

海洋链霉菌来源的天然产物*

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摘要 海洋链霉菌(*Streptomyces* spp.)由于其独特的生理和代谢功能,成为海洋微生物活性物质的主要来源。对 2010~2013 年初的海洋放线菌天然产物的统计表明,研究最多的放线菌是链霉菌,占海洋放线菌新天然产物的 60%。本文综述了自 1976 年第一个海洋链霉菌天然产物到 2016 年 6 月的 40 年间报道的 547 个海洋链霉菌天然产物的结构、生物活性及其微生物来源。其结构包括含氮化合物(如生物碱)、聚酮、萜类、甾体等,其中含氮化合物是其主要类型,占海洋链霉菌天然产物总数的 61%;而 67% 的海洋链霉菌天然产物表现出细胞毒、抑菌、抗疟和抗寄生虫等生物活性。

关键词 海洋放线菌;链霉菌;天然产物;来源;结构;生物活性

中图分类号 R282.77 doi: 10.12036/hyxxjk20160711002

海洋链霉菌由于其独特的生理和代谢功能,成为海洋微生物活性天然产物的重要来源。本实验室对 2010~2013 年初海洋放线菌新天然产物的统计表明,海洋放线菌研究最多的是链霉菌(*Streptomyces*),占海洋放线菌新天然产物的 60%(赵成英等, 2013)。海洋链霉菌新天然产物的研究始于 1976 年, Okami 课题组报道了首例海洋链霉菌天然产物 aplasmomycins A-C (150~152)(Okami et al., 1976);截至 2016 年 6 月的 40 年时间里,已报道了 547 个海洋链霉菌新天然产物。这些天然产物的结构类型包括生物碱、聚酮、萜类、甾体、卤代物、聚醚类等;并具有多种生物活性,包括抗肿瘤、

抗菌、抗疟和抗寄生虫等。因此,海洋链霉菌天然产物可能是发现药物先导化合物的重要的资源宝库,本文将从海洋链霉菌的来源出发,综述这些天然产物的结构及其生物活性。

1 海洋动物来源的海洋链霉菌天然产物

1.1 海绵来源的海洋链霉菌天然产物

海绵来源的(下同)链霉菌 *Streptomyces* sp. Ni-80 代谢产生 urauchimycins A(1)和 B(2),两个化合物在 10 μ g/mL 时具有抑制白色念珠菌(*Canidia albicans*)活性(Imamura et al., 1993)。*Streptomyces* sp. KM86-9B 代谢产生具有拓扑

* 资助项目: 国家自然科学基金项目(81561148012, U1501221, U1406402-1, 41376148)。王聪, 男, 博士研究生, E-mail: wangcong123206@163.com

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收稿日期: 2016-07-11, 收修改稿日期: 2016-08-02

异构酶 I 抑制活性的化合物 **3~9** (Lee et al., 1998)。环肽 dehydroxynocardamine (**10**)和 desmethylenynocardamine (**11**)来自 *Streptomyces* sp. M1087, 具有微弱的重组酶 sortase B 抑制活性, EC_{50} 分别为 88.3 $\mu\text{g/mL}$ 和 126.4 $\mu\text{g/mL}$ (Lee et al., 2005)。*Streptomyces* sp. HB202 代谢产生吩嗪类化合物 streptophenazines A-H (**12~19**), 化合物 **12**、**14~16** 和 **19** 对枯草芽胞杆菌(*Bacillus subtilis*)的最小抑菌浓度(minimum inhibitory concentration, MIC)分别为 46.9 $\mu\text{g/mL}$ 、15.6 $\mu\text{g/mL}$ 、62.5 $\mu\text{g/mL}$ 、62.5 $\mu\text{g/mL}$ 和 15.6 $\mu\text{g/mL}$, 化合物 **12~14**、**17** 和 **18** 对金黄色葡萄球菌(*Staphylococcus aureus*)的 MIC 分别为 62.5 $\mu\text{g/mL}$ 、62.5 $\mu\text{g/mL}$ 、46.9 $\mu\text{g/mL}$ 、62.5 $\mu\text{g/mL}$ 和 62.5 $\mu\text{g/mL}$ (Mitova et al., 2008)。*Streptomyces* sp. SpC080624SC-11 代谢产生 3 个吩嗪类化合物 **20~22** (Izumikawa et al., 2010b), *Streptomyces* sp. Sp080513GE-23 代谢产生 2 个含有氯代吡啶单元的二肽类化合物 **23** 和 **24** (Motohashi et al., 2010c), *Streptomyces* sp. NBRC105896 代谢产生化合物 **25**、对人宫颈癌 Hela 细胞和恶性胸膜间皮瘤细胞 ACC-MESO-1 的 IC_{50} 分别为 49 $\mu\text{mol/L}$ 和 88 $\mu\text{mol/L}$ (Izumikawa et al., 2010a), *Streptomyces* sp. Sp080513GE-26 产生 2 个新的萜环类化合物 **26** 和 **27**、化合物 **26** 对 Hela 细胞和 HL-60 细胞的 IC_{50} 分别为 120 $\mu\text{mol/L}$ 和 210 $\mu\text{mol/L}$ (Motohashi et al., 2010a)。*Streptomyces* sp. SpD081030ME-02 代谢产生水杨酰胺衍生物 **28**, 对 Hela 细胞的 IC_{50} 为 28 $\mu\text{mol/L}$ (Ueda et al., 2010)。联苯萜糖苷 **29** 来自 *Streptomyces* sp. HB202 (Schneemann et al., 2010), 化合物 **29** 对 HepG2、HT-29、GXF251L、LXF529L 等 8 种人肿瘤细胞的 IC_{50} 为 0.13~0.33 $\mu\text{mol/L}$, 对鼠成纤维细胞 NIH-3T3 的 IC_{50} 为 0.22 $\mu\text{mol/L}$, 且对包括耐甲氧西林金黄色葡萄球菌、表皮葡萄球菌(*Staphylococcus epidermidis*)、人皮肤杆菌和痤疮丙酸杆菌(*Propionibacterium acnes*)等 9

种细菌的 IC_{50} 为 2.5~8.4 $\mu\text{mol/L}$ 。Tetromycins 化合物 **30~33** 产自链霉菌 *S. axinellae* Pol001^T, 可以抑制布氏锥虫(*Trypanosoma bruce*) (Pimentel-Elardo et al., 2011)。化合物 Lobophorins C (**34**) 和 D (**35**) 产自肉质链霉菌 *S. carnosus* AZS17, 化合物 **34** 和 **35** 对人肝癌细胞株 7402 的 IC_{50} 分别为 0.6 $\mu\text{g/mL}$ 和 723.1 $\mu\text{g/mL}$ 、对人乳腺癌细胞株 MDA-MB-435 的 IC_{50} 分别为 61.8 $\mu\text{mol/L}$ 和 7.5 $\mu\text{mol/L}$ (Wei et al., 2011)。细黄链霉菌(*S. microflavus*)代谢产生 3-乙酰基-5-甲基-2'-脱氧尿嘧啶 **36** (Li et al., 2011); *Streptomyces* sp. SpD081030SC-03 代谢产生小肽 JBIR-56 (**37**) 和 JBIR-57 (**38**) (Motohashi et al., 2011)。吡啶生物碱 streptomycindole (**39**) 产自链霉菌 *Streptomyces* sp. DA22, 对 HL-60、结肠癌 HCT-116、卵巢上皮性癌 HO-8910 和人肝癌细胞 HepG2 没有活性 (Huang et al., 2011)。3 个曲古抑菌素 **40~42** 是链霉菌 *Streptomyces* sp. RM72 的代谢产物, 对组蛋白脱乙酰化酶 HDAC1 的 IC_{50} 分别为 48 $\mu\text{mol/L}$ 、74 $\mu\text{mol/L}$ 和 57 $\mu\text{mol/L}$ (Hosoya et al., 2012)。环脂肽 **43~46** 产自 *Streptomyces* sp. RV15 (Abdelmohsen et al., 2012); 苯并萜醌糖苷 **47~49** 产自 *Streptomyces* sp. BCC45596 (Supong et al., 2012), 其对疟原虫的 IC_{50} 为 0.053 $\mu\text{g/mL}$ 、0.142 $\mu\text{g/mL}$ 和 2.93 $\mu\text{g/mL}$, 对结核杆菌的 MIC 分别为 3.13 $\mu\text{g/mL}$ 、12.50 $\mu\text{g/mL}$ 和 6.25 $\mu\text{g/mL}$, 化合物 **47** 对 KB、MCF-7、NCI-H187 和 Vero 细胞的 IC_{50} 分别为 0.179 $\mu\text{g/mL}$ 、0.196 $\mu\text{g/mL}$ 、0.092 $\mu\text{g/mL}$ 和 1.71 $\mu\text{g/mL}$, 化合物 **48** 对 KB、MCF-7、NCI-H187 和 Vero 细胞的 IC_{50} 分别为 0.324 $\mu\text{g/mL}$ 、0.45 $\mu\text{g/mL}$ 、0.242 $\mu\text{g/mL}$ 和 3.05 $\mu\text{g/mL}$, 化合物 **49** 对 KB、MCF-7、NCI-H187 和 Vero 细胞的 IC_{50} 分别为 6.96 $\mu\text{g/mL}$ 、3.41 $\mu\text{g/mL}$ 、3.97 $\mu\text{g/mL}$ 和 10.07 $\mu\text{g/mL}$ 。链霉菌 *S. tateyamensis* 代谢产生化合物 JBIR-107(**50**) (Izumikawa et al., 2013)。吩嗪类化合物 streptophenazines I-K

(51~53)来自链霉菌 *Streptomyces* HB202, 化合物 52 对磷酸二酯酶的 IC_{50} 为 $12.0\mu\text{mol/L}$, 化合物 53 对枯草芽胞杆菌、表皮葡萄球菌、磷酸二酯酶的 IC_{50} 分别为 $21.6\mu\text{mol/L}$ 、 $14.5\mu\text{mol/L}$ 和 $12.2\mu\text{mol/L}$ (Kunz et al., 2014)。环圈链霉菌 *S. anulatus* S71 代谢产生化合物 54 (Sun et al., 2014b)。 *Streptomyces* sp. M7_15 代谢产生 monacyclonones A-F (55~60), 化合物 57、59 和 60 对横纹肌肉瘤 X 细胞 SJCRH30 的 IC_{50} 分别为 $160\mu\text{mol/L}$ 、 $270\mu\text{mol/L}$ 和 $0.73\mu\text{mol/L}$ (Vicente et al., 2015)。二肽 xestostreptin (61) 产自 *Streptomyces* sp. S.4, 其对恶性疟原虫的 IC_{50} 为 $50\mu\text{mol/L}$ (Rakotondraibe et al., 2015)。化合物 quinomycin G (62) 和环二肽 63 来源于 *Streptomyces* sp. LS298, 化合物 63 对 ACHN、786-O、U87 MG 和 Jurkat 肿瘤细胞的 IC_{50} 分别为 $0.552\mu\text{mol/L}$ 、 $0.721\mu\text{mol/L}$ 、 $0.627\mu\text{mol/L}$

和 $0.414\mu\text{mol/L}$ (Zhen et al., 2015)。 *Streptomyces* sp. SBT345 代谢产生氯化化合物 ageloline A (64), 对沙眼衣原体的 IC_{50} 为 $9.54\mu\text{mol/L}$ (Cheng et al., 2016)。

1.2 珊瑚来源的海洋链霉菌天然产物

珊瑚来源的(下同)的链霉菌 *Streptomyces* sp. 代谢产生 octalactins A (65) 和 B (66), 化合物 65 对 B-16-F10 和 HCT-116 细胞的 IC_{50} 分别为 $0.0072\mu\text{g/mL}$ 和 $0.5\mu\text{g/mL}$ (Tapiolas et al., 1991)。多氯代聚酮 strepchloritides A (67) 和 B (68) 产自 *Streptomyces* sp. OUCMDZ-1703, 其对 MCF-7 细胞的 IC_{50} 分别为 $9.9\mu\text{mol/L}$ 和 $20.2\mu\text{mol/L}$ (Fu et al., 2013)。Axinelline A (69) 来自链霉菌 *S. axinellae* SCSIO02208, 对环氧化酶 COX-2 的 IC_{50} 为 2.8mmol/L (Ai et al., 2014)。Nahuoicacids 70~73 来自 *Streptomyces* sp. SCSGAA 0027 (Nong et al., 2016) (图 1)。

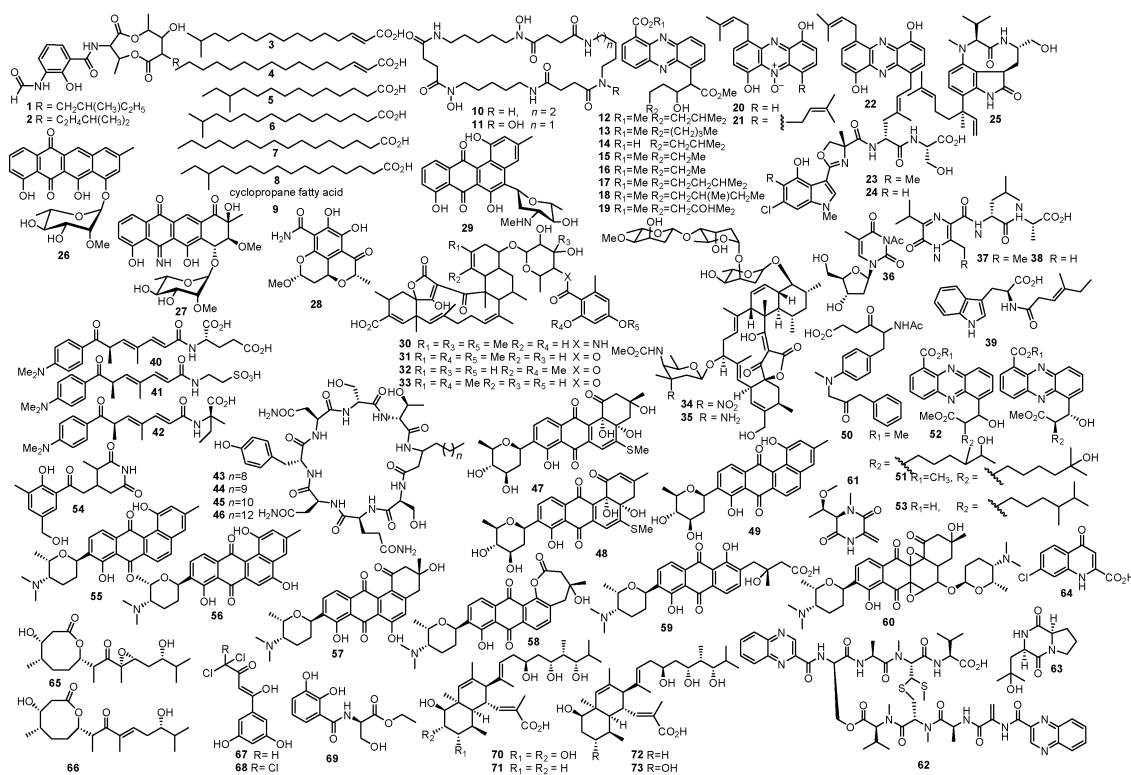


图 1 化合物 1~73 的结构
Fig.1 Structures of compounds 1~73

1.3 其他动物来源的链霉菌天然产物

其他海洋动物来源的(下同)链霉菌 *S. hygroscopicus* 代谢产生 salinamides A(**74**)和 B(**75**), 其对肺炎链球菌 *Streptococcus pneumoniae* 的 MIC 均为 4 μ g/mL、对酿脓葡萄球菌 (*Staphylococcus pyrogenes*) 的 MIC 分别为 4 μ g/mL 和 2 μ g/mL; 化合物 **74** 和 **75** 还有抗炎活性, 浓度为 59 μ g/mL 时, 其对佛波醇酯诱导的小鼠耳水肿的抑制率分别为 84%和 83% (Trischman et al., 1994)。Halichomycin(**76**)来自链霉菌 *S. hygroscopicus*, 对小鼠白血病 P388 细胞的 ED₅₀ 为 0.13 μ g/mL(Takahashi et al., 1994)。大环内酰胺 aburatubolactam A (**77**)产自 *Streptomyces* sp. SCRC-A20, 可抑制 TPA 诱导的超氧化阴离子的产生(Bae et al., 1996)。吡啶衍生物 **78~80** 产自 *Streptomyces* sp. BL-49-58-005 (Sánchez et al., 2003), 化合物 **78** 对白血病 K562 细胞的 GI₅₀ 为 8.46 μ mol/L; 化合物 **79** 对不同肿瘤细胞株表现出中等细胞毒活性, GI₅₀ 在微摩尔级, 并且无明显选择性; 化合物 **80** 对所测试的肿瘤细胞株没有活性。粉蝶霉素 piericidins C7(**81**)and C8(**82**)来自 *Streptomyces* sp. YM14-060, 可抑制小鼠神经母细胞瘤细胞 Neuro-2a 增殖而不杀死细胞, IC₅₀ 分别为 0.83 nmol/L 和 0.2nmol/L (Hayakawa et al., 2007)。 *Streptomyces* sp. JP90 代谢产生 cinnamoylphosphoramidate (**83**), 其对乙酰胆碱酯酶的 IC₅₀ 为 250 μ mol/L(Quitschau et al., 2008)。 *Streptomyces* sp. CP32 的代谢产生噻唑类衍生物 **84~88**, 化合物 **84** 和 **87** 可选择性地结合 5-HT_{2B} 受体(K_i 分别为 0.50 μ mol/L 和 1.54 μ mol/L) (Lin et al., 2010)。化合物 **89** 产自 *Streptomyces* sp. BOSC-022A(Lorente et al., 2010)。Nobilamides A-E(**90~94**)和 F-H(**95~97**)分别产自链霉菌 HQ696493 和 HQ696492, 化合物 **91** 具有拮抗 TRPV1 作用(Lin et al., 2011)。化合物 **98** 产自 *Streptomyces* sp., 对 P388 细胞有细胞毒活性(Mahyudin et al.,

2012)。 *Streptomyces* sp. 1053U.I.1a.1b 的代谢产生化合物 **99** 及其糖苷 **100**(Lin et al., 2012)。化合物 violapyrones H (**101**)和 I (**102**)来自 *Streptomyces* sp. 112CH148, 化合物 **101** 对 HCT-15 细胞的活性最高, GI₅₀ 为 1.10 μ g/mL (Shin et al., 2014)。聚酮类 lobophorins H (**103**)和 I (**104**)产自 *Streptomyces* sp. 1053U.I.1a.3b, 化合物 **104** 对结核分枝杆菌和枯草杆菌的 MIC 分别为 2.6mmol/L 和 10.6mmol/L(Lin et al., 2014)。Hyaluromycin(**105**)来自 *Streptomyces* sp. MB-PO13, 化合物 **105** 对透明质酸酶的 IC₅₀ 为 14 μ mol/L(Harunari et al., 2014)。大环内酯类化合物 PM100117 (**106**) 和 PM100118 (**107**) 产自链霉菌 *S. caniferus* GUA-06-05-006A, 其对 A549 细胞的 GI₅₀ 分别为 1.3 μ mol/L 和 0.83 μ mol/L、对 MDA-MB-231 细胞的 GI₅₀ 分别为 2.7 μ mol/L 和 1.7 μ mol/L、对人结肠癌细胞 HT29 的 GI₅₀ 分别为 3.8 μ mol/L 和 9.2 μ mol/L (Pérez et al., 2016)。

2 海洋植物来源的海洋链霉菌天然产物

2.1 海藻来源的海洋链霉菌天然产物

海藻链霉菌 *Streptomyces* sp. #N1-78-1 代谢产生蒽醌类化合物 **108~110**, 3 个化合物对金黄色葡萄球菌的 IC₅₀ 分别为 0.15 μ mol/L、0.36 μ mol/L 和 31 μ mol/L(Socha et al., 2006)。化合物 streptobactin (**111**)、dibenarthin (**112**)和 tribenarthin (**113**)产自海藻链霉菌 *Streptomyces* sp. YM5-799(Matsuo et al., 2011)。

2.2 红树林来源的海洋链霉菌天然产物

红树植物来源的链霉菌(下同) *Streptomyces* sp. GT2002/1503 代谢产生吡啶并倍半萜烯 xiamycin B (**114**)、indospene (**115**)和 sespenine (**116**), 化合物 **114** 具有选择性抑制 HIV 活性 (Ding et al., 2010)(图 2)。

Streptomyces sp. HK10552 代谢产生化合物 **117~120**(Wang et al., 2010); 吡啶生物碱 **121** 和吡啶生物碱 **122** 产自 *Streptomyces* sp. GT2002/1503, **121** 和 **122** 对 HT-29、GXF 251L、LXFA 629L 等 12 种人癌细胞的平均 IC₅₀ 值分别为大于 30μmol/L 和 10.1μmol/L; 化合物 **121** 选择性地抑制 HIV 病毒的 R5 受体活性(Ding et al., 2010)。化合物 divergolides A-D (**123~126**)产自 *Streptomyces* sp. HKI0576, 化合物 **123** 对肺癌细胞 LXFA 629L、胰腺癌细胞 PANC-1、肾癌细胞 RXF 486L 和恶性毒瘤 Saos-2 的 IC₅₀ 值为 1.0~2.0μmol/L(Ding et al., 2011)。化合物 divergolides A-D (**127~130**)也产自该菌(Xu et al., 2014)。链霉菌 *S. lusitanus* XM52 代谢产生 **131~132**, 其中 **132**

2.3 其他植物来源的链霉菌天然产物

其他海洋植物来源的链霉菌 *Streptomyces* sp. CANU Fox 21-2-6 代谢产生化合物 **138~140**, 对小鼠白血病细胞 P388 的 IC₅₀ 值为 0.4~0.06 μg/mL (Phipps et al., 2004)。来自草绿盐角草 (*Salicornia herbacea*) 的链霉菌 *Streptomyces* sp. FX-58 代谢产生化合物 **141** (Huang et al., 2006a) 和化合物 **142~143** (Huang et al., 2006b), 化合物 **143** 对 HL-60、BCTC-823 和 MDA-MB-

435 细胞的 IC_{50} 值分别为 $6.83\mu\text{g/mL}$ 、 $82.2\mu\text{g/mL}$ 和 $56.59\mu\text{g/mL}$ 。黄酮类化合物 **144** 产自 *Streptomyces* sp. MA-12, 浓度为 0.25mmol/L 时, 对香蕉炭疽病菌、小麦赤霉病菌和桔青霉 3 种植物病原菌有抑制作用(Ding et al., 2013)。不饱和脂肪酸 **145** 产自链霉菌 *S. violans* HTTA-F04129, 对 A2780 细胞的 IC_{50} 值为 $4.36\mu\text{mol/L}$ (Huang et al., 2014)。*Streptomyces* sp. LC6 代谢产生 juanlimycins A (**146**)和 B (**147**), 可抑制沙门氏菌毒力岛-1 的分泌(Zhang et al., 2014a)。来源于浒苔的链霉菌 *Streptomyces* sp. OUCMDZ-3434 代谢产生结构新颖的二聚体 wailupemycins H (**148**)和 I (**149**), 其对 α -糖苷酶的 K_i 值分别为 $16.8\mu\text{mol/L}$ 和 $6.0\mu\text{mol/L}$ 、 IC_{50} 值分别为 $19.7\mu\text{mol/L}$ 和 $8.3\mu\text{mol/L}$ (Chen et al., 2016)。

3 海泥和海水来源的链霉菌天然产物

3.1 海泥来源的链霉菌天然产物

海泥来源的链霉菌(下同)*S. griseus* SS-20 代谢产生 aplasmomycins A-C (**150~152**), 能抑制多种革兰氏阳性细菌(包括分枝细菌), 同时具有抗疟原虫的活性。感染了疟原虫的小鼠口服后, 疟原虫大大减少, 且小鼠全部存活, 而未经过治疗的小鼠在 8d 内全部死亡(Okami et al., 1976; Nakamura et al., 1977)。链霉菌 *S. tenjimariensis* SS-939 代谢产生氨基糖苷类化合物 istamycins A 和 istamycins B (**153** 和 **154**), 对革兰氏阳性菌和阴性菌都有很好的抑制作用(Okami et al., 1979)。生物碱 altemicidin(**155**)产自 *S. sioyaensis* SA-1758, 具有抗肿瘤和杀螨活性(Okami et al., 1989)。4 个罕见的吩嗪生物碱类化合物 **156~159** 来自 *Streptomyces* sp. CNB-253, 化合物 **156** 对嗜血杆菌属流感的 IC_{50} 值可达到 $1\mu\text{g/mL}$ 、对梭菌属产气荚膜杆菌 IC_{50} 值可达到 $4\mu\text{g/mL}$ (Pathirana et al., 1992)。N-乙酰- β -D-氨基葡萄糖苷酶抑制剂 pyrostatins A (**160**)和 B (**161**)产自 *Streptomyces*

sp. SA-3501(Aoyama et al., 1995)。二酮哌嗪 maremycins A (**162**)和 B (**163**)产自 *Streptomyces* sp. B 9173 (Balk-Bindseil et al., 1995)。*Streptomyces* sp. BD-26T(20)代谢产生 wailupemycins A-C (**164~166**)和 3-epideoxyenterocin (**167**), 化合物 **167** 浓度在 $1\text{mg}/6\text{mm}$ disk 时, 对金黄色葡萄球菌的抑菌圈为 18mm ; 化合物 **164** 浓度在 $0.1\text{mg}/6\text{mm}$ disk 时, 对大肠杆菌 *E. coli* 的抑菌圈为 15mm (Sitachitta et al., 1996)。多色霉素类抗生素 δ -indomycinone **168** 产自 *Streptomyces* sp. B 8300, 对枯草芽孢杆菌 *B. subtilis* 的 MIC 为 $100\mu\text{g/mL}$ (Biabani et al., 1997)。Actinoflavoside (**169**)产自 *Streptomyces* sp. CNB-689, 对革兰氏阳性菌肺炎链球菌(*S. pneumonia*)、酿脓葡萄球菌(*S. pyrogenes*)、金黄色葡萄球菌和藤黄微球菌(*M. luteus*)的 MIC 均为 $64\mu\text{g/mL}$ (Jiang et al., 1997)。*Streptomyces* sp. B 8251 代谢产生生物碱 **170**, 具有微弱的抑制大肠杆菌(*E. coli*)和枯草芽孢杆菌(*B. subtilis*)的活性(Pusecker et al., 1997)。Anthranilamide (**171**)产自 *Streptomyces* sp. B7747, 浓度为 $100\mu\text{g}/\text{disk}$, 对淡水小球藻(*C. sorokiniana*)的抑制圈直径为 11mm 、对普通小球藻(*C. vulgaris*)的抑制圈直径为 13mm 、对栅藻(*S. subspicatus*)的抑制圈直径为 12mm (Biabani et al., 1998)。*Streptomyces* sp. BD-18T(41)代谢产生多环苯醌类化合物 halawanones A-D(**172~175**)(Ford et al., 1998)。两个弱的抗菌活性的芳香族胺类化合物 lornemides A(**176**)和 B(**177**)产自 *Streptomyces* sp. MSTMA190, **176** 对枯草杆菌(*B. subtilis*)的 LD_{99} 为 $50\mu\text{g/mL}$ (Capon et al., 2000)。化合物 **178~181** 来自 *Streptomyces* sp. B5632 和 B3497(Mukku et al., 2000)。化合物 **182** 和 **183** 分别来自 *Streptomyces* sp. SS99BA-2 (Hernandez et al., 2000)和 *Streptomyces* sp. 1010(Ivanova et al., 2001), 化合物 **183** 对藤黄微球菌(*M. luteus*)和枯草芽孢杆菌(*B. subtilis*)的 MIC 分别为 $15\mu\text{g/mL}$ 和 $50\mu\text{g/mL}$, 而对白

色念珠菌(*C. albicans*)和大肠杆菌(*E. coli*)没有抑制活性。*Streptomyces* sp. M02750 代谢产生化合物 **184~189**, 无抗白色念珠菌(*C. albicans*)活性(Cho et al., 2001)。大环内酯 chalcone B (**190**)产自 *Streptomyces* sp. B7064, 其在浓度为 10 μ g/9mm disk 时, 对金黄色葡萄球菌、大肠杆菌(*E. coli*)、枯草杆菌(*B. subtilis*)的抑菌圈直径分别为 23mm、28mm 和 21mm (Asolkar et al., 2002)。化合物 parimycin(**191**)来自 *Streptomyces* sp. B8652, 其对 GXF251L、H460、LXFA629L、LXFL529L、MCF-7、MAXF401NL、MEXF462NL 和 MEXF 514L 细胞的 IC₇₀ 为 0.9~6.7 μ g/mL(Maskey et al., 2002)。化合物 gutingimycin(**192**)也来源于该链霉菌(Maskey et al., 2004)。链霉菌 *Streptomyces* sp. BD21-2 代谢产生 bonactin (**193**), 在测试浓度为 1mg/mL 时, 对金黄色葡萄球菌、芽孢杆菌(*B. megaterium*)和酿酒酵母菌(*S. cerevisiae*)的抑菌圈直径分别为 7mm、8mm 和 7.5mm (Schumacher et al., 2003)。Komodoquinone A (**194**)产自 *Streptomyces* sp. KS3, 在 1 μ g/mL 时, 即可诱导神经母细胞瘤细胞株 Neuro 2A 的形态变化(Itoh et al., 2003)。内酯类化合物 **195~196** 和大环内酰胺类化合物 **197** 分别产自 *Streptomyces* sp. B6007 (Stritzke et al., 2004) 和 *S. aureoverticillatus* NPS001583(Mitchell et al., 2004), 对 HT-29、B16-F10 和人外周白血病细胞的 EC₅₀ 分别为 3.6 μ mol/L、2.2 μ mol/L 和 2.3 μ mol/L。

Lajollamycin (**198**)产自链霉菌 *S. nodosus* NPS007994, 对耐青霉素肺炎双球菌(*S. pneumonia*)和耐甲氧西林葡萄球菌(*S. aureus*)的 MIC 分别为 1.5 μ g/mL 和 5 μ g/mL, 对小鼠黑色素瘤细胞系 B16-F10 的 EC₅₀ 为 9.6 μ mol/L (Manam et al., 2005)。氯代手霉素衍生物 chinikomycins A (**199**)和 B (**200**)来自 *Streptomyces* sp. M045, 化合物 **199** 对乳腺癌细胞 MAXF 401NL、黑色素瘤细胞 MEXF 462NL 和肾癌细胞 RXF 944L 的 IC₅₀ 分别为 2.41 μ g/mL、

4.15 μ g/mL 和 4.02 μ g/mL, 化合物 **200** 对 MAXF 401NL 的 IC₅₀ 为 3.04 μ g/mL(Li et al., 2005)。*Streptomyces* sp. NPS008187 代谢产生 glaciapyrroles A-C (**201~203**), 其中 **201** 对结肠腺癌细胞 HT-29 和黑色素瘤细胞 B16-F10 的 IC₅₀ 均为 180 μ mol/L(Macherla et al., 2005)。拒霉素衍生物 **204** 产自 *Streptomyces* sp. B8005, 抑制大肠杆菌(*E. coli*)、金黄色葡萄球菌和绿色产色链霉菌(*S. viridochromogenes*)的 MIC 大于 40 μ g/mL(Kock et al., 2005)。Actinofuranones A (**205**)和 B(**206**)产自 *Streptomyces* sp. CNQ766 (Cho et al., 2006a), 该菌株还代谢产生 azamerone (**207**)(Cho et al., 2006b)。Daryamides A-C (**208~210**)、化合物 **211** 来自 *Streptomyces* sp. CNQ-085, 化合物 **208** 对 HCT-116 细胞的 IC₅₀ 为 3.15 μ g/mL, 化合物 **208~209** 对白色念珠菌的 MIC 分别为 62.5 μ g/mL 和 125 μ g/mL (Asolkar et al., 2006) (图 3)。

星孢菌素 N-carboxamidostaurosporine (**212**)、倍半萜类 **213** 和生物碱类 **214** 来自链霉菌 *Streptomyces* sp. QD518, 化合物 **214** 对膀胱、中枢神经系统、结肠、胃、头、颈、肺、乳房、胰腺、前列腺, 以及黑色素瘤等 37 个人癌细胞的平均 IC₅₀ 和 IC₇₀ 值分别为 0.016 μ g/mL 和 0.17 μ g/mL, 化合物 **214** 在 40 μ g/disc 时对金黄色葡萄球菌的抑菌圈直径为 11mm(Wu et al., 2006)。*Streptomyces* sp. CNQ-583 代谢产生吡咯生物碱 bohemamine B (**215**)、bohemamine C (**216**)和 5-chlorobohemamine C(**217**)(Bugni et al., 2006)。化合物 urauchimycin C (**218**)来自 *Streptomyces* sp. B1751(Yao et al., 2006)。*Streptokordin* (**219**)产自 *Streptomyces* sp. KORDI- 3238, 对细胞 MDA-MB-231、HCT15、PC-3、NCI-H23、ACHN、LOX-IMVI、K-562 的 IC₅₀ 值分别为 7.5 μ g/mL、7.8 μ g/mL、3.2 μ g/mL、3.5 μ g/mL、4.7 μ g/mL、7.4 μ g/mL 和 8.6 μ g/mL(Jeong et al., 2006)。*Streptomyces* sp. B8000 代谢产生

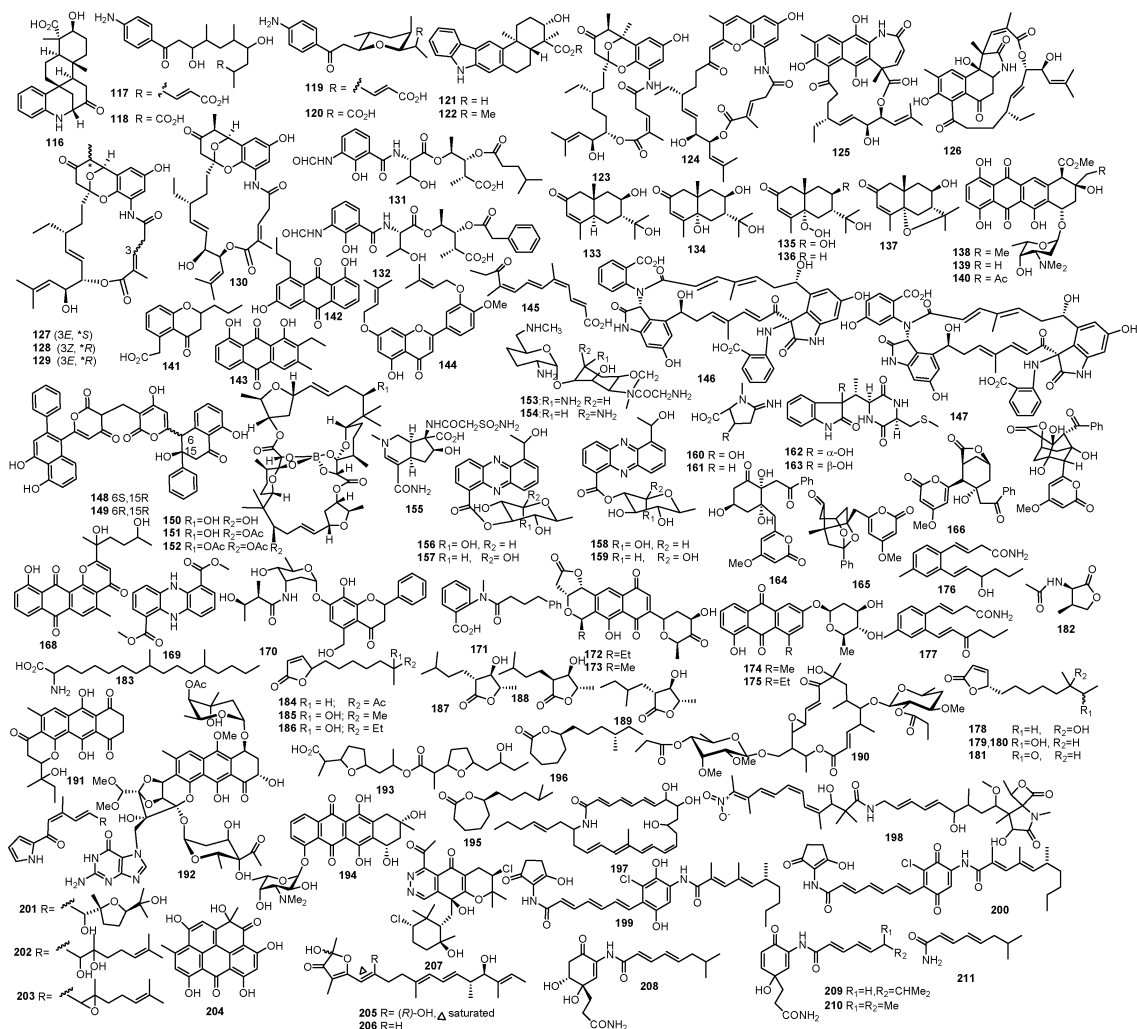


图3 化合物 116~211 的结构

Fig.3 Structures of compounds 116~211

化合物 220 和 221, 化合物 220 在 40 μ g/disc 时, 对金黄色葡萄球菌和绿色链霉菌的抑菌圈直径分别为 14mm 和 12mm(Poumale et al., 2006)。化合物 octalactin C (222) 来自 *Streptomyces* sp. V5(陈光英等, 2007)。*Streptomyces* sp. M491 代谢产生倍半萜化合物 223~225(Wu et al., 2007)和 226~231(Ding et al., 2009), 化合物 226 对多种肿瘤细胞的平均 IC₅₀ 为 6.7 μ g/mL。*Streptomyces* sp. CNH990 代谢产生醌类化合物 marmycins A (232)和 marmycins B(233), 化合物 232 对人结肠癌细胞 HCT-116

的 IC₅₀ 为 60.5nmol/L, 是其氯代同系物 227 的 18 倍(IC₅₀ 为 1.09 μ mol/L), 232 还具有 G1 期阻滞活性 (Martin et al., 2007)。环六肽 piperazimycins A-C (234~236) 产自链霉菌 *Streptomyces* sp. CNQ-593, 其对人结肠癌细胞 HCT-116 的平均 GI₅₀ 均为 76ng/mL (Miller et al., 2007)。吡咯生物碱 marinopyrroles A (237)和 B (238) 来自链霉菌 *Streptomyces* sp. CNQ-418, 其对耐甲氧西林金黄色葡萄球菌 (MRSA) 的 MIC₉₀ 分别为 0.61 μ mol/L 和 1.1 μ mol/L、对 HCT-11 细胞的 IC₅₀ 分别为

8.8 μ mol/L 和 9.0 μ mol/L(Hughes et al., 2008); 对该菌株优化后又得到 marinopyrroles C-F (239~245), 对抑制人结肠癌 HCT-116 细胞的 IC₅₀ 为 1~5 μ g/mL, 化合物 239 抑制 MRSA 的 MIC 小于 1 μ g/mL(Hughes et al., 2010)。*Streptomyces* sp. MS239 代谢产生吡啶类化合物 243 和萘类化合物 244, 化合物 243 对枯草杆菌 ATCC6633 有弱的抑菌活性(Motohashi et al., 2008)。化合物 essramycin (245)来自于 *Streptomyces* sp. Merv8102, 其对革兰阳性菌和革兰阴性菌的 MIC 为 1.0~8.0 μ g/mL。对大肠杆菌(ATCC 10536)、铜绿假单胞菌(ATCC 10145)、枯草杆菌(ATCC 6051)、金黄色葡萄球菌(ATCC 6538)和藤黄微球菌(ATCC 9341)的 MIC 分别为 8 μ g/mL、3.5 μ g/mL、1 μ g/mL、1 μ g/mL 和 1.5 μ g/mL(El-Gendy et al., 2008)。

Streptomyces sp. H668 代谢产生聚醚类化合物 246, 有抗疟疾活性, IC₅₀ 为 100~200ng/mL(Na et al., 2008)。有机酸 247 和 248 来自 *Streptomyces* sp. Act8015(Shaaban et al., 2008)。聚酮 phaechromycins F-H (249~251)产自 *Streptomyces* sp. DSS-18(Li et al., 2008)。*Streptomyces* sp. CNQ-617 代谢产生 marineosins A 和 B(252~253), 其对入结肠癌细胞 HCT-116 的 IC₅₀ 分别为 0.5 μ mol/L 和 46 μ mol/L(Boonlarppradab et al., 2008); 对 marineosins 的生物合成研究, 又从该链霉菌的代谢产物中获得了化合物 254~257, 其中 256 对 HepG2 细胞的 IC₅₀ 为 4.17 μ mol/L; 化合物 256 对氯喹敏感(CQS)、氯喹拮抗, 以及采用氯喹处理过的菌株 *P. falciparum* 的 IC₅₀ 分别为 2.3nmol/L、12nmol/L 和 1.5nmol/L(Salem et al., 2014)。三环聚丙酸酯类 indoxamycins A-F (258~263)产自 *Streptomyces* sp. NPS-643, 化合物 258 和 263 对人结肠癌细胞 HT-29 的 IC₅₀ 为 0.3~3 μ mol/L(Sato et al., 2009)。氯代生物碱 ammosamides A (264)和 B (265)产自链霉菌

Streptomyces sp. CNR-698, 264 暴露在空气中可逐渐转化为 265, 其对入结肠癌 HCT-116 细胞的 IC₅₀ 均为 320nmol/L, 作用靶点为肌球蛋白(Hughes et al., 2009)。化合物 splenocins A-J (266~275)产自 *Streptomyces* sp. CNQ431, 抑制脾脏细胞因子的 IC₅₀ 为 2~50nmol/L, 且对哺乳动物细胞的细胞毒性较小, 具有治疗哮喘的潜力(Strangman et al., 2009)。*Streptomyces* sp. NTK 227 代谢产生 albidopyrone A (276), 具有蛋白酪氨酸磷酸酶 B(PTP1B)抑制活性, IC₅₀ 为 128 μ g/mL(Hohmann et al., 2009)。细胞毒活性的 mansouramycins A-D (277~280)和 tartrolon D (281)分别产自 *Streptomyces* sp. Mei37(Hawas et al., 2009)和 *Streptomyces* sp. MDG-04-17-069(Pérez et al., 2009), 化合物 281 对 A549、HT29 和 MDA-MB-231 的 GI₅₀ 分别为 0.16 μ mol/L、0.31 μ mol/L 和 0.79 μ mol/L。二酮哌嗪 naseazones A (282)和 B (283)产自 *Streptomyces* sp. CMB-MQ030(Raju et al., 2009)。Lorneic acids A (284)和 B (285)产自 *Streptomyces* sp. NPS554, 其抑制人血小板磷酸二酯酶 5(PDE5)的 IC₅₀ 分别为 12.6 μ mol/L 和 87.1 μ mol/L(Iwata et al., 2009); 多环聚酮类化合物 akaeolide (286)也产自该菌, 其对大鼠成纤维细胞 3Y1 的 IC₅₀ 为 8.5 μ mol/L(Igarashi et al., 2013)。Tirandamycins C (287)和 D (288)产自 *Streptomyces* sp. 307-9, 抑制耐万古霉素肠球菌(VRE)的 MIC 分别为 110 μ mol/L 和大于 9 μ mol/L(Carlson et al., 2009)。化合物 289 来自 *S. xiamenensis* 318, 具有治疗肺纤维化的潜力(Xu et al., 2012)。肿大链霉菌(*S. tumescens*) YM23-260 产生环肽类化合物 290 和 291, 化合物 290 在浓度为 100 μ mol/L 时, 具有抑制阿尔兹海默病活性(Motohashi et al., 2010b)。环肽类化合物 292 产自 *Streptomyces* sp. MWW064, 具有抑制鼠肿瘤细胞 26-L5 的转移作用(Igarashi et al., 2010)。*Streptomyces* sp. CMB-M0406 产生 heronamides A-C (293~295)

(Raju et al., 2010a)和 8-deoxyheronamide C (296)(Sugiyama et al., 2014), 296 对裂殖酵母细胞的 MIC 可达 $5.8\mu\text{mol/L}$ 。化合物 297~299

为 *Streptomyces* sp. CMB-M0423 的代谢产物, 对革兰阳性菌的 IC_{50} 为 $0.6\sim 6.5\mu\text{mol/L}$ (Raju et al., 2010b)(图 4)。

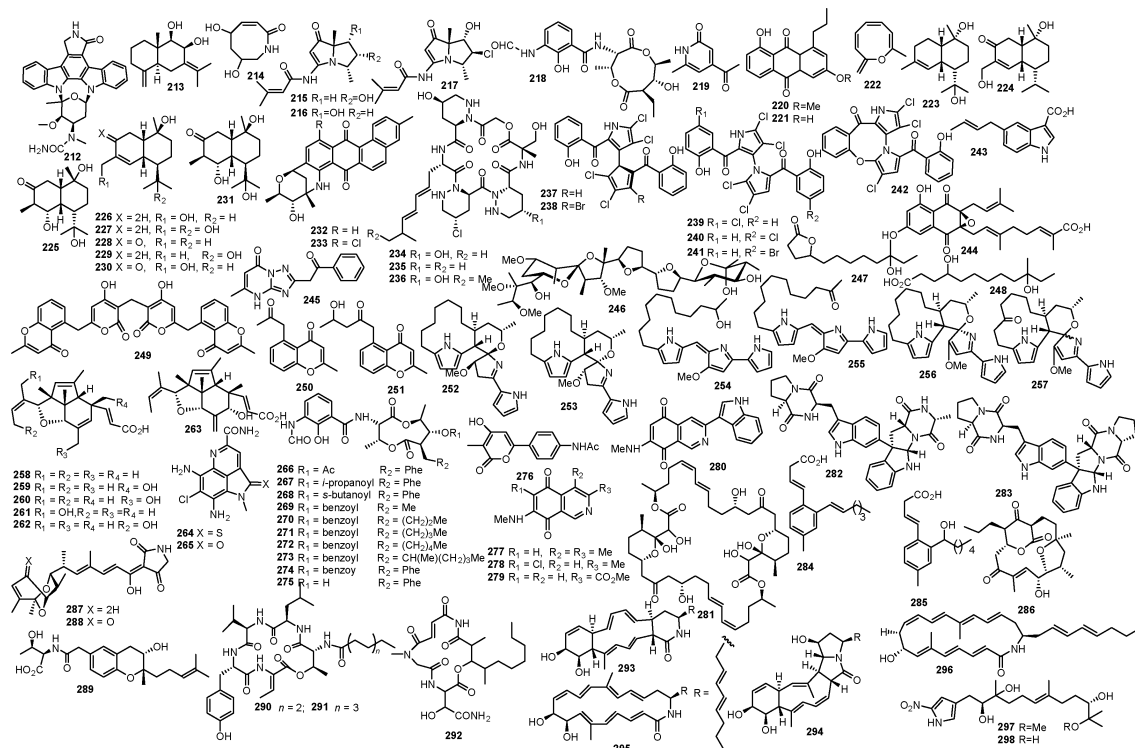


图 4 化合物 212~298 的结构

Fig.4 Structures of compounds 212~298

化合物 300~304 产自 *Streptomyces* CNQ-509, 化合物 300, 302 和 303 对 HCT-116 细胞的 IC_{50} 分别为 $31.1\mu\text{mol/L}$ 、 $31.0\mu\text{mol/L}$ 和 $5.7\mu\text{mol/L}$ (Kwon et al., 2010); *Streptomyces* sp. B6219 代谢产生化合物 305(Abdalla et al., 2010)。吡喃酮类化合物 306~309 产自 *S. albus* POR-04-15-053, 化合物 306 和 309 对 MDA-MB-231、HT-29 和 A549 的 GI_{50} 为 $0.24\sim 0.69\mu\text{mol/L}$ (Schleissner et al., 2011)。抗霉素 antimycins A_{19} 和 A_{20} (310~311) 产自 *S. antibioticus* H74-18, 其抑制白色念珠菌(*C. albicans*)的 MIC 为 $5\sim 10\mu\text{g/mL}$ (Xu et al., 2011)。*Streptomyces* sp. CNQ-027 代谢产生 actinoramides A-C (312~314)(Nam et al., 2011)和 actinoranone

(315)(Nam et al., 2013), 化合物 315 对 HCT-116 细胞的 LD_{50} 为 $2.0\mu\text{g/mL}$ 。*Streptomyces* sp. RJA2928 代谢产生 pandanamide B (316)(Williams et al., 2011)、nahuic acid A (317)(Williams et al., 2013)和 nahuic acids D-E (318~319)(Williams et al., 2016), 化合物 316 抑制 T 淋巴细胞细胞的 IC_{50} 为 $20\mu\text{g/mL}$ 、化合物 317 和 319 对组蛋白甲基化酶的 IC_{50} 分别为 $6.5\mu\text{mol/L}$ 和 $13\mu\text{mol/L}$ 。缩酚酸肽 fijimycins A-C (320~322)来自 *Streptomyces* sp. CNS-575, 其对 MRSA (ATCC33591)、Sanger 252 和 UAMS1182 的 MIC_{100} 为 $4\sim 16\mu\text{g/mL}$ (Sun et al., 2011)。*Streptomyces* sp. 211726 代谢产生化合物 323~324(Yuan et al., 2011)和 325~331(Yuan

et al., 2013), 对白色念珠菌(*C. albicans*)和人结肠癌细胞 HCT-116 有抑制活性。化合物 **332** 产自 *Streptomyces* sp. 061316 (Chen et al., 2011)。安沙霉素类化合物 ansalactam A (**333**)来自 *Streptomyces* sp. CNH-189(Wilson et al., 2011); 该菌还代谢产生混源萜 **334~337** (Kaysser et al., 2012)和 ansalactams B-D (**338~340**)(Le et al., 2016), 化合物 **338~340** 对 MRSA 的 MIC 分别为 31.2 μ g/mL、31.2 μ g/mL 和 62.5 μ g/mL。化合物 benzoxacystol (**341**)来自 *Streptomyces* sp. NTK 935, 抑制糖原合成酶激酶 GSK-3 β 的 IC₅₀ 为 1.35 μ mol/L, 对小鼠成纤维细胞 NIH- 3T3 有弱抑制活性(Nachtigall et al., 2011)。*Streptomyces* sp. B8112 代谢产生

glucopiericidin C (**342**), 有抗米黑毛霉菌活性和细胞毒活性 (Shaaban et al., 2011)。*Streptomyces* sp. MST- MA568 代谢产生螺环缩酮 reveromycin E (**343**)(Fremlin et al., 2011)。吡喃酮 A-C (**344~346**)产自 *Streptomyces* sp. CNQ-301 (Fukuda et al., 2011)。*Streptomyces* sp. WuXin 代谢产生化合物 **347** 和 **348**, 对 HL-60 有细胞毒活性(Li et al., 2011); 化合物 usabamycin A-C (**349~351**)产自 *Streptomyces* sp. NPS853, 对人宫颈癌 HeLa 细胞有弱细胞毒活性并可选择性抑制对 5-羟色胺的摄取 (Sato et al., 2011)。*Streptomyces* sp. W007 代谢产生化合物 **352**, 对 A549 细胞有细胞毒性(Zhang et al., 2011)(图 5)。

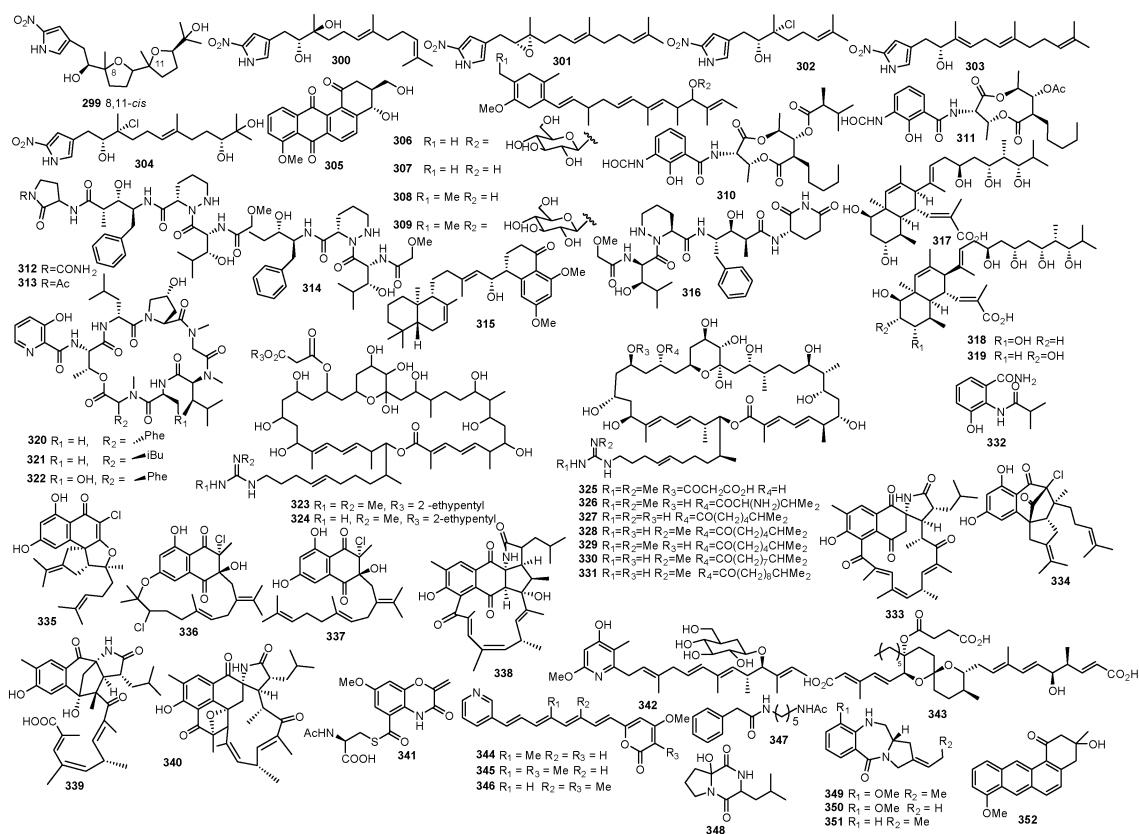


图 5 化合物 299~352 的结构
Fig.5 Structures of compounds 299~352

化合物 **353** 产自杆菌状链霉菌 *S. bacillaris* SNB-019(Hu and MacMillan, 2012)。

对弗氏链霉菌 *S. fradiae* 007 进行紫外照射和亚硝基胍诱变, 得到突变株 *S. fradiae* 007M135, 该突变株代谢产生吡嗪生物碱 **354~356**, 其对 HL-60、K562、A549、BEL-7402 细胞均有抑制活性, 对蛋白激酶 C (PKC- α) 的 IC_{50} 值为 0.001~4.6 $\mu\text{mol/L}$ (Fu et al., 2012a)。糖苷类化合物 **357~361** 来自 *S. lusitanus* SCSIO LR32, **357~360** 对多个肿瘤细胞的 IC_{50} 值为 1.1~31 $\mu\text{mol/L}$ (Huang et al., 2012)。*Streptomyces* sp. CMB-M0392 代谢产生化合物 **362**, 对枯草杆菌 ATCC6052 和 ATCC6633 的 IC_{50} 分别为 8 $\mu\text{mol/L}$ 和 14 $\mu\text{mol/L}$ (Raju et al., 2012)。化合物 **363** 和 **364** 产自 *Streptomyces* sp. CNQ343, 化合物 **363** 对白色念珠菌有较强的抑制活性 (Kim et al., 2012)。*Streptomyces* sp. SCSIO 03032 代谢产生吡嗪生物碱 **365~368** (Zhang et al., 2012)、indimicins A-E (**369~373**)、lynamicin F (**374**) 和 lynamicin G (**375**) (Chen et al., 2014), 以及 piericidin A1 (**376**) (Zhang et al., 2014a)、heronamides D-F (**377~379**) (Zhang et al., 2014b), 化合物 **366~368** 对多种肿瘤细胞的 IC_{50} 为 4~15 $\mu\text{mol/L}$ 、**370** 对 MCF-7 的 IC_{50} 为 10.0 $\mu\text{mol/L}$ 。吩嗪类化合物 **380** 为 *Streptomyces* sp. LB173 的代谢产物, 有微弱的抗菌活性, 是一种乙酰胆碱酯酶抑制剂 (Ohlendorf et al., 2012)。化合物 **381** 产自 *Streptomyces* sp. M268 (Xie et al., 2012); 化合物 **382~385** 产自 *Streptomyces* sp. SCSIO 02999 (Zhang et al., 2012), 4 个化合物对致病菌的 MIC 分别为 *E.coli* ATCC 25922 (8 $\mu\text{g/mL}$ 、8 $\mu\text{g/mL}$ 、16 $\mu\text{g/mL}$ 和 4 $\mu\text{g/mL}$)、*S.aureus* ATCC29 213 (8 $\mu\text{g/mL}$ 、16 $\mu\text{g/mL}$ 、16 $\mu\text{g/mL}$ 、8 $\mu\text{g/mL}$)、*B.subtilis* SCSIO BS01 (64 $\mu\text{g/mL}$ 、128 $\mu\text{g/mL}$ 、大于 128 $\mu\text{g/mL}$ 、64 $\mu\text{g/mL}$) 和 *B.thuringiensis* SCSIO BT01 (64 $\mu\text{g/mL}$ 、64 $\mu\text{g/mL}$ 、大于 128 $\mu\text{g/mL}$ 、大于 128 $\mu\text{g/mL}$)。化合物 **386** 产自 *Streptomyces* sp. CP13-10, 对酵母 Sir2p 基因的 MIC 为 2.5 mmol/L、对人类 SIRT1 和

SIRT2 基因的 IC_{50} 分别为 3.7 mmol/L 和 4.5 mmol/L (Amagata et al., 2012)。

S. variabilis SNA-020 代谢产生生物碱 **387**, **387** 对胰腺细胞 MIA PaCa-2 的 IC_{50} 为 3.2 $\mu\text{mol/L}$ (Pan et al., 2012)。化合物 **388** 产自 *Streptomyces* sp. TP-A0879, 对小鼠结肠癌细胞 26-L5 的 IC_{50} 为 0.25 $\mu\text{mol/L}$ (Igarashi et al., 2012)。吡嗪生物碱 **389** 和 **390** 产自 *Streptomyces* sp. FMA, 化合物 **390** 对 HL-60、A549 和 Hela 细胞的 IC_{50} 值分别为 1.4 $\mu\text{mol/L}$ 、5.0 $\mu\text{mol/L}$ 和 34.5 $\mu\text{mol/L}$ (Fu et al., 2012b)。*Streptomyces* sp. CNT-179 代谢产生 cyanosporasides D-F (**391~393**) (Lane et al., 2013); *S. antibioticus* PTZ0016 代谢产生 **394~396**, 化合物 **394~396** 对金黄色葡萄球菌 ATCC6538 的 MIC 分别为 6.0 mg/mL、6.0 mg/mL 和 8.0 mg/mL (Lian and Zhang, 2013)。生物碱 nitrosporeusines A (**397**) 和 B (**398**) 产自 *S. nitrosporeus* CQT1424, 具有抑制甲型 H1N1 流感病毒活性 (Yang et al., 2013a)。*S. niveus* SCSIO 3406 代谢产生倍半萜 marfuraquinocins A-D (**399~402**)、phenaziterpenes A (**403**) 和 B (**404**), 化合物 **399** 和 **401** 对肺癌细胞 NCI-H460 的 IC_{50} 值分别为 3.7 $\mu\text{mol/L}$ 和 4.4 $\mu\text{mol/L}$, 化合物 **399**、**401** 和 **402** 对金黄色葡萄球菌 ATCC292138 的 MIC 值均为 8 $\mu\text{g/mL}$; 化合物 **401** 和 **402** 对耐甲氧西表皮葡萄球菌 shhs-E1 的 MIC 值为 8 $\mu\text{g/mL}$ (Song et al., 2013)。*Streptomyces* sp. CNH-287 代谢产生 chlorizidine A (**405**), 其对 HCT-116 细胞的 IC_{50} 为 3.2~4.9 $\mu\text{mol/L}$ (Alvarez-Mico et al., 2013)。脱氢二酮哌嗪 **406~410** 产自 *Streptomyces* sp. FXJ7.328, 化合物 **407** 抑制 H1N1 病毒的 IC_{50} 为 41.5 $\mu\text{mol/L}$ (Wang et al., 2013)。*Streptomyces* sp. MS100061 代谢产生 lobophorin G1 (**411**), 其对枯草芽胞杆菌和结核分支杆菌 H37Rv 的 MIC 分别为 3.1 $\mu\text{g/mL}$ 和 32 $\mu\text{g/mL}$ (Chen et al., 2013) (图 6)。

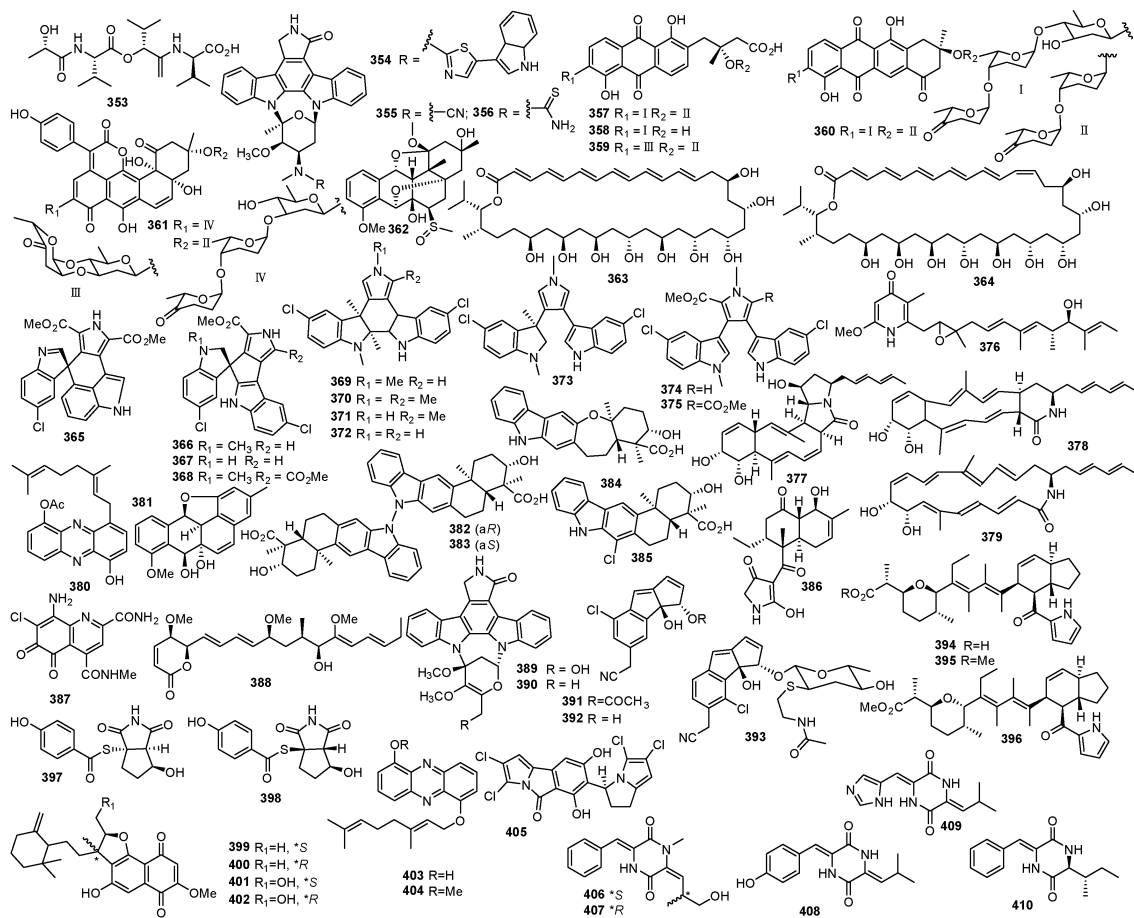


图 6 化合物 353~410 的结构
Fig.6 Structures of compounds 353~410

Streptomyces sp. SNJ013 代谢产生化合物 sungsanpin (**412**)(Um et al., 2013a)。*Streptomyces* sp. CNQ-329 代谢产生 napyradiomycins A-E(**413~417**), 化合物 **413**、**416** 和 **417** 对 HCT-116 细胞的 IC_{50} 为 4.2 μ g/mL、16.1 μ g/mL 和 4.8 μ g/mL, 化合物 **413** 和 **414** 对 MRSA 的 MIC 分别为 26 μ g/mL 和 64 μ g/mL(Cheng et al., 2013)。*Streptomyces* sp. CNH-070 产生 napyradiomycin F (**418**), 其对 HCT-116 细胞的 IC_{50} 为 9.42 μ g/mL(Cheng et al., 2013)。*Streptomyces* sp. SCSIO 10428 代谢产生化合物 **419~421**, 化合物 **419** 对金黄色葡萄球菌 ATCC29213、枯草芽胞杆菌 SCSIO BS01 和苏云金杆菌 SCSIO BT01 的 MIC 分别为 4 μ g/mL、4 μ g/mL 和

8 μ g/mL, 化合物 **420** 对金黄色葡萄球菌 ATCC29213、枯草芽胞杆菌 SCSIO BS01 和苏云金杆菌 SCSIO BT01 的 MIC 分别为 0.5 μ g/mL、1 μ g/mL 和 1 μ g/mL, 化合物 **421** 对枯草芽胞杆菌 SCSIO BS01 和苏云金杆菌 SCSIO BT01 的 MIC 分别为 8 μ g/mL 和 16 μ g/mL(Wu et al., 2013a)。化合物 anthracimycin (**422**) 来自 *Streptomyces* sp. CNH365, 对炭疽芽胞杆菌 UM23C1-1、金黄色葡萄球菌 ATCC 13709、粪肠球菌 ATCC 29212、肺炎链球菌 ATCC 51916、流感嗜血杆菌 ATCC 31517KO 的 MIC 分别为 0.03125 μ g/mL、0.0625 μ g/mL、0.125 μ g/mL、0.25 μ g/mL 和 4 μ g/mL(Jang et al., 2013)。环肽 surugamides A-E (**423~427**)来自

Streptomyces sp. JAMM992, 对牛组织蛋白酶 B 的 IC_{50} 分别为 $21\mu\text{mol/L}$ 、 $27\mu\text{mol/L}$ 、 $36\mu\text{mol/L}$ 、 $18\mu\text{mol/L}$ 和 $16\mu\text{mol/L}$ (Takada et al., 2013)。*Streptomyces* sp. SCSIO 03219 代谢产生萜类化合物 03219A (**428**) (Zhang et al., 2013)。*Streptomyces* sp. Eg25 代谢产生 maroxazinone (**429**), 对 MCF7、HEPG2 和 HCT116 细胞的 IC_{50} 分别为 $4.32\mu\text{g/mL}$ 、 $2.90\mu\text{g/mL}$ 和 $8.51\mu\text{g/mL}$ (Abdelfattah, 2013)。*Streptomyces* sp. CNT-372 代谢产生 farnesides A (**430**) 和 B (**431**), **430** 对恶性疟原虫的 IC_{50} 为 $69.3\mu\text{mol/L}$ (Zafirir et al., 2013)。*Streptomyces* sp. 7-145 代谢产生化合物 **432** 和 **433**, 对耐甲氧西林金黄色葡萄球菌和耐万古霉素肠球菌有很好的抗菌活性(Wu et al., 2013b)。环肽 ohmyungsamycin A(**434**)和 ohmyungsamycin B(**435**)产自链霉菌 *Streptomyces* sp. SNJ042, 化合物 **434** 对枯草芽胞杆菌 ATCC6633、藤黄微球菌 NBRC12708 和变形杆菌 NBRC3851 的 MIC 分别为 $4.28\mu\text{mol/L}$ 、 $1.07\mu\text{mol/L}$ 和 $2.14\mu\text{mol/L}$, 化合物 **435** 对藤黄微球菌 NBRC12708 的 MIC 为 $8.5\mu\text{mol/L}$, 化合物 **434** 对 HCT116、A549、SNU-638、MDAMB-231 和 SKHEP-1 细胞的 IC_{50} 分别为 $0.359\mu\text{mol/L}$ 、 $0.551\mu\text{mol/L}$ 、 $0.532\mu\text{mol/L}$ 、 $0.688\mu\text{mol/L}$ 和 $0.816\mu\text{mol/L}$ (Um et al., 2013b)。Separacenes A-D(**436~439**) 产自 *Streptomyces* sp. SNJ210, 化合物 **436** 对白色念珠菌异柠檬酸裂解酶、人癌细胞 HCT-116 和 A549 有弱活性(Bae et al., 2013)。*Streptomyces* sp. 12A35 代谢产生 lobophorins H (**440**)和 I (**441**), 化合物 **440** 对金黄色葡萄球菌 ATCC29213 和枯草芽胞杆菌 CMCC63501 的 MIC 分别为 $50\mu\text{g/mL}$ 和 $1.57\mu\text{g/mL}$ (Pan et al., 2013)。Strepsesquitriol (**442**)来自 *Streptomyces* sp. SCSIO 10355, 具有抑制 $\text{TNF-}\alpha$ 的活性(Yang et al., 2013b)。Mollemycin A (**443**) 产自 *Streptomyces* sp. CBM0244, 对金黄色葡萄球菌 ATCC

25293 和 ATCC 9144、表皮葡萄球菌 ATCC12228、枯草芽胞杆菌 ATCC 6051 和 ATCC 6633、大肠杆菌 ATCC 25922、绿脓杆菌 ATCC 27853 和牛结核杆菌的 IC_{50} 值分别为 50nmol/L 、 10nmol/L 、 50nmol/L 、 10nmol/L 、 10nmol/L 、 10nmol/L 、 50nmol/L 和 3200nmol/L ; 对药敏型和多药耐药的恶性疟原虫的 IC_{50} 分别为 9nmol/L 和 7nmol/L , 活性远大于氯喹, 与青蒿素相当(Raju et al., 2014)。*S. drozdowiczii* SCSIO 10141 代谢产生 marformycins A-F (**444~449**), 化合物 **444~448** 对藤黄微球菌的 MIC 分别为 0.25mg/mL 、 4.0mg/mL 、 0.25mg/mL 、 0.063mg/mL 和 4.0mg/mL (Zhou et al., 2014)。*S. nitrosporeus* YBH10-5 代谢产生 nitrosporeunols A-G (**450~456**)(Liu et al., 2014)。*S. scopuliridis* SCSIO ZJ46 代谢产生化合物 **457~459**, **457** 对金黄色葡萄球菌 ATCC 29213、肺炎双球菌 NCTC 7466、耐甲氧西林表皮葡萄球菌的 MIC 值分别为 $16.0\mu\text{g/mL}$ 、 $12.5\mu\text{g/mL}$ 和 $32.0\mu\text{g/mL}$ (Song et al., 2014)(图 7)。

Streptomyces sp. LZ35DgdmAI 代谢产生 echosides A-E (**460~464**), 化合物 **460** 有很明显的拓扑异构酶 I 活性, 化合物 **462** 有拓扑异构酶 IIa 活性(Deng et al., 2014)。化合物 **465~468** 产自 Streptomycetaceae CNQ525, 可以诱导 HCT-116 细胞凋亡(Farnaes et al., 2014)。*Streptomyces* sp. ACT232 代谢产生 ahpatinin Ac (**469**)和 ahpatinin Pr (**470**), 对胃蛋白酶的 IC_{50} 为 $11\sim 50\text{nmol/L}$ (Sun et al., 2014a)。Carpatamides A-C(**471~473**)来自 *Streptomyces* sp. SNE-011, 化合物 **471** 和 **473** 对 NSCLC、HCC366、A549 和 HCC44 细胞的 IC_{50} 为 $2.2\sim 8.4\mu\text{mol/L}$ (Fu et al., 2014)。化合物 anmindenols A (**474**) 和 B (**475**) 产自 *Streptomyces* sp. CMDD10D111, 抑制 NO 产生的 IC_{50} 值为 $23\mu\text{mol/L}$ 和 $19\mu\text{mol/L}$ (Lee et al., 2014)。Arcticoside (**476**)和 C-1027

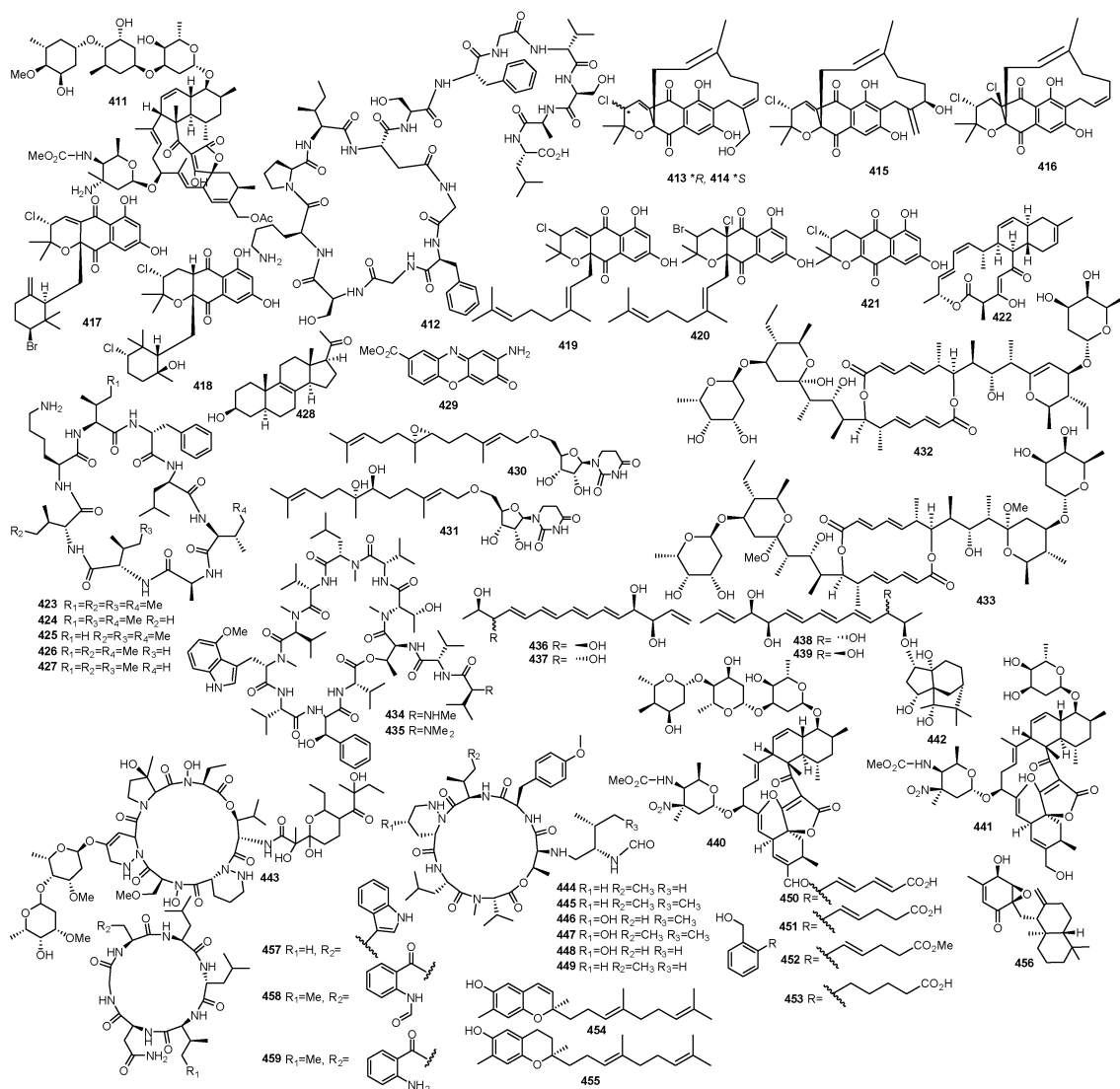


图7 化合物411~459的结构
Fig.7 Structures of compounds 411~459

chromophore-V (477) 产自 *Streptomyces* sp. ART5, 化合物 476 和 477 对白色念珠菌异柠檬酸(裂合)酶的 IC₅₀ 分别为 30.4μmol/L 和 37.9μmol/L; 化合物 477 对癌细胞 MDA-MB231 和 HCT-116 的 IC₅₀ 分别为 0.9μmol/L 和 2.7μmol/L(Moon et al., 2014)。Lajollamycins B-D (478~480) 产自链霉菌 *Streptomyces* sp. SMC72, 对白色念珠菌异柠檬酸裂解酶的 IC₅₀ 分别为 40μmol/L、50μmol/L 和 120μmol/L

(Ko et al., 2014)。Streptomyces sp. SNM55 代谢产生 mohangamides A (481) 和 B (482)(Bae et al., 2015b)、hormaomycins B (483) 和 C (484)(Bae et al., 2015a), 化合物 481 和 482 对白色念珠菌 ICL 的 IC₅₀ 分别为 4.4μmol/L 和 20.5μmol/L, 化合物 483/484 对金黄色葡萄球菌 ATCC 25923、枯草芽胞杆菌 ATCC 6633、藤黄微球菌 NBRC 12708、化脓性链球菌 ATCC 19615、肠道沙门菌 ATCC 14028 和 *P.*

hauseri NBRC 3851 的 MIC 分别为 7/7 μ mol/L、14/56 μ mol/L、0.4/0.23 μ mol/L、14/8 μ mol/L、29/114 μ mol/L 和 29/14 μ mol/L。*Streptomyces* sp. IFM 11440 代谢产生 nubosins A-C (**485~487**), 化合物 **486** 具有 Ngn2 基因启动子的活性、促进神经干细胞分化基因有关的 mRNA 的表达 (Arai et al., 2015)。*Streptomyces* sp. SCSIO 11594 代谢产生 marangucyclines A (**488**)和 B (**489**), 化合物 **489** 对 A549、CNE2、MCF-7、HepG2 和 HL7702 细胞的 IC₅₀ 分别为 0.45 μ mol/L、0.56 μ mol/L、0.24 μ mol/L、0.43 μ mol/L 和 3.67 μ mol/L (Song et al., 2015)。Suncheonosides A-D (**490~493**)来自 *Streptomyces* sp. SSC21, 化合物 **490**、**491** 和 **493** 能促进脂联素的产生, 具有降糖的潜力 (Shin et al., 2015)。二酮哌嗪 **494** 产自 *Streptomyces* sp. SCSIO 04496 (Luo et al., 2016)。Rocheicoside A (**495**)和 rocheicoside **496** 产自 *S. rochei* 06CM016, 化合物 **495** 对大肠杆菌 O157: H7 RSKK 234、耐甲氧西林金黄色葡萄球菌 DSM 11729 和人白色念珠菌 DSM 5817 的 MIC 分别为 16 μ g/mL、8 μ g/mL 和 4 μ g/mL; 化合物 **496** 对这 3 株致病菌的 MIC 分别为 16 μ g/mL、16 μ g/mL 和 8 μ g/mL (Aksoy et al., 2016)。*Streptomyces* sp. IFM11490 代谢产生 elmonin (**497**)、elmenols A (**498**)和 elmenols B (**499**), 化合物 **497** 和 **499** 对 AGS 细胞有弱细胞毒活性 (Yixizhuoma et al., 2015)。*Streptomyces* sp. SNB-048 代谢产生 spinoxazines A (**500**)和 spinoxazines B (**501**)、bohemamine D-I (**502~507**) (Fu et al., 2016)。*Streptomyces* sp. CHQ-64 代谢产生 drimentine I (**508**), 对 HeLa 的 IC₅₀ 为 16.7 μ mol/L (Che et al., 2016)。*Streptomyces* sp. 10A085 代谢产生 anithiactins A-C (**509~511**), 其对乙酰胆碱酯酶的 IC₅₀ 分别为 63 μ mol/L、53 μ mol/L 和 68 μ mol/L (Kim et al., 2014) (图 8)。

多环萜醌 **512** 和 **513** 来自 *Streptomyces* sp. 182SMLY, 对 C6、U251、U87-MG 和 SHG-44c

4 种胶质瘤细胞的 IC₅₀ 为 0.5~7.3 μ mol/L; 化合物 **512** 对 *S. aureus* 的 MIC 为 20.0 μ mol/L (Liang et al., 2016b); 该菌株还代谢产生吩嗪类化合物 **514~516** (Liang et al., 2016a)。*Mohangic acids* A-E (**517~521**) 来自 *Streptomyces* sp. SNM31, 化合物 **521** 对醌还原酶具有良好的活性, 当浓度为 20 μ mol/L 时, 活性是阳性药 β -萘黄酮的 2.1 倍 (Bae et al., 2016)。*Actinoquinolines* A (**522**) 和 B (**523**) 产自 *Streptomyces* sp. CNP975, 对环氧化酶 COX-1 的 IC₅₀ 分别为 7.6 μ mol/L 和 2.13 μ mol/L, 对环氧化酶 COX-2 的 IC₅₀ 分别为 24.9 μ mol/L 和 1.42 μ mol/L (Hassan et al., 2016)。麦角脂醇类化合物 ananstreps A-C (**524~526**) 来自 *S. anandii* H41-59, 其中化合物 **526** 对 SF-268、MCF-7 和 NCI-H460 的 IC₅₀ 分别为 13.0 μ g/mL、18.1 μ g/mL 和 23.5 μ g/mL (Zhang et al., 2016)。

3.2 海水来源的链霉菌天然产物

海水来源的链霉菌(下同)*Streptomyces* sp. Z00045 代谢产生 cycloheximide acid A (**527**) (Xu et al., 2013)。*Streptomyces* sp. F001 代谢产生 diazaquinomycins E-G (**528~530**), **528** 对卵巢癌 OVCAR5 细胞的 IC₅₀ 为 9.0 μ mol/L (Mullowney et al., 2014)。*Streptomyces* sp. TPU1236A 代谢产生 streptcytosines A-E (**531~535**), **531** 对耻垢分枝杆菌的 MIC 为 32 μ g/mL (Bu et al., 2014)。一株 gntR 基因突变的链霉菌代谢产生化合物 **536~538** (Liu et al., 2015)。

4 未知来源的海洋链霉菌天然产物

来源未知的链霉菌(下同)*Streptomyces* sp. GWS-BW-H5 产生内酯类化合物 **539~544** (Dickschat et al., 2005)。降倍半萜 **545** 来自 *Streptomyces* sp. 0616208, 对肝癌细胞 SMMC-7721 有细胞毒活性 (Xie et al., 2006)。吩嗪类化合物 **546** 和 **547** 产自 *Streptomyces* sp. CNS284, 其对 TNF- α 介导的 NF κ B 有抑制作

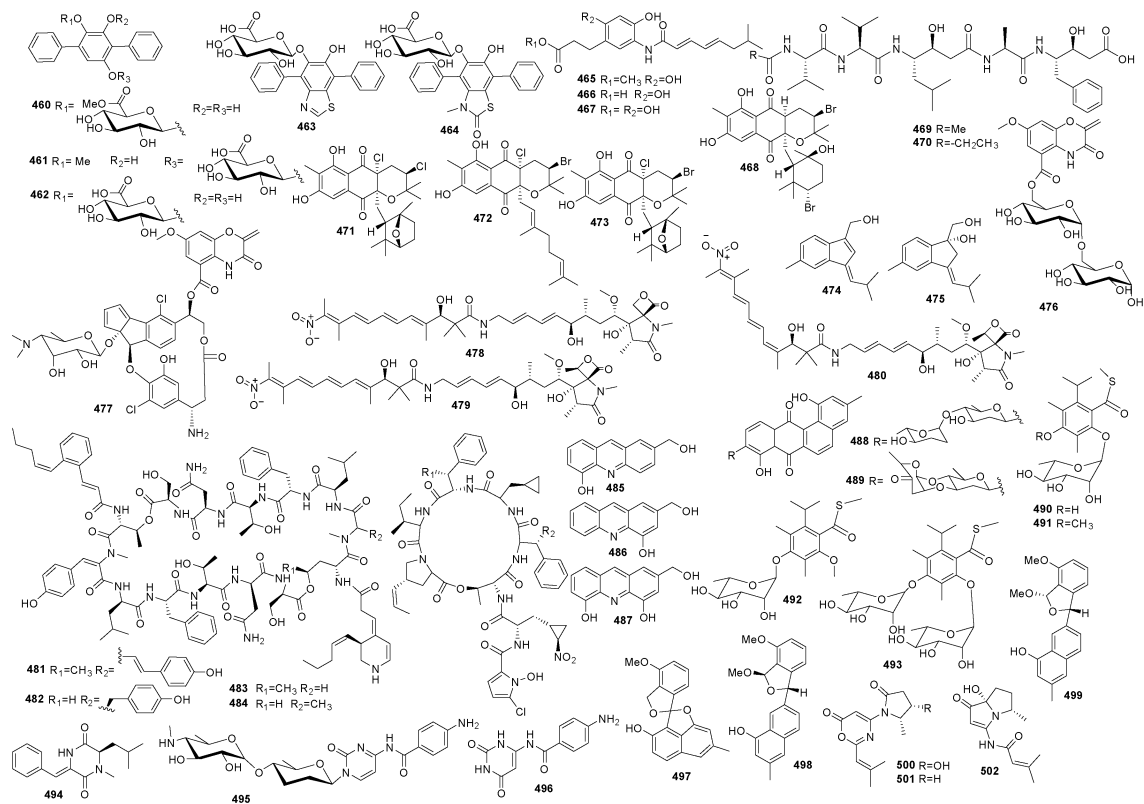


图 8 化合物 460~502 的结构
Fig.8 Structures of compounds 460~502

用, IC_{50} 分别为 $4.1\mu\text{mol/L}$ 和 $24.2\mu\text{mol/L}$; 抑制 LPS 介导的 NO 的 IC_{50} 分别为 $48.6\mu\text{mol/L}$ 和 $15.1\mu\text{mol/L}$; 对细胞生长和调节因子——前列腺素 E2(PGE2)有抑制作用, IC_{50} 分别是 $7.5\mu\text{mol/L}$ 和 $0.89\mu\text{mol/L}$ (Kondratyuk et al., 2012)(图 9)。

综上所述, 从 1976 年报道的首例海洋链霉菌来源的 aplasmomycins A-C(Okami et al., 1976)到 2016 年 6 月的 40 年时间里, 一共报道了 547 个海洋链霉菌新天然产物(表 1)。其结构类型呈现多样性, 涉及含氮化合物, 如生物碱、聚酮、萜类、甾体、糖苷、聚醚类及其卤代物等, 且 67.3% 的化合物表现出肿瘤细胞毒、抗菌、抗疟、抗寄生虫, 以及糖苷酶抑制等生物活性(表 1), 是发现海洋活性化合物的重要资源。

(1) 从海洋链霉菌 NPs 的数量看, 新化合物的数量呈现年递增的趋势。从 2006 年开始, 新化合物递增的趋势越来越显著, 2014 年最多, 报道了 82 个(图 10)。

(2) 从海洋链霉菌的样品来源看, 产生新化合物最多的海洋链霉菌的来源依次是海泥(377 个)、海绵(64 个)和其他海洋动物(34 个), 分别占 68.9%、11.7%和 6.2%(图 11)。

(3) 从化合物的结构类型看, 化合物最多的类型依次是含氮(336 个)和聚酮(196 个), 分别占海洋链霉菌 NPs 总数的 61.4%和 35.8%(图 12)。

(4) 约 67.3% 的海洋链霉菌 NPs(368 个)表现出肿瘤细胞毒、抗菌、抗疟和抗寄生虫等生物活性, 而肿瘤细胞毒活性(141 个)和抑菌活性(117 个)是主要的活性类型, 分别占活性

时间范围	天然产物数量
1976~1990年	6
1991~1999年	40
2000~2005年	34
2006年	24
2007年	17
2008年	22
2009年	34
2010年	42
2011年	54
2012年	54
2013年	67
2014年	82
2015年	47
2016年1月~2016年6月	24

29.8%的海洋链霉菌 NPs(图 14 见文后彩图); 欧美、中国和其他亚洲国家的学者分别发表了 93 篇、63 篇和 52 篇文章, 其他国家发表了 9 篇文章, 分别占 42.9%、29.0%、24.0%和 4.1%。

表 1 海洋链霉菌来源的新天然产物(1976 年至 2016 年 6 月)
Tab.1 New marine natural products from marine-derived *Streptomyces* sp. (1976~2016.6)

化合物	来源菌株	环境来源	生物活性	参考文献
1~2	<i>Streptomyces</i> sp. Ni-80	Unidentified sponge, Urauchicove, Iriomote, Japan	Antibacterial activity	Imamura et al., 1993
3~9	<i>Streptomyces</i> sp. KM86-9B	Sponge, Keomun Island, Korea	Topo I inhibition	Lee et al., 1998
10~11	<i>Streptomyces</i> M1087	Unidentified sponge, Jeju Island	Recombinase sortase B inhibition	Lee et al., 2005
12~19	<i>Streptomyces</i> sp. HB202	<i>Halichondria panicea</i> sponge, Baltic Sea (Germany)	Antibacterial activity	Mitova et al., 2008
20~22	<i>Streptomyces</i> sp. Sp. C080624SC-11	<i>Cinachyra</i> sp. Sponge, Okinawa, Japan	/	Izumikawa et al., 2010b
23~24	<i>Streptomyces</i> sp. Sp080513GE-23	<i>Haliclona</i> sp. Sponge, Chiba, Japan	/	Motohashi et al., 2010c
25	<i>Streptomyces</i> sp. NBRC105896	<i>Haliclona</i> sp. Sponge, Chiba, Japan	Cytotoxicity	Izumikawa et al., 2010a
26~27	<i>Streptomyces</i> sp. Sp080513GE-26	<i>Haliclona</i> sp. Sponge, Chiba, Japan	26: Cytotoxicity	Motohashi et al., 2010a
28	<i>Streptomyces</i> sp. Sp. D081030ME-02	Demospongiae sponge, ishigaki, Japan	Cytotoxicity	Ueda et al., 2010
29	<i>Streptomyces</i> sp. HB202	<i>Halichondria panicea</i> sponge, Baltic Sea	Cytotoxicity, Antibacterial activity	Schneemann et al., 2010
30~33	<i>S. axinellae</i> Pol001 ^T	<i>Axinella polypoides</i> sponge, Banyuls-sur-Mer	Anti-parasitic activity	Pimentel-Elardo et al., 2011
34~35	<i>S. carnosus</i> AZS17	<i>Hymeniacidon</i> sp. sponge, East China Sea	Cytotoxicity	Wei et al., 2011
36	<i>S. microflavus</i> HVG29	<i>Hymeniacidon perlevis</i> sponge (Dalian, China).	/	Li et al., 2011
37~38	<i>Streptomyces</i> sp. SpD081030SC-03	demospongiae sponge, Okinawa, Japan	/	Motohashi et al., 2011
39	<i>Streptomyces</i> sp. DA22	<i>Craniella australiensis</i> Sponge, South China Sea	Cytotoxicity	Huang et al., 2011
40~42	<i>Streptomyces</i> sp. RM72	Sponge, kagoshima	HDAC1 inhibition	Hosoya et al., 2012
43~46	<i>Streptomyces</i> sp. RV15	<i>Dysidea tupa</i> sponge, Croatian	/	Abdelmohsen et al., 2012
47~49	<i>Streptomyces</i> sp. BCC45596	<i>Xestospongia</i> sp. sponge, Thailand	Anti-malaria, anti- tuberculosis activity, Cytotoxicity	Supong et al., 2012
50	<i>S. tateyamensis</i> NBRC 105047	<i>Haliclona</i> sp. sponge, Tate-yama	/	Izumikawa et al., 2013
51~53	<i>Streptomyces</i> HB202	<i>Halichondria panacea</i> sponge, Baltic Sea	53: Antibacterial activity	Kunz et al., 2014

续表

化合物	来源菌株	环境来源	生物活性	参考文献
54	<i>S. anulatus</i> S71	<i>Aplysina aerophoba</i> sponge, South China Sea	/	Sun et al., 2014b
55~60	<i>Streptomyces</i> sp. M7_15	<i>S. ruetzleri</i> sponge, Caribbean	57, 59-60: Cytotoxicity	Vicente et al., 2015
61	<i>Streptomyces</i> sp. S.4	<i>Xestospongia muta</i> sponge, Florida Island.	Anti-plasmodium activity	Rakotondraibe et al., 2015
62~63	<i>Streptomyces</i> sp. LS298	<i>Gelliodes carnosus</i> sponge, South China Sea	63: Cytotoxicity	Zhen et al., 2015
64	<i>Streptomyces</i> sp. SBT345	<i>Agelas oroides</i> sponge, Mediterranean Sea	Anti-chlamydia activity	Cheng et al., 2016
65~66	<i>Streptomyces</i> sp. PG-19	Coral <i>Pacifigorgia</i> sp., Sea of Cortez	65: Cytotoxicity	Tapiolas et al., 1991
67~68	<i>Streptomyces</i> sp. OUCMDZ-1703	Unidentified soft coral, Weizhou Island, Guangxi, China	Cytotoxicity	Fu et al., 2013
69	<i>S. axinellae</i> SCSIO02208	Coral, South China Sea	/	Ai et al., 2014
70~73	<i>Streptomyces</i> sp. SCSGAA 0027	<i>Melittodes squamata</i> , South China Sea	<i>Shewanella oneidensis</i> MR-1 biofilm inhibition	Nong et al., 2016
74~75	<i>S. hygroscopicus</i>	Jellyfish <i>Cassiopeia xamachana</i> , Florida Keys	Antibacterial, Anti-inflammatory activity	Trischman et al., 1994
76	<i>S. hygroscopicus</i>	Fish <i>Halichoeres bleekeri</i> , unknown place	Cytotoxicity	Takahashi et al., 1994
77	<i>Streptomyces</i> sp. SCRC-A20	Unidentified marine mollusk, Aburatubo, Japan	Superoxide anion production inhibitor	Bae et al., 1996
78~80	<i>Streptomyces</i> sp. BL-49-58-005	Unidentified marine invertebrate, Mexico	78-79: Cytotoxicity	Jose et al., 2003
81~82	<i>Streptomyces</i> sp. YM14-060	Unidentified ascidian, Palau	Cytotoxicity	Hayakawa et al., 2007
83	<i>Streptomyces</i> sp. JP90	Ascidian <i>Aplidium lenticulum</i> , Great Barrier Reef, Australia	Acetylcholinesterase inhibitor	Quitschau et al., 2008
84~88	<i>Streptomyces</i> sp. CP32	Snail, Cebu Island	Serotonin 5-HT2B receptor binding activity	Lin et al., 2010
89	<i>Streptomyces</i> sp. BOSC-022A	Tunicate, the Scottish coast	/	Lorente et al., 2010
90~94	<i>Streptomyces</i> HQ696493	<i>Chicoreus nobilis</i> , Cebu Island	TRPV1 antagonist	Lin et al., 2011
95~97	<i>Streptomyces</i> HQ696492	<i>Chicoreus nobilis</i> , Cebu Island	/	Lin et al., 2011
98	<i>Streptomyces</i> sp.	Tunicate, New Zealand	Cytotoxicity	Mahyudin et al., 2012

续表

化合物	来源菌株	环境来源	生物活性	参考文献
99~100	<i>Streptomyces</i> sp. 1053U.I.1a.1b	<i>Lienardia totopotens</i> , Mactan Island, Cebu, Philippines	/	Lin et al., 2012
101~102	<i>Streptomyces</i> sp. 112CH148	<i>Acanthaster planci</i> , the Federated States of Micronesia	Cytotoxicity	Shin et al., 2014
103~104	<i>Streptomyces</i> sp. 1053U.I.1a.3b	<i>L. totopotens</i> , Mactan Island, Cebu, Philippines	104: Antibacterial activity	Lin et al., 2014
105	<i>Streptomyces</i> sp. MB-PO13	<i>Molgula manhattensis</i> , Minato-ku, Tokyo	Hyaluronic acid enzyme inhibition	Harunari et al., 2014
106~107	<i>S. Caniferus</i> GUA-06-05-006A	<i>Polychaeta Filograna</i> sp., Guadalupe Island	Cytotoxicity	Pérez et al., 2016
108~110	<i>Streptomyces</i> sp. # N1-78-1	Unidentified green algae, Rhode Island	Antibacterial activity	Socha et al., 2006
111~113	<i>Streptomyces</i> sp. YM5-799	<i>Analphus japonicus</i> , Muroran, Japan	/	Matsuo et al., 2011
114~116	<i>Streptomyces</i> sp. GT2002/1503	Mangrove tree stem, unknown place	Anti-HIV activity	Ding et al., 2010
117~120	<i>Streptomyces</i> sp. HK10552	Leaves of <i>A. corniculatum</i> , Xiamen, China	/	Wang et al., 2010
121~122	<i>Streptomyces</i> sp. GT2002/1503	Mangrove root, unknown place	Cytotoxicity; 121: Anti-HIV activity	Ding et al., 2010
123~130	<i>Streptomyces</i> sp. HK10576	Mangrove tree stem, unknown place	123-126: Antibacterial activity, Cytotoxicity	Ding et al., 2011; Xu et al., 2014
131~132	<i>S. lusitanus</i> XM52	Mangrove root, Fujian, China	132: Antibacterial activity	Han et al., 2012
133~137	<i>Streptomyces</i> sp. HK10595	Stem of <i>K. candel</i> , Xiamen, China	Antibacterial activity	Ding et al., 2012
138~140	<i>Streptomyces</i> sp. CANU Fox 21-2-6	Driftwood, West coast, New Zealand	Cytotoxicity	Phipps et al., 2004
141~143	<i>Streptomyces</i> sp. FX-58	<i>Salicornia herbacea</i> , Qingdao, China	143: Cytotoxicity	Huang et al., 2006a, 2006b
144	<i>Streptomyces</i> sp. MA-12.	Myoporium root, Leizhou Peninsula	Antibacterial activity	Ding et al., 2013
145	<i>S. violans</i> HTTA-F04129	<i>Salicornia herbacea</i> , Rushan, China	Cytotoxicity	Huang et al., 2014
146~147	<i>Streptomyces</i> sp. LC6	Leaves of <i>Kandelia candel</i> , Longhai, Fujian, China	Antibacterial activity	Zhang et al., 2014c
148~149	<i>Streptomyces</i> sp. OUCMDZ-3434	Green algae <i>Enteromorpha prolifera</i> , Zhanqiao, Qingdao, China	α -glucosidase inhibition	Chen et al., 2016
150~152	<i>S. griseus</i> SS-20	shallow sea sediment, Sagami Bay	Antibacterial, anti-plasmodium activity	Okami et al., 1976; Nakamura et al., 1977

续表

化合物	来源菌株	环境来源	生物活性	参考文献
153~154	<i>S. tenjimariensis</i> SS-939	sea mud sample, Tenjin-island, Sagami-Bay	Antibacterial activity	Okami et al., 1979
155	<i>S. siroyaensis</i> SA-1758	sea mud sample, Gamo, Miyagi Prefecture, Japan	Acaricidal activity, Cytotoxicity	Okami et al., 1989
156~159	<i>Streptomyces</i> sp. CNB-253	Sediment, Bodega Bay, CA	156: antiviral activity; Antibacterial activity	Pathirana et al., 1992
160~161	<i>Streptomyces</i> sp. SA-3501	Sediment, Otsuchi Bay, Japan	<i>N</i> -acetyl- β -D-aminoglucose enzyme inhibition	Aoyama et al., 1995
162~163	<i>Streptomyces</i> sp. B 9173	Sediment, Pacific coast of Chile	/	Balk-Bindseil et al., 1995
164~167	<i>Streptomyces</i> sp. BD-26T(20)	Sediment, Hawaii	164, 167: Antibacterial activity	Sitachitta et al., 1996
168	<i>Streptomyces</i> sp. B 8300	Sediment, Gulf of Mexico	Antibacterial activity	Biabani et al., 1997
169	<i>Streptomyces</i> sp. CNB-689	Sediment, Christchurch, New Zealand	Antibacterial activity	Jiang et al., 1997
170	<i>Streptomyces</i> sp. strain B 8251	Sediment, Gulf of Mexico	Antibacterial activity	Pusecker et al., 1997
171	<i>Streptomyces</i> sp. B7747	Sediment, Gulf of Mexico	Anti- <i>C. sorokiniana</i>	Biabani et al., 1998
172~175	<i>Streptomyces</i> sp. BD-18T(41)	Sediment, Oahu	/	Ford et al., 1998
176~177	<i>Streptomyces</i> MSTMA190	Sediment, Victorian	176: Antibacterial activity	Capon et al., 2000
178~181	<i>Streptomyces</i> strains B 5632 and B 3497	Sediment, North Atlantic and Oakland	/	Mukku et al., 2000
182	<i>Streptomyces</i> sp. SS99BA-2	Sediment, coast of St Paul, Brazil	/	Hernandez et al., 2000
183	<i>Streptomyces</i> sp. 1010	Sediment, Livingston	Antibacterial activity	Ivanova et al., 2001
184~189	<i>Streptomyces</i> sp. M02750	Sediment, Tongyoung Bay, Korea	/	Cho et al., 2001
190	<i>Streptomyces</i> sp. B7064	Sediment, Hawaii	Antibacterial activity	Asolkar et al., 2002
191~192	<i>Streptomyces</i> .sp B8652	Sediment, Laguna de Terminos, Gulf of Mexico	Cytotoxicity	Maskey et al., 2002
193	<i>Streptomyces</i> sp. BD21-2	Sediment, Kailua Beach, Oahu, Hawaii	Antibacterial activity	Schumacher et al., 2003
194	<i>Streptomyces</i> sp. KS3	Sediment, Komodo Island, Indonesia	Cytotoxicity	Itoh et al., 2003
195~196	<i>Streptomyces</i> sp. B6007	Sediment, Papua New Guinea	/	Stritzke et al., 2004
197	<i>S. aureoverticillatus</i> NPS001583	Sediment, Unknown place	Cytotoxicity	Mitchell et al., 2004

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化合物	来源菌株	环境来源	生物活性	参考文献
198	<i>S. nodosus</i> NPS007994	Sediment, Scripps Canyons, La Jolla	Antibacterial activity	Manam et al., 2005
199~200	<i>Streptomyces</i> sp. M045	Sediment, Jiaozhou Bay, China	Cytotoxicity	Li et al., 2005
201~203	<i>Streptomyces</i> sp. NPS008187	Sediment, Alaska	Cytotoxicity	Macherla et al., 2005
204	<i>Streptomyces</i> sp. B8005	Sediment, Gulf of Mexico	Antibacterial activity	Koek et al., 2005
205~207	<i>Streptomyces</i> sp. CNQ766	Sediment, Island of Guam	/	Cho et al., 2006a, 2006b
208~211	<i>Streptomyces</i> sp. CNQ-085	Sediment, San Diego, CA.	208: Cytotoxicity 208-209: Antibacterial	Asolkar et al., 2006
212~214	<i>Streptomyces</i> sp. QD518	Sediment, Jiaozhou Bay, China	212: Cytotoxicity, Antibacterial activity	Wu et al., 2006
215~217	<i>Streptomyces</i> sp. CNQ-583	Sediment, Island of Guam	/	Bugni et al., 2006
218	<i>Streptomyces</i> sp. B1751	Sediment, Northeast of the Shetland Islands (59°00'N, 00°00'W)	/	Yao et al., 2006
219	<i>Streptomyces</i> sp. KORDI-3238	Sediment, Western Pacific Ocean	Cytotoxicity	Jeong et al., 2006
220~221	<i>Streptomyces</i> sp. B8000	Sediment, Gulf of Mexico	220: Antibacterial activity	Pounale et al., 2006
222	<i>Streptomyces</i> sp. V5	rhizosphere soil of mangrove root, South China Sea	/	陈光英等, 2007
223~231	<i>Streptomyces</i> sp. M491	Sediment Jiaozhou Bay, China	226: Cytotoxicity	Wu et al., 2007; Ding et al., 2009
232~233	<i>Streptomyces</i> sp. CNH990	Sediment, Cabo San Lucas, Mexico.	Cytotoxicity	Martin et al., 2007
234~236	<i>Streptomyces</i> sp. CNQ-593	Sediment, Island of Guam	Cytotoxicity	Miller et al., 2007
237~242	<i>Streptomyces</i> sp. CNQ-418	Sediment, La Jolla, CA	Cytotoxicity	Hughes et al., 2008, 2010
243~244	<i>Streptomyces</i> sp. MS239	Sediment, Tokushima, Japan.	243: Antibacterial activity	Motohashi et al., 2008
245	<i>Streptomyces</i> sp. Merv8102	Sediment, Mediterranean Sea, Egypt	Antibacterial activity	El-Gendy et al., 2008
246	<i>Streptomyces</i> sp. H668	Sediment, Hawaiian	Antimalarial activity	Na et al., 2008
247~248	<i>Streptomyces</i> sp. Act8015	Sediment, Gulf of Mexico	/	Shaaban et al., 2008
249~251	<i>Streptomyces</i> sp. DSS-18	Sediment, west Pacific	Cytotoxicity	Li et al., 2008
252~257	<i>Streptomyces</i> CNQ-617	Sediment, La Jolla	252-253, 255: Cytotoxicity 256: Antibacterial activity	Boonlappradab et al., 2008; Salem et al., 2014

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化合物	来源菌株	环境来源	生物活性	参考文献
258~263	<i>Streptomyces</i> sp. NPS-643	Sediment, Kochi Harbor, Japan	Cytotoxicity	Sato et al., 2009
264~265	<i>Streptomyces</i> sp. CNR-698	Sediment, Bahamas Islands	Cytotoxicity	Hughes et al., 2009
266~275	<i>Streptomyces</i> sp. CNQ431	Sediment, La Jolla, CA	anti-inflammatory;	Strangman et al., 2009
276	<i>Streptomyces</i> sp. NTK 227	Sediment, Atlantic	anti-protein-tyrosin phosphatase B	Hohmann et al., 2009
277~280	<i>Streptomyces</i> sp. Mei37	Sediment, Jade Bay, German	Cytotoxicity	Hawas et al., 2009
281	<i>Streptomyces</i> sp. MDG-04-17-069	Sediment, the east coast, Madagascar	Cytotoxicity	Pérez et al., 2009
282~283	<i>Streptomyces</i> sp. CMB-MQ030	Sediment, Figi island	/	Raju et al., 2009
284~286	<i>Streptomyces</i> sp. NPS554	Sediment, Miyazaki Harbor, Japan	284-285 : phosphodiesterase inhibition; 286 : Cytotoxicity	Iwata et al., 2009; Igarashi et al., 2013
287~288	<i>Streptomyces</i> sp. 307-9	Sediment, Salt Cay, U.S. Virgin Islands	Antibacterial activity	Carlson et al., 2009
289	<i>S. xiamenensis</i> 318	Sediment, mangrove, Fujian, China	lung excessive fibrotic inhibition	Xu et al., 2012
290~291	<i>S. tumescens</i> YM23-260	Sediment, Palau	290 : the insulin-degrading enzyme promoter	Motohashi et al., 2010b
292	<i>Streptomyces</i> sp. MW064	Sediment, Samut Sakhon, Thailand.	Cytotoxicity	Igarashi et al., 2010
293~296	<i>Streptomyces</i> sp. CMB-M0406	Sediment, Heron island, Australai	296 : Antibacterial activity	Raju et al., 2010a; Sugiyama et al., 2014
297~299	<i>Streptomyces</i> sp. CMB-M0423	Sediment Heron Island, Queensland	Antibacterial activity	Raju et al., 2010b
300~304	<i>Streptomycetaceae</i> CNQ509	Sediment, California	300, 302-303 : Cytotoxicity	Kwon et al., 2010
305	<i>Streptomyces</i> sp. B6219	mangrove Sediment, Galapagos	/	Abdalla et al., 2010
306~309	<i>S. albus</i> POR-04-15-053	Sediment, Punta Sagres, Portugal	306,309 : Cytotoxicity 307 : subnanomolar activity	Schleissner et al., 2011
310~311	<i>S. antibioticus</i> H74-18	Sediment, South China Sea	Antibacterial activity	Xu et al., 2011
312~315	<i>Streptomyces</i> CNQ-027	Sediment, San Diego, CA.	315 : Cytotoxicity	Nam et al., 2011; Nam et al., 2013
316~319	<i>Streptomyces</i> sp. RJA2928	sediment, Papua New Guinea	316 : Cytotoxicity; 317 : SETD8 inhibition activity	Williams et al., 2011, 2013, 2016
320~322	<i>Streptomyces</i> sp. CNS-575	Sediment, Figi island	Antibacterial activity	Sun et al., 2011

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化合物	来源菌株	环境来源	生物活性	参考文献
323-331	<i>Streptomyces</i> sp. 211726	rhizosphere soil of <i>Heritiera globose</i> , Wenchang, China	Antibacterial activity, Cytotoxicity	Yuan et al., 2011, 2013
332	<i>Streptomyces</i> sp. No. 061316	rhizosphere soil, Wenchang, China	/	Chen et al., 2011
333-340	<i>Streptomyces</i> sp. CNH-189	Sediment, Oceanside, California	338-340 : Antibacterial activity	Wilson et al., 2011; Kaysser et al., 2012; Le et al., 2016
341	<i>Streptomyces</i> NTK 935	Sediment, Canary Islands, Atlantic Ocean	glycogen synthase kinase 3 β Inhibition	Nachtigall et al., 2011
342	<i>Streptomyces</i> species B8112	Sediment, Gulf of Mexico	Antibacterial, Cytotoxicity	Shaaban et al., 2011
343	<i>Streptomyces</i> sp. MST-MA568	Sediment, Glenelg River, South Australia	/	Fremlin et al., 2011
344-346	<i>Streptomyces</i> sp. CNQ-301	Sediment, La Jolla, California	/	Fukuda et al., 2011
347-348	<i>Streptomyces</i> sp. WuXin	Sediment, Bohai Bay of China	Cytotoxicity	Li et al., 2011
349-351	<i>Streptomyces</i> sp. NPS853	Sediment, Usa Bay, Kochi, Japan	Cytotoxicity	Sato et al., 2011
352	<i>Streptomyces</i> sp. W007	Sediment, Jiaozhou Bay, China	Cytotoxicity	Zhang et al., 2011
353	<i>S. bacillaris</i> SNB-019	Sediment, Galveston Bay, Texas	/	Hu and MacMillan, 2012
354-356	<i>S. fradiae</i> 007M135	Sediment, Jiaozhou Bay, China	354 : Cytotoxicity	Fu et al., 2012b
357-361	<i>S. lusitanus</i> SCSIO LR32	Sediment, South China Sea	Cytotoxicity	Huang et al., 2012
362	<i>Streptomyces</i> sp. CMB-M0392	Sediment, Heron Island, Queensland	Antibacterial activity	Raju et al., 2012
363-364	<i>Streptomyces</i> sp. CNQ343	Sediment, North Cat Cay, Bahamas	363 : Antibacterial activity	Kim et al., 2012
365-379	<i>Streptomyces</i> sp. SCSIO 03032	Sediment, Bay of Bengal	366-368, 370 : Cytotoxicity	Zhang et al., 2012, 2014a, 2014b; Chen et al., 2014
380	<i>Streptomyces</i> sp. LB173	Sediment, Baltic Sea, Germany	Acetylcholinesterase inhibition	Ohlendorf et al., 2012
381	<i>Streptomyces</i> sp. M268	Sediment, Jiaozhou Bay, China	/	Xie et al., 2012
382-385	<i>Streptomyces</i> sp. SCSIO 02999	Sediment, South China Sea	Antibacterial activity	Zhang et al., 2012
386	<i>Streptomyces</i> sp. CP13-10	Sediment, San Francisco Bay, CA	Antibacterial activity; human SIRT2 inhibition activity	Amagata et al., 2012
387	<i>S. variabilis</i> SNA-020	Sediment, Bahamas	Cytotoxicity	Pan et al., 2012
388	<i>Streptomyces</i> sp. TP-A0879	Sediment, Otsuchi Bay, Iwate, Japan	Cytotoxicity	Igarashi et al., 2012

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化合物	来源菌株	环境来源	生物活性	参考文献
389-390	<i>Streptomyces</i> sp. FMA	Sediment, Sanya, China	390 : Cytotoxicity	Fu et al., 2012a
391-393	<i>Streptomyces</i> sp. CNT-179	Sediment, Bahamas	/	Lane et al., 2013
394-396	<i>S. antibioticus</i> PTZ0016	Sediment, Unknown place	Antibacterial activity	Lian and Zhang, 2013
397-398	<i>S. nitrosporeus</i> QQT1424	Sediment, Arctic Chukchi Sea	Anti- H1N1 activity	Yang et al., 2013a
399-404	<i>S. niveus</i> SCSIO 3406	Sediment, South China Sea	399, 401 : Cytotoxicity 399, 401-402 : Antibacterial	Song et al., 2013
405	<i>Streptomyces</i> sp. CNH-287	Sediment, San Diego, CA.	Cytotoxicity	Alvarez-Mico et al., 2013
406-410	<i>Streptomyces</i> sp. FXJ7.328	Sediment, Dalian, China	407 : Anti- H1N1 activity	Wang et al., 2013
411	<i>Streptomyces</i> sp. MS100061	Sediment, South China Sea	Antibacterial activity	Chen et al., 2013
412	<i>Streptomyces</i> sp. SNJ013	Sediment, jeju	/	Um et al., 2013a
413-417	<i>Streptomyces</i> sp. CNQ-329	Sediment, San Diego, CA.	413, 416-417 : Cytotoxicity 413-414 : Antibacterial	Cheng et al., 2013
418	<i>Streptomyces</i> sp. CNH-070	Sediment, Encinitas, California	Cytotoxicity	Cheng et al., 2013
419-421	<i>Streptomyces</i> sp. SCSIO 10428	Sediment, Beihai, Guangxi, China	Antibacterial activity	Wu et al., 2013a
422	<i>Streptomyces</i> sp. CNH365	Sediment, Santa Barbara, CA	Antibacterial activity	Jang et al., 2013
423-427	<i>Streptomyces</i> sp. JAMM992	Sediment, Kinko Bay	Cathepsin B inhibition activity	Takada et al., 2013
428	<i>Streptomyces</i> sp. SCSIO 03219	Sediment, South China Sea	/	Zhang et al., 2013
429	<i>Streptomyces</i> sp. Ege25	Sediment, MarsaMatruhcity, Egypt	Cytotoxicity	Abdelfattah et al., 2013
430-431	<i>Streptomyces</i> sp. CNT-372	Sediment, Figi island	Antimalarial activity	Zafir et al., 2013
432-433	<i>Streptomyces</i> sp. 7-145	Sediment, Heishijiao Bay, China,	Antibacterial activity	Wu et al., 2013b
434-435	<i>Streptomyces</i> sp. SNJ042	Sediment, jeju Island	Antibacterial activity 435 : Cytotoxicity	Um et al., 2013b
436-439	<i>Streptomyces</i> sp. SNJ210	Sediment, jeju Island	436 : Cytotoxicity	Bae et al., 2013
440-441	<i>Streptomyces</i> sp. 12A35	Sediment, South China Sea	Antibacterial activity	Pan et al., 2013
442	<i>Streptomyces</i> sp. SCSIO 10355	Sediment, Indian Ocean	Inhibition of lipopolysaccharide-induced TNF α	Yang et al., 2013b

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化合物	来源菌株	环境来源	生物活性	参考文献
443	<i>Streptomyces</i> sp. CMBM0244	Sediment, Molle Island, Queensland	Antibacterial, Antimalarial	Raju et al., 2014
444~449	<i>S. drozdowiczii</i> SCSIO 10141	Sediment, South China Sea	Antibacterial activity	Zhou et al., 2014
450~456	<i>S. nitrosporeus</i> YBH10-5	Sediment, Arctic Chukchi Sea	/	Liu et al., 2014
457~459	<i>S. scopuliridis</i> SCSIO ZJ46	Sediment, South China Sea	457: Antibacterial activity	Song et al., 2014
460~464	<i>Streptomyces</i> sp. LZ35DgdmAI	Sediment, Jimei, Xiamen, China	460: Topo I inhibition 462: Topo IIa inhibition	Deng et al., 2014
465~468	<i>Streptomyces</i> sp. CNQ525	Sediment, La Jolla, CA	Cytotoxicity	Farnaes et al., 2014
469~470	<i>Streptomyces</i> sp. ACT232	Sediment, Sagami-Bay, Japan	Pepsin Inhibition activity	Sun et al., 2014a
471~473	<i>Streptomyces</i> sp. SNE-011	Sediment, South Carolina	Cytotoxicity	Fu et al., 2014
474~475	<i>Streptomyces</i> sp. CMDD10D111	Sediment, Anmyeon Island, Korea	nitric oxide Inhibition	Lee et al., 2014
476~477	<i>Streptomyces</i> sp. ART5	Sediment, East Siberian, Arctic Ocean	476: Inhibition of <i>Candida albicans</i> isocitrate lyase 477: Cytotoxicity	Moon et al., 2014
478~480	<i>Streptomyces</i> sp. SMC72	Sediment, jeju Island	<i>Candida albicans</i> isocitrate lyase Inhibition	Ko et al., 2014
481~484	<i>Streptomyces</i> sp. SNM55	Sediment, Buan, Korea	Antibacterial activity	Bae et al., 2015a, 2015b
485~487	<i>Streptomyces</i> sp. IFM 11440	Sediment, Choshi City, Japan	486: Ngn2 promoter activity	Arai et al., 2015
488~489	<i>Streptomyces</i> sp. SCSIO 11594	Sediment, South China Sea	489: Cytotoxicity	Song et al., 2015
490~493	<i>Streptomyces</i> sp. SSC21	Sediment, Suncheon Bay, Korea	Insulin Sensitivity activity	Shin et al., 2015
494	<i>Streptomyces</i> sp. SCSIO 04496	Sediment, South China Sea	/	Luo et al., 2016
495~496	<i>S. rochei</i> 06CM016	Sediment, Kaş, Turkey	Antibacterial activity	Aksoy et al., 2016
497~499	<i>Streptomyces</i> sp. IFM11490	Sediment, Chiba, Japan	497, 499: Cytotoxicity	Yixizhuoma et al., 2015
500~507	<i>Streptomyces</i> sp. SNB-048	Sediment, Bahamas	/	Fu et al., 2016
508	<i>Streptomyces</i> sp. CHQ-64	Mangrove soil, Guangdong, China	Cytotoxicity	Che et al., 2016
509~511	<i>Streptomyces</i> sp. 10A085	Sediment	Acetylcholinesterase inhibition	Kim et al., 2014
512~516	<i>Streptomyces</i> sp. 182SMLY	Sediment, East China Sea	512-513: Cytotoxicity	Liang et al., 2016a, 2016b

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化合物	来源菌株	环境来源	生物活性	参考文献
517~521	<i>Streptomyces</i> sp. SNM31	Sediment, Buan, Korea	quinone reductase induction	Bae et al., 2016
522~523	<i>Streptomyces</i> sp. CNP975	Sediment, La Jolla, USA	cyclooxygenase inhibition	Hassan et al., 2016
524~526	<i>S. anandii</i> H41-59	Sediment, South China Sea	526 : Cytotoxicity	Zhang et al., 2016
527	<i>Streptomyces</i> sp. Z00045	Seawater, East China Sea	/	Xu et al., 2013
528~530	<i>Streptomyces</i> sp. F001	Seawater, Unknown place	528 : Cytotoxicity	Mullowney et al., 2014
531~535	<i>Streptomyces</i> sp. TPU1236A	Seawater, Okinawa, Japan	531 : Antibacterial activity	Bu et al., 2014
536~538	<i>S. olivaceus</i> FXJ8.012Δ1741)	Seawater, South Atlantic Oceans	/	Liu et al., 2015
539~544	<i>Streptomyces</i> GWS-BW-H5	Unknown sample	/	Dickschat et al., 2005
545	<i>Streptomyces</i> sp. 0616208	Unknown source	Cytotoxicity	Xie et al., 2006
546~547	<i>Streptomyces</i> sp. CNS284	Unknown source	TNF- α -induced NF κ B, LPS-induced nitric oxide	Kondratyuk et al., 2012

注: /表示没有测到生物活性

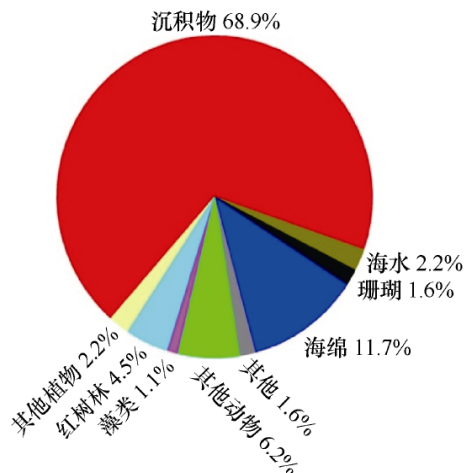


图 11 海洋链霉菌天然产物的来源
Fig.11 Origin categories of marine-derived *Streptomyces* actinomycetes MNPs

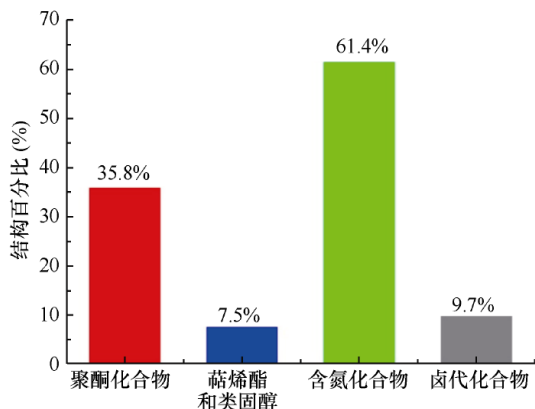


图 12 海洋链霉菌天然产物的结构分类
Fig.12 The main structure types of marine-derived *Streptomyces* actinomycetes MNPs

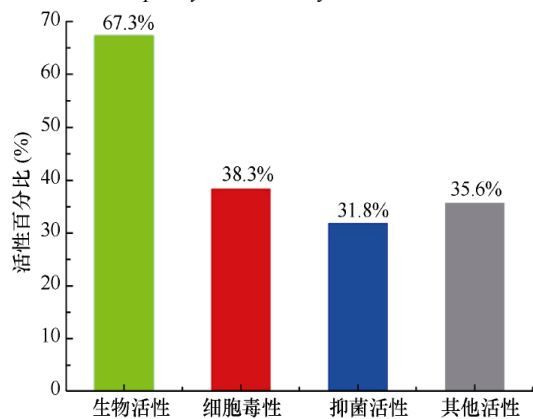


图 13 海洋链霉菌天然产物的活性分类
Fig.13 Bioactive categories of marine-derived *Streptomyces* actinomycetes MNPs

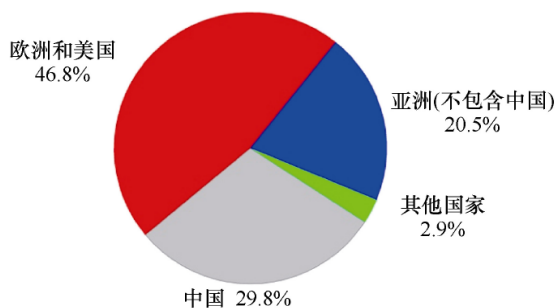


图 14 海洋链霉菌天然产物的主要发现者国别
Fig.14 Country categories of the main discoverers on *Streptomyces* MNPs

(6) 我国学者在 63 篇学术文章中贡献了 163 个海洋链霉菌 NPs, 在天然产物化学类、有机化学类和海洋药物类的主流杂志, 如 *J Nat Prod*、*Org Lett*、*J Org Chem* 和 *Mar Drugs* 的学术文章分别有 11 篇、7 篇、1 篇和 13 篇, 占其文章总数的 17.5%、11.1%、1.6%和 20.6% (图 15)。

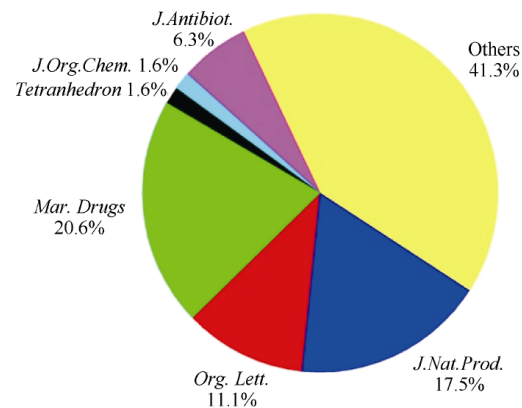


图 15 中国学者发表论文的期刊分类
Fig.15 Journal categories of Chinese scholars for publishing *Streptomyces* MNPs

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New Natural Products From the Marine-Derived *Streptomyces* Actinobacteria

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Abstract Marine-derived *Streptomyces* were the chief source of the bioactive marine natural products (MNPs) from marine microbial origin owing to their unique physiological and metabolic functions. According to statistic results for MNPs from 2010 to 2013, marine-derived *Streptomyces* attributed to 60% MNPs sourced from marine-derived actinobacteria. This paper reviews the sources, structures and bioactivities of the 547 new MNPs of *Streptomyces* origin in 40 years from 1976 to June 2016. These MNPs have diverse structures including alkaloids, polyketides, sterols and terpenoids, and so on. Nitrogen compounds are the major structural types making up 61% MNPs from *Streptomyces*. And 67% MNPs sourced from *Streptomyces* showed bioactivities such as cytotoxicity, antimicrobial activity, antimalaric and insecticidal activity.

Key words marine-derived actinobacteria; *Streptomyces* sp.; natural products; sources; chemical structures; bioactivities