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·综 述·

刘璞 兰州大学生命科学学院副教授。近年一直从事利用微生物资源来减除环境污染物如重金属、抗生素等对生物的危害的机理与应用研究。已在 *Journal of Hazardous Materials*、*Nutrients* 等期刊上发表相关 SCI 论文 20 余篇，申请国内发明专利 3 项。本课题组所属的环境微生物研究团队结合近年研究成果，提出了应对环境污染物的“肠道修复”策略，获得了领域内专家的认可。

环境抗生素污染的微生物修复进展

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摘 要: 近年来随着抗生素在畜牧业、水产养殖业以及医疗行业的广泛应用，大量抗生素通过排泄物进入环境，导致我国大面积水体及土壤环境中抗生素残留量急剧增高。环境中不同种类的抗生素的残留导致微生物种群结构失衡，对生态环境及人类造成极大危害。因此，解决抗生素残留问题是 21 世纪新型环境污染物领域的一个重要课题。已有研究显示，一些微生物能够以抗生素为碳源生存，可用于降解环境中残留抗生素，但人们对微生物降解抗生素的降解机制了解较少。文中概括了近十年来抗生素降解菌株和菌群对抗生素的去除情况，以及应用微生物菌群处理抗生素残留的技术方法，同时对未来利用微生物修复法减少环境中抗生素残留进行了展望。

关键词: 抗生素，生物降解，菌株，微生物群落，合成生物学

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Progress in microbial remediation of antibiotic-residue contaminated environment

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Abstract: In recent years, antibiotics have been widely used in animal husbandry, aquaculture and the medication in China. Many antibiotics are discharged into the environment, resulting in dramatic increase of antibiotic residues in domestic water and soil. Residues of different antibiotics in the environment change the microbial structure, which is extremely harmful to the ecological environment and humans. Therefore, remediation of antibiotic contamination is significantly important. Studies have shown that some microorganisms can degrade and utilize antibiotics, and thus have good application prospects on bioremediation of antibiotic contamination. However, little is known about the microbial degradation mechanism of antibiotics. This article summarizes the removal of antibiotics by antibiotic-degrading strains and bacterial flora in recent ten years, and the methods of using microbial flora to treat antibiotic residues. The future prospect of using microbial remediation to reduce antibiotic residues in the environment has also been discussed.

Keywords: antibiotics, biodegradation, strains, microbial communities, synthetic biology

自 1928 年弗莱明发现青霉素后，抗生素作为一种新的应对病原体感染的方式被广泛应用于医学、畜牧、水产养殖等领域[1-2]。抗生素是具有抗菌活性的天然、合成和半合成化合物，能对其他活性细胞的发育产生干扰作用，主要包括磺胺类、四环素类、β-内酰胺类、氟喹诺酮类、大环内脂类等。中国是世界上使用抗生素最频繁的国家之一，调查显示，2013 年我国抗生素的使用量达到 16 万 t，其中 52%用于畜牧业；2018 年，我国约 70%的住院病人和 20%的门诊病人使用抗生素类药物，约为发达国家使用率的两倍。抗生素在人类疾病治疗和畜禽生产等方面作出巨大贡献的同时也带来了新的问题。有数据表明，2001 年至 2005 年间，约有 60 万名患者死于抗生素滥用[3]。研究还发现，动物体摄入的磺胺类药物中约有 50%不经修饰直接排放至水体和土壤环境中，进而对人类和生态系统产生潜在的威胁[4]，例如导致多种耐药致病菌的出现、抗生素抗性基因的扩散等[5-6]。因此，抗生素广泛使用带来的环境污染问题已成为新型有机污染物领域的重要课题。

近年来，研究者对去除环境中抗生素残留的问题已进行了大量的研究，目前已将理化方法、微生物降解法应用于环境中抗生素的去除。理化方法如活性炭吸附法、低温等离子技术、土壤渗滤系统法和超声降解法等，主要用于去除环境中的有机污染物，在抗生素去除方面的应用存在成本较高、去除效率低的问题[7]。微生物降解法作为一种去除环境抗生素残留的生物方法，具有成本低、效能高以及环境污染小等特点，是处理抗生素污染的有效途径之一[8]。本文对近年来抗生素降解菌株和菌群及其在去除环境中抗生素残留方面的应用进行了系统综述，并对部分抗生素的微生物降解机制进行总结，为今后抗生素的微生物修复研究提供参考。

1 降解抗生素的菌株、降解途径和应用现状

1.1 降解抗生素的菌株

1.1.1 降解抗生素的细菌

抗生素的生物降解以微生物代谢为主。近年来通过筛选、富集和驯化等方式分离获得了许多具有抗生素降解能力的细菌菌株 (表 1)，这些细菌参与分解的抗生素包括磺胺类 (Sulfonamide antibiotics,

SAs)、四环素类 (Tetracycline antibiotics, TCs)、氟喹诺酮类 (Fluoroquinolones, FQ)、大环内脂类 (Macrolides antibiotics, MA)、β-内酰胺类和多肽等五类，其中以 SAs 和 TCs 为主，可能与其在环境中的残留量有关[15,31]。获得的具有抗生素降解能力的细菌来自无色杆菌属、产碱杆菌属、微杆菌属、氨氧化细菌、苍白杆菌属、戈登式菌属、葡萄球菌属、鞘氨醇菌属、栖热菌属、拉乌尔菌属、伯克氏菌属、芽孢杆菌属和假单胞菌属等。这些细菌是土壤、污水中的常见菌株，80%属于厚壁菌门和变形菌门，少部分来自栖热菌门、拟杆菌门、放线菌门和浮霉菌门等。

表 1　近五年文献中的抗生素特异性降解细菌

Table 1　Antibiotic-degrading bacterial strains reported in recent 5 years

Antibiotics		Bacterial species	Concentration (mg/L)	Removal rate (%)	Sources	References
Sulfonamides	Sulfamethoxazole	*Microbacterium* sp. BR1	100	40–60 (1 h)	Laboratory	[9]
	Sulfamethoxazole	*Nitrosomonas Ammonia oxidizing bacteria*	100	86 (70 d)	Domestic wastewater	[10]
	Sulfamethoxazole	*Achromobacter* sp. S-3	100	80 (25 d)	Aerobic sludge	[11]
	Sulfamethoxazole	*Achromobacter denitrificans* PR1	250	44 (16 h)	Activated sludge wastewater	[4]
	Sulfamethoxazole	*Pseudomonas mandelii* McBPA4	50	73 (15 d)	Laboratory	[12]
	Sulfamethoxazole	*Acinetobacter* sp. W1	5–240	100 (10 h)	Activated sludge	[13]
	Sulfadimidine	*Bacillus cereus* J2	50	100 (36 h)	Municipal sewage	[14]
	Sulfamethoxazole	*Ochrobactrum* sp. SMX-PM1-SA1	5	45.2 (8 d)	Wastewater	
	Sulfamethoxazole	*Labrys* sp. SMX-W11	5	62.2 (8 d)	Activated sludge	[15]
	Sulfamethoxazole	*Gordonia* sp. SMX-W2-SCD14	5	51.4 (8 d)	Pig manure	
Tetracyclines	Tetracycline	*Advenella* sp.4002	50	57.8 (5 d)	Factory	[16]
	Tetracycline	*Stenotrophomonas maltophilia* DT1	10	70 (3 d)	Factory sewage	[17]
	Tetracycline	*Raoultella* sp. XY-1	20	70.68 (8 d)	Pig farm sediment	[18]
	Tetracycline	*Sphingobium* sp. PHE3	20	40.1 (90 d)	Contaminated farmland soil	[19]
	Oxytetracycline	*Pseudomonas* sp. T4	100	26.88 (7 d)	Livestock manure	[20]
	Oxytetracycline	*Ochrobactrum* sp. KSS10	30	63.33 (4 d)	Municipal sludge	[21]
	Oxytetracycline	*Achromobacter* sp. TJ-2#	50	58.3 (3 d)	Contaminated soil	
	Tetracycline	*Achromobacter* sp. TJ-2#	50	63.9 (3 d)		[22]
	Aureomycin	*Achromobacter* sp. TJ-2#	50	65.5 (3 d)		
Fluoroquinolones	Ciprofloxacin	*Thermus thermophiles* C419	5	57 (5 d)	Pharmaceutical sludge	[23]
	Norfloxacin	*Staphylococcus caprae* NOR-36	5	92.6 (10 d)	Pharmaceutical wastewater	[24]
	Ofloxain	*Labrys portucalensis* F11	0.45	34.6 (28 d)	Fluorobenzene	[25]
	Ofloxain	*Rhodococcus* sp. FR1	0.45	39.3 (28 d)		
Beta-lactam	Cefalexin	*Pseudomonas* sp. CE21	10	46.7 (1 d)	Activated sludge	[26]
	Cefalexin	*Pseudomonas* sp. CE22	10	90 (1 d)	Activated sludge	[26]
	Cefalexin	*Shewanella* strain	5	47.9 (40)	EBPR SBR system	[27]
	Amoxicillin	*Shewanella* strain	10	90 (40)	EBPR SBR system	[27]
Macrolides	Tylosin	*Achromobacter*	50	96.08 (56 d)	Spinach soil	[28]
	Tylosin	*Burkholderia vietnamiensis*	50–500	99 (7 d)	Laboratory soil	[29]
Polypeptides	Polymyxins	*Baxillus licheniformis* DC-01	10	92.1 (1d)	Laboratory	[30]

目前，少部分有降解抗生素能力的细菌菌株被用于处理含抗生素的土壤或废水，均获得较高的去除率。如章程等从添加抗生素的菠菜土壤中筛选到对泰乐菌素去除率为 96.08%的无色杆菌，并将其应用于盆栽土壤中，发现泰乐菌素的残留率在 20%以下，表明无色杆菌可以有效促进土壤中泰乐菌素的去除[28]；Shao 等探究了不同条件下嗜铬菌 KSS10 对土霉素 (Oxytetracycline，OTC) 的生物降解特性，发现 KSS10 菌株在 96 h 内对 OTC 的转化率为 63.33%。随后对菌株 KSS10 进行生物固定化并联合生物膜反应器处理合成的水产养殖废水，OTC 的清除率约为 76.42%[21]。目前，利用抗生素特异性降解细菌菌株处理环境中残留抗生素的应用实例不多，其主要原因可能是在实际应用中存在耐药基因扩散的风险。

1.1.2 降解抗生素的真菌

真菌是抗生素的来源之一，同时一些真菌已被证明可以分解抗生素类药物。真菌对高浓度污染物的耐受性比细菌更强，能够降解多种难降解的化合物。另外，真菌细胞内含有细胞色素 P450 复合物，能够像哺乳动物细胞一样代谢抗生素，使其成为消除环境中残留抗生素的强有力候选者[2,46](表 2)。

大量的研究表明通过筛选降解抗生素的真菌来去除环境中残留的抗生素是可行的。卿纯等探究了黄孢原毛平革菌应用于四环素 (Tetracycline，TC) 模拟废水，发现在 72 h 内该菌株对 10 mg/L 的 TC 去除率高达 80%[40]；Copete-Pertuz 等将从哥伦比亚麦德林山谷中分离得到的小光壳属真菌 *Leptosphaerulia* sp.用于处理实验规模的医疗废水，第 6 天未检测到抗生素的存在，且降解产物无毒害，无抗菌效果[41]；崔辉将曲霉属真菌 Y-7 接种到含有 OTC (50 mg/kg) 的土壤中，对 OTC 的降解率可达到 30.63%[39]；Aydin 发现分离自活性污泥中的真菌组合变色栓菌和烟管菌对红霉素 (Erythromycin，E)、磺胺甲恶唑(Sulfamethoxazole，SMX) 和 TC 组成的混合抗生素的降解效率在 85%–94%之间[37]；Lucas 等将变色栓菌 ATCC42530 用于处理废水，对 7 种不同类型 (SAs、TCs 和 FQ 等) 的 47 种抗生素的去除率达到 77%，远高于传统的处理方法[47]。

表 2 近十年文献中的抗生素特异性降解真菌

Table 2 Antibiotic-degrading fungi reported in recent 10 years

Antibiotics		Fungus	Concentration (mg/L)	Degradation enzyme	Removal rate (%)	References
Sulfonamides	Sulfamethazine	*Trametes versicolor* ATCC42530	9	Lac, P450	100 (20 h)	[32]
	Sulfapyridine	*Trametes versicolor*	10	Lac, P450	100 (2 d)	[33]
	Sulfathiazole	*Trametes versicolor*	10	Lac, P450	100 (2 d)	[33]
	Sulfamethazine	*Phanerochaete chrysosporium*	10–30	Lac	53 (1 d)	[34]
	Sulfadiazine	*Fusarium solani* KS256	1.5	——	18.53 (7 d)	[35]
	Sulfamethoxazole	*Phanerochaete Chrysosporium*	10	Lac, P450, Mnp	100 (2 d)	[36]
	Sulfamethoxazole	*Pycnoporus sanguineus*	10	Lac, P450, Mnp	85 (30 d)	[36]
	Sulfamethoxazole	*Trametes versicolor* ATCC42530	10	——	94 (30 d)	[37]
	Sulfamethoxazole	*Bjerkandera adusta* ATCC28314	10	——	94 (30 d)	[37]

待续

续表 2

Tetracyclines	Tetracycline	*Phanerochaete chrysosporium*	50	Mnp	72.5 (4 h)	[38]
	Oxytetracycline	*Phanerochaete chrysosporium*	50	Mnp	84.3 (4 h)	[38]
	Oxytetracycline	*Aspergillus* sp. Y7	200	——	31.86 (7 d)	[39]
	Tetracycline	*Phanerochaete chrysosporium*	10	Lip, Mnp	80 (3 d)	[40]
	Tetracycline	*Trametes versicolor* ATCC 42530	2	——	92 (30 d)	[41]
	Tetracycline	*Bjerkandera adusta* ATCC 28314	2	——	92 (30 d)	[41]
	Oxytetracycline	*Trichoderma Harzianum*	250	——	92 (21 d)	[42]
	Oxytetracycline	*Trichoderma deliquescens*	250	——	85 (21 d)	[42]
	Oxytetracycline	*Penicillium crustosum*	250	——	83 (21 d)	[42]
	Oxytetracycline	*Rhodotorula mucilaginosa*	250	——	73 (21 d)	[42]
	Oxytetracycline	*Talaromyces atroroseus*	250	——	72 (21 d)	[42]
	Oxytetracycline	*Penicillium janthinellum* KS272	1.5	——	40.29 (7 d)	[35]
Fluoroquinolones	Ciprofloxacin	*Phanerochaete chrysosporium*	2	Lac, P450	90 (7 d)	[43]
	Norfloxacin	*Phanerochaete chrysosporium*	2	Lac, P450	90 (7 d)	[43]
	Norfloxacin	*Irpex lacteus*	10	Mnp	100 (14 d)	[44]
	Norfloxacin	*Trametes versicolor*	10	Mnp	100 (14 d)	[44]
	Ofloxacin	*Irpex lacteus*	10	Mnp	100 (14 d)	[44]
	Ofloxacin	*Trametes versicolor*	10	Mnp	100 (14 d)	[44]
	Ciprofloxacin	*Irpex lacteus*	10	Mnp	100 (14 d)	[44]
	Ciprofloxacin	*Trametes versicolor*	10	Mnp	100 (14 d)	[44]
	Ciprofloxacin	*Phanerochaete chrysosporium*	10	Lac, P450	98 (2 d)	[36]
	Ciprofloxacin	*Pycnoporus sanguineus*	10	Lac, P450	98 (2 d)	[36]
	Norfloxacin	*Phanerochaete chrysosporium*	10	Lac, P450	97 (2 d)	[36]
	Norfloxacin	*Pycnoporus sanguineus*	10	Lac, P450	97 (2 d)	[36]
	Norfloxacin	*Penicillium janthinellum* KS272	1.5	——	10.49 (7 d)	[35]
Beta-lactam	Oxacillin	*Leptosphaerulina* sp.	16	Lac, Mnp, Lip	100 (6 d)	[41]
	Cloxacillin	*Leptosphaerulina* sp.	17.5	Lac, Mnp, Lip	100 (6 d)	[41]
	Dicloxacillin	*Leptosphaerulina* sp.	19	Lac, Mnp, Lip	100 (8 d)	[41]
	Cephadroxyl	*Leptosphaerulina* sp. CECT20913	15.2	Lac, Mnp	100 (15 d)	[45]
	Cephadroxyl	*Trametes versicolor* ATCC 42530	6	Lac, Mnp	100 (15 d)	[45]
Macrolipids	Erythromucin	*Bjerkandera adusta* ATCC28314	1.5	——	85 (30 d)	[28]

酵母作为一种单细胞真菌，在环境抗生素污染修复方面也具有潜在的价值。Selvi 等从制药废水中分离得到一株假丝酵母菌 *Candida* sp. SMN04，它可以利用头孢地尼 (250 mg/L) 作为唯一碳源生长，6 d 内的降解率达到 84%[48]；冯福鑫等发现，在适当的条件下酵母菌 XPY-10 在 7 d 内对初始浓度为 600 mg/L 的 TC 去除率为 83.63%[49]。以上的研究均说明酵母菌具有高效降解各类抗生素的能力。

菌株的抗生素降解能力受到抗生素种类、菌株类型、碳源、氮源、温度、废水组分等多种因素的影响。为促进抗生素降解菌在实际环境废水中的应用，需要关注以下几点：1) 不同抗生素的微生物降解率存在差异。2) 不同的菌株类型对不同的抗生素降解效果存在显著差异。3) 当环境中的抗生素浓度较低时，作为碳源不足以促进菌群生长，抗生素的降解效率将大大降低。如外加碳源可以有效增强无色杆菌的能量利用效率，提高对磺胺甲恶唑的降解能力[50]。4) 菌株在不同的温度条件下对抗生素的降解率具有显著差异[13]。Zheng 等长期监控发现，夏季抗生素降解率远高于冬季[51]。5) 废水中金属离子的存在会影响氨氧化菌等降解菌还原抗生素的能力[52]。6) 抗生素代谢的中间产物如果具有抑菌性会降低菌株的抗生素去除率[10,23]。7) 多株具有降解能力的菌株共培养可以增强对抗生素的降解[53]。

1.2 抗生素的微生物降解途径、基因和降解酶

1.2.1 抗生素的微生物降解途径

微生物对抗生素的降解过程比较复杂，不同种类的抗生素由于结构不同，降解途径存在显著的差异。总的来说，微生物对抗生素降解途径的主要反应包括：羟基化、乙酰化、硝基化、氧化作用、取代作用等。近年来，有关 SAs 和 TCs 的微生物降解机理的报道较多，我们选取了这两类中研究较为透彻的抗生素进行总结。

SMX 是 SAs 中最常用的抗生素之一。其降解主要涉及 3 个过程：1) 主链 S-N 键断裂；2) 异恶唑环裂解；3) 发生羟基化、乙酰化或硝基化修饰[54] (图 1)。但在有氧和厌氧条件下，SMX 的微生物降解产物存在差异。有氧条件下，SMX 作为代谢基质被菌株降解时，途径 A 产生中间产物 3-氨基-5-甲基异恶唑和 4-氨基苯磺酸盐或 4-苯胺，最终生成产物 1,2,4-三羟基苯与 3-氨基异恶唑；而途径 B 产生 3-氨基-5-甲基异恶唑和 4-苯胺，最终生成产物磺胺、苯胺及 3-氨基异恶唑[53] (图 1A, B)。最近研究显示，厌氧条件下，SMX 有两条降解通路：1) SMX 先发生羟基化作用，随后异恶唑环破裂；2) 降解菌先攻击异恶唑环，异恶唑环破裂后，形成一个不稳定的自由基阴离子 ($SMX^{\cdot-}$)，随后发生氢化作用 (图 1C) 最终形成 3-氨基异恶唑[32,55-56]，但是具体的反应步骤有待进一步研究。

OTCs 的微生物降解通路目前还不是十分明确，推测可能涉及取代反应、苯环破裂、氧化反应、去羟基化作用。图 2 表示了 OTC 的微生物降解过程：OTCs 首先发生了胺基化，形成 4-差向土霉素 (EOTC)；随后发生去羟基化反应形成 2-乙酰基-2-去酰胺土霉素 (ADOTC)，然后氧化形成两种不同构型的产物 α-apo-OTC 和 β-apo-OTC，最终氧化形成 3-羟基环己酮[57-58]。

1.2.2 基因和降解酶

目前，关于抗生素降解基因的研究主要来自抗生素的耐药菌，这些基因编码的降解酶包括氨基糖类修饰酶、β-内酰胺酶、大环内酯类灭活酶等[60]。Richen 报道了 SadA、SadB 与 SadC 基因参与了磺胺甲恶唑的生物降解过程，其中 SadA、SadB 基因编码单加氧酶，SadC 基因编码 FMN 还原酶，这些基因广泛存在于磺胺类的降解菌株中[61]。

近年分离获得的具有抗生素降解能力的真菌以白腐真菌为主，它依赖自身的非特异性酶系统来转化或矿化抗生素等有害的异源物质[38,62]。

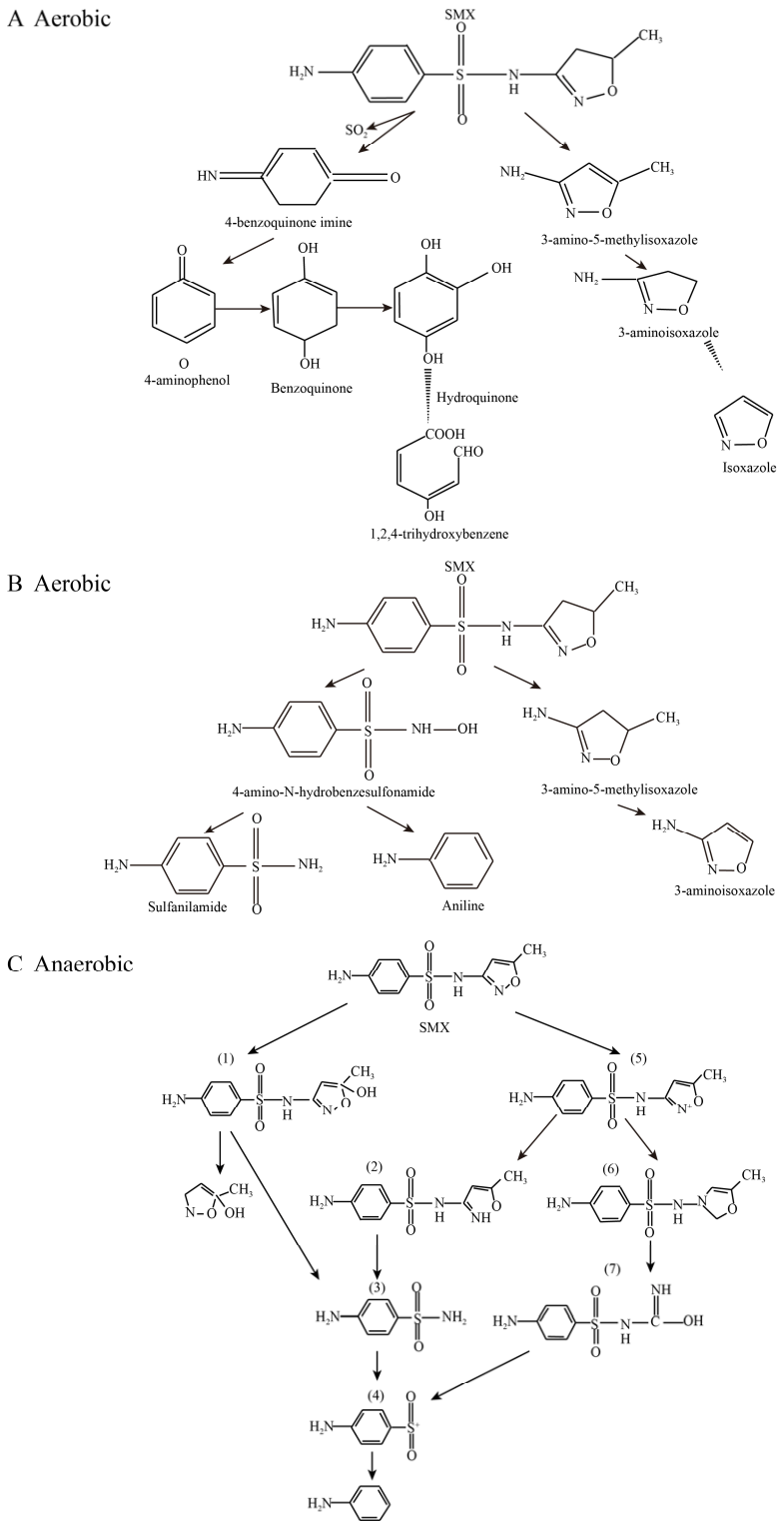

图 1　SMX 的微生物降解途径[53,55-56]

Fig. 1　Microbial degradation pathways of SMX[53,55-56]. (A–B) Biodegradation pathways of SMX under aerobic conditions. (C) Biodegradation pathway of SMX under anaerobic conditions.

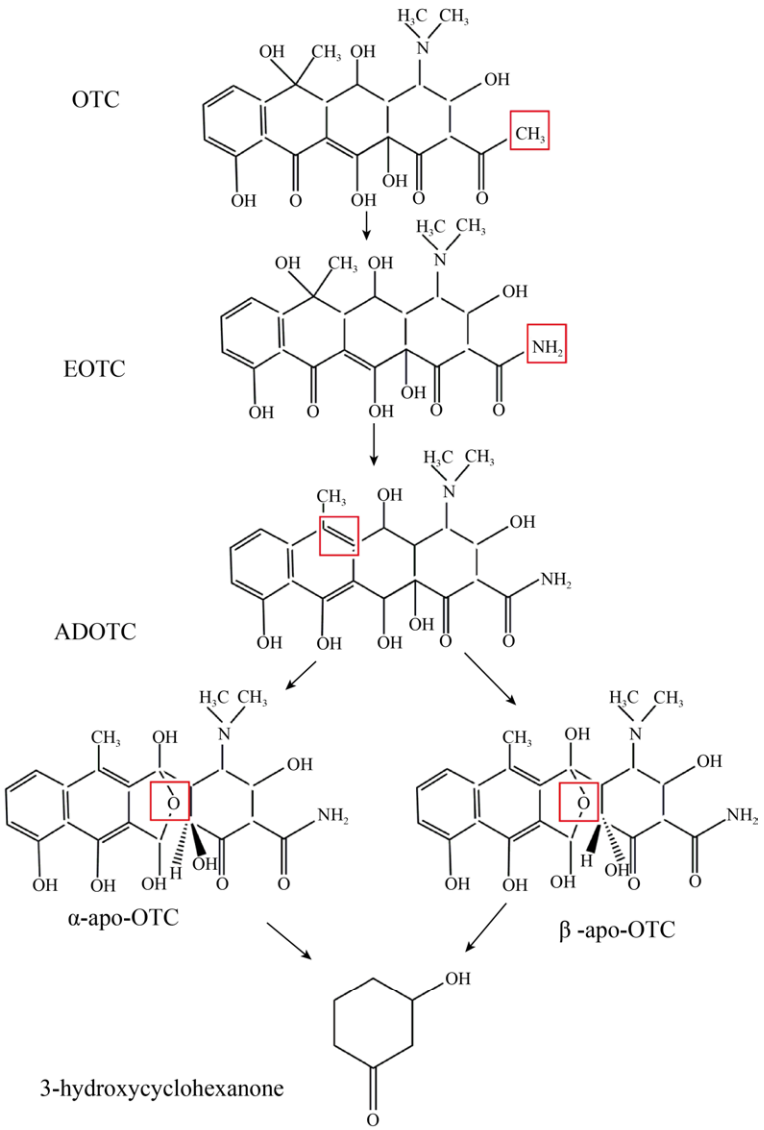

图 2　土霉素的微生物降解途径[48,59](土霉素通过胺基化、去羧基化和氧化反应，最终形成产物 3-羟基环己酮)

Fig. 2　Microbial degradation pathway of OTC. OTC can be converted into 3-hydroxycyclohexanone by amination, decarboxylation and oxidation[48,59].

该酶系统包括胞外的木质素修饰酶木质素过氧化物酶 (Lignin peroxidase, Lip)、锰过氧化物酶 (Manganese-dependent peroxidase, Mnp)、漆酶 (Laccase, Lac) 和胞内的细胞色素 P450 (Cytochrome P450)。其中，Lac 可以利用 O_2 作为电子受体氧化底物；Mnp 可以氧化 Mn^{2+}转变为 Mn^{3+}与有机酸螯合，随后发生氧化反应[46,62]。

由于木质素修饰酶是非特异性酶，可以降解环境中难降解的污染物，因此近年来有大量关于木质素修饰酶在抗生素修复方面的应用报道。Llorca 等应用漆酶降解四环素和红霉素，去除率达到了 78%[63]。Ding 等利用 SAs 和 TCs 容易被漆酶系统氧化、FQ 易被土壤吸附的特点，将漆酶与土壤结合起来，对 SAs、TCs 和 FQ 进行去除，其去除率在 7.5 d 后达到 100%[64]。Yang 等将漆酶固定化形成磁性交联酶聚合体，TC (100 mg/L) 的

去除率达到了 100%[65]。Marco-Urea 等在膜反应器中进行漆酶固定化，并联合介质丁香醛去除高达 38 种抗生素的混合物，24 h 后 32 种抗生素的降解率大于 50%。另有研究将漆酶与细菌进行共培养，提高了漆酶对抗生素的去除效率[66]。Lueangjaroenkit 等发现，在金属离子存在的条件下，Mnp 和 Lac 有效地灭活 TC、多西环素、阿莫西林和环丙沙星等抗生素[67]。

2 分解抗生素的微生物菌群及应用

2.1 分解抗生素的微生物菌群

抗生素降解菌群主要由变形菌门、拟杆菌门、酸杆菌门、放线菌门、疣微菌门、浮霉菌门的细菌组成。其中，以 β-变形菌门最为丰富，主要负责有机物和养分的去除；亚优势菌门是拟杆菌门、酸杆菌门和绿弯菌门。而真菌中子囊菌门最多，占 6%以上。抗生素的添加会影响微生物群落的结构组成，但降解不同种类抗生素的微生物群落的结构差异并不是十分明显[68]。Bai 等研究表明，抗生素加入污泥后，微生物群落的丰度显著下降，但多样性增加[69]。降解菌群的组成还受到地理位置、温度及氧气含量的影响。在预脱氮池的系统中，α-变形杆菌的丰度受温度影响，而 β-变形杆菌、放线菌和氯氧杆菌在微生物种群中的比例相对稳定。在厌氧条件下，硝化螺旋菌属、生丝微菌属、微丝菌属、甲烷丝菌属、亚硝化单胞菌属的丰度更高，相比于好氧环境，各菌属丰度的分布更加均匀，可能更有利于提高抗生素的降解能力[70-71]。

2.2 应用微生物菌群处理抗生素的方法

2.2.1 活性污泥法

活性污泥法 (Activated sludge process, ASP) 是国内外处理污水的常用方法。它的主要机制是，好氧细菌分泌胞外酶，将水中的胶质有机物分解为可溶解有机物。可溶解有机物通过渗透作用进入细菌细胞膜，诱导细胞内特异性基因的表达，随后被分解。同时细菌利用有机物分解释放的能量增殖，进一步加强有机物的降解。ASP 自 1914 年至今经历了漫长的发展历程，现如今已成功应用于抗生素废水的处理。

SAs 在活性污泥中的去除以降解为主吸附为辅。如 Jia 等利用硫酸盐还原菌污泥系统去除 SMX，发现 SMX 起初依赖污泥的快速吸附，随后菌株破坏异恶唑环降解 SMX[55]。ASP 对不同种类 SAs 的降解效果存在一定的差异。如 Yang 等研究发现，ASP 对 SMX、磺胺二甲氧基嘧啶和磺胺甲氧基嘧啶的降解率分别为 24%、30%和 19%，降解顺序为 SMX>磺胺二甲氧基>磺胺甲嗪[56,72]。

TCs 主要通过生物吸附的方式转移到污泥中，微生物降解的贡献极少[73]。其主要原因是 TCs 是两性化合物，极易与周围的环境发生反应，形成稳定的化合物，失去抑菌能力[74]。另一可能的原因是特异性降解菌属丰度低。如 Wang 等发现在原污泥中 TC 的优势降解菌属如希瓦氏菌、芽孢杆菌、假单胞菌、氨氧化菌等丰度低，降解能力弱。当以 TC 为唯一碳源时，这些菌属转变为优势菌属，TC 降解率显著提高[75]。因此，通过增加活性污泥中抗生素特异性降解菌属的比例，可以提高 ASP 中微生物群落对抗生素的去除能力。

FQ 在 ASP 的去除以吸附为主微生物降解为辅，高浓度的 FQ 对 ASP 的菌群会产生抑制作用。高温、好氧、优势菌株的丰度、硝化作用有助于增强菌群对 FQ 降解能力[60]。Wang 等发现，在有氧、高温条件下，通过硝化过程中的共代谢，显著提高了菌群的 FQ 去除率[76]。Jia 等发现厌氧污泥系统中含有对 FQ 高耐受性的脱硫杆菌属，能长期有效去除制药及医院废水中的 FQ[77]。另外，β-lactams 在 ASP 中的去除也以微生物为辅，高浓度的 β-lactams 会显著抑制微生物的降解能力。通常将 ASP 与 Fenton 氧化、微电解等非生物技术联

用提高 β-lactams 的去除率[78-79]。Chen 等将头孢菌素 C 与活性污泥共堆肥，头孢菌素 C 的降解率仅为 6.58%[80]。传统的 ASP 存在污泥生产量大、成本高、易膨胀等问题，使其实际应用受到一定的限制[60]。目前，已有不少研究将现代工艺与活性污泥法结合起来，在提高污染物降解率的同时，降低废水处理成本。如 Sodhi 采用膜生物反应器、厌氧消化池、与 CAS 反应器连接形成活性污泥改良版系统，促进污泥中微生物的富集，污泥产量减少了 72%[81]；Meerburg 等利用高速率活性污泥，增加了微生物群落的丰度，提高了污泥的质量，为各种污水类型的低容量活性污泥处理设施提供了一种可持续的实用选择[82]。

另外菌群、碳源、反应时间及温度也会影响 ASP 中抗生素的降解效率：1) 抗生素可作为降解菌株的碳源或氮源，当外加乙酸盐和硝酸铵进行共代谢时，抗生素的微生物降解率显著提高[83]；2) 菌群的丰度和种类会影响抗生素的去除率，其中不动杆菌和假单胞菌是污泥中磺胺降解的主要菌属，脱硫杆菌属是 FQ 的主要菌属[71]；3) 反应时间也会影响抗生素的去除效果，细菌对磺胺类抗生素的吸附是一个可逆的过程，当反应时间过长，SAs 会被重新释放出来；4) 温度影响活性污泥中菌群的生长，如 Huang 等发现 SMZ 的吸附速率随温度的升高而降低[11,51]；5) 污泥龄在 5–25 d 时，SMZ 的去除率也从 45%提高到 80%。

2.2.2 膜生物反应器法

膜生物反应器 (Membrane bioreactor，MBR) 是活性污泥处理与微滤或超滤技术相结合的产物。与传统活性污泥处理相比，MBR 具有出水水质好、污泥消耗低、占地面积小的特点[60]。近年来，还出现了将微滤或超滤等低压膜与活性污泥系统相结合形成的一种高保留率膜生物反应器。目前有 3 种高保留率膜生物反应器应用于抗生素废水的处理，即渗透膜生物反应器、膜蒸馏生物反应器和纳滤膜生物反应器，对抗生素具有良好的去除效果，但存在膜污染、膜消耗量大的问题[84-85]。

MBR 既包括好氧膜生物反应器，也包括厌氧膜生物反应器 (Anaerobic membrane bioreactors, AnMBRs)。AnMBRs 是近年来出现的一种处理抗生素废水的新技术。它在处理过程中将废水中的有机物转化为富含甲烷的沼气，并可以通过产生的沼气抵消废水处理过程中的能源需求，与传统的活性污泥和好氧膜生物反应器相比具有许多优点[86]。如 Huang 等在利用 AnMBR 系统处理含有 β-lactams 废水的过程中发现头孢曲松、头孢哌酮等抗生素的去除率达到了 50%[87]。另外，AnMBRs 膜在阻止抗生素和带有抗性基因的微生物从反应器逃逸到环境中起着重要作用。该系统不仅能降解抗生素，有效地控制细菌污染，而且能提高废水的能量回收，是一种很有前途的抗生素废水处理技术[88]。

随着近年来污水排放标准的提高，越来越多的污水处理厂开始对现有的 MBR 处理工艺进行改进。如 Karaolia 将 MBR 与太阳能芬顿法结合，氧化去除 SMX、红霉素和克拉霉素，与单独的 MBR 相比，克拉霉素的去除率显著提升[89]。Cheng 等研究发现将 MBRs 与生物膜载体 (如颗粒活性炭、海绵) 相结合可以降低膜污染，提高抗生素的去除率[90]。

MBR 的性能还受到盐度、菌群、温度等多种因素的影响。盐分积累会干扰 MBR 膜的生物性能，出现膜污染、微生物对抗生素的去除能力下降等问题[91]。耐盐菌群的增加会维护 MBR 的性能。Luo 等研究发现，在高盐度条件下，大部分菌属受到抑制，耐盐/嗜盐微生物与非嗜盐微生物的比例显著升高，MBR 的生物学性能随耐盐菌的增加缓慢恢复，因此可以通过增加耐盐菌或嗜盐菌的量来维持 MBR 的性能[85]。温度过高或过低对 MBR 的抗生素去除效率有显著性影响[92]。

2.2.3 堆肥法

堆肥法是一种将原生有机质转化为有价值的有机土壤的改良技术,它通过多种微生物的作用,将生物残体、粪便和药渣等进行矿质化、腐殖化和无害化,使得各种复杂的有机养分转化为可溶性养分和腐殖质,可作为去除动物粪便中抗生素的一种有效方法。堆肥法在 20 世纪初由英国农业学家霍华德提出,主要有好氧堆肥和厌氧堆肥两种类型,在不同类型抗生素的降解中均有应用。好氧堆肥是一种通过酶、微生物和氧气的作用降解有机物的过程[93]。厌氧堆肥则是一个发酵的过程,它利用畜禽粪便产生环境友好型能源 (沼气),主要由 4 个阶段组成,即水解、酸生成、乙酰生成和甲烷生成。

Shi 等在粪便中添加 4 种典型的抗生素进行好氧堆肥,20 d 内抗生素的去除率达到了 90%以上[94]。Inastrazysch 等研究发现厌氧发酵对 7 种磺胺类药物和甲氧苄啶均有去除效果,而且代谢物的抗菌活性显著降低[95];Spielmeyer 等发现通过半连续发酵,磺胺嘧啶、四环素和氯四环素的去除率在 14%–89%之间,并且抗生素的存在对甲烷产量没有抑制作用[96]。

堆肥法的抗生素清除率受到堆肥底物、温度等多种因素的影响。(1) 共堆肥有利于抗生素的清除[97]。Zhang 等将青霉素发酵菌渣与猪粪进行好氧共堆肥后,超过 99%的青霉素在堆肥 7 d 后被清除[97-98];Liu 等利用庆大霉素发酵残基和洛伐他汀发酵残基进行室内共堆肥,庆大霉素去除率在 90%以上[8]。(2) 温度、pH。Huang 等研究发现,堆肥的最佳 pH 值在 5.5–8.0 之间[99];Ma 等发现高温能有效促进堆肥发酵[100]。(3) 过少的曝气会导致厌氧环境,而过多的曝气会导致过早冷却,破坏了适宜的高温条件,从而影响分解速率[93,101]。

2.2.4 生物电化学系统

生物电化学系统 (Bioelectrochemical systems, BESs) 由微生物燃料电池 (MFCs) 和微生物电解细胞 (MECs) 两部分组成,是一种将微生物代谢和电化学氧化还原反应结合起来,利用电化学性微生物回收能量的装置,被认为是降解污染物的有效的替代方法,近年被应用到抗生素的降解中[102-103]。

大部分的 MFC 是由生物阳极和非生物阴极组成的。在非生物阴极中,通常铁氰化钾或氧作为电子受体;在生物阳极中,抗生素作为电子供体和碳源。产电菌和降解菌附着在阳极上,在细胞外聚合物中形成生物膜,负责降低可降解抗生素及其代谢物的电位,无需提供外源能量[102]。

目前,已有不少证据表明 BESs 系统对抗生素具有良好的去除效果。如 MFC 对磺胺嘧啶、SMX 等 SAs 降解率在 85%以上,对 TC 的降解率能达到 99%,对氯霉素也具有良好的去除效果[102,104]。与其他技术相比,BESs 具有以下优势:(1) 运行成本低[106];(2) 抗生素去除效果好[105-106];(3) 可以与其他技术如人工湿地联用,降解不同类型的抗生素,但它的降解能力也受到盐度、固相以及金属的影响[107-108]。

2.2.5 微藻的光解

藻类是一类结构类似于细菌的真核生物。微藻在水生环境中具有最多的生物量,对污染物的耐受性也高于细菌,并且具有良好的有机物去除能力[109]。微藻广泛应用于各种新型污染物废水的处理,近年也出现了利用微藻去除废水中抗生素的报道。如 Liu 等将铜绿微囊藻置于 50 μg/L–1 ng/L 螺旋霉素和阿莫西林水溶液中培养 7 d,降解了 12.5%–32.9%的螺旋霉素和 30.5%–33.6%的阿莫西林,表明蓝藻细胞具有一定的抗生素去除能力[110]。Hom-Diaz 等采用光藻反应器处理实际废水,可高效去除废水中的环丙沙星 (2 mg/L)[111]。Yu 等研究发现,在海藻处理 6 h 后,未处理的头孢噻啶

残留率为 96.93%，处理后的头孢噻啶的残留率仅为 7.35%[112]。有研究发现光照强度、CO_2 浓度有利于藻类生长和抗生素的去除[113]。微藻对抗生素的处理主要由 3 个步骤组成：1) 快速吸附，藻类具有较大的表面积和体积比，其细胞壁带有负电荷，因此能吸附大量的有机物；2) 缓慢的细胞壁传输进入微藻细胞；3) 光解作用，将光电子的光激发与微藻的光催化耦合，在抗生素光解过程中促进了光电子的传递[109]。

近年来，也有研究将微藻与活性污泥联用来处理抗生素废水。Guo 等利用藻类和活性污泥联合系统去除头孢菌素，14 d 内单活性污泥的去除率为 46.3%，联合去除效果达到了 97.91%[114]。

3 总结与展望

抗生素作为一类新型污染物，给水体、土壤造成的污染成为全球面临的重大环境问题。在自然环境中，生物降解是天然存在于生态系统中的有机物降解途径。相较于传统修复方法，其成本低、效能高、适用范围广，是一种具有前景的消除环境抗生素残留的生物修复法。目前，关于不同种类抗生素微生物代谢通路的研究已有大量文献报道。但现有研究主要集中于抗生素特异性降解菌株的筛选与降解产物的分析，对降解过程所涉及的基因及产物、降解机理的研究及特异性菌株的实际应用很少。为了能使微生物修复法得到更广泛的应用，今后的环境抗生素污染的微生物修复研究可以从以下方面开展：1) 探究在自然和实验条件下，抗生素特异性降解菌株生存和降解能力的差异。2) 筛选对特定类别多种抗生素具有极强降解能力的菌株。3) 加强对抗生素生物降解机制的研究，挖掘参与抗生素降解过程的关键基因元件、降解酶，加速对抗生素降解酶制剂的研究。4) 应用合成生物学方法构建和改造工程菌株，提高菌株对多种抗生素的分解能力[31]。5) 抗生素降解菌株、菌群与非生物修复技术联用，并优化组合工艺，提高抗生素的降解效率。

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