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Reviews 综 述

畜禽粪便中抗生素抗性基因的分布特征及消减技术研究进展

李纤慧，李建政，张成成，刘文斌，孟佳*

城市水资源与水环境国家重点实验室(哈尔滨工业大学)，黑龙江 哈尔滨 150090

李纤慧，李建政，张成成，刘文斌，孟佳. 畜禽粪便中抗生素抗性基因的分布特征及消减技术研究进展. 微生物学报，2022, 62(12): 4740–4755.
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摘 要：随着集约化畜禽养殖业的不断发展，兽用抗生素的长期使用导致畜禽粪便抗生素抗性基因污染日益严重，对生态环境和人类健康造成严重危害。如何有效消减畜禽粪便中的抗生素抗性基因成为当前研究热点。本文系统总结了畜禽粪便中抗生素抗性基因的产生途径、分布和影响因素，并阐述了好氧堆肥、厌氧消化及其强化工艺消减畜禽粪便抗生素抗性基因的研究进展，根据现有工艺研究存在的问题展望了今后的重点研究方向，为畜禽粪便中抗生素抗性基因的消减提供理论基础和技术支撑。

关键词：畜禽粪便；抗生素抗性基因；生物技术；好氧堆肥；厌氧消化

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***Corresponding author.** E-mail: jiameng@hit.edu.cn

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Distribution characteristics of antibiotic resistance genes in livestock manure and the reduction techniques: a review

LI Xianhui, LI Jianzheng, ZHANG Chengcheng, LIU Wenbin, MENG Jia*
State Key Laboratory of Urban Water Resource and Environment (Harbin Institute of Technology), Harbin 150090, Heilongjiang, China

Abstract: As the intensive livestock breeding industry develops, veterinary antibiotics have been frequently used, allowing the emergence of antibiotic resistance genes in livestock manure. These genes pose great risks to ecological environment and human health. Thus, it has been a research hotspot to reduce antibiotic resistance genes in the livestock manure. This paper summarizes the source, distribution and influencing factors of antibiotic resistance genes in livestock manure, as well as the removal of antibiotic resistance genes from livestock manure by aerobic composting, anaerobic digestion, and their enhanced processes. Finally, in view of the problems in the available techniques, we summed up the future research directions, hoping to provide theoretical basis and technical support for the removal of antibiotic resistance genes in livestock manure.

Keywords: livestock manure; antibiotic resistance genes; biotechnology; aerobic composting; anaerobic digestion

抗生素是一类对微生物具有抑制或杀灭作用的化学物质，其主要来源是生物合成(发酵)，少数利用化学合成或半合成制得。抗生素作为饲料添加剂能够降低动物患病率、促进动物生长、提高饲料转化率，被广泛应用于畜禽养殖产业[1]。随着我国畜禽养殖业的集约化发展，畜禽抗生素的使用量也日益增加，不可避免地出现了抗生素的泛用和滥用。2013 年我国抗生素的使用量达到了 16.2 万 t，其中约 52%的抗生素用于畜禽养殖业[2]。为有效遏制动物源细菌耐药、整治兽药残留超标，全面提升畜禽绿色健康养殖水平，农业农村部制定了一系列兽用抗菌药减量化政策。即便如此，我国近几年的兽用抗生素使用量也达到了约 3 万 t/年[3]。畜禽养殖业中抗生素的过量使用造成了畜禽粪便中抗生素残留，诱导抗生素抗性菌(antibiotic resistant bacteria，ARB)和抗生素抗性基因(antibiotic resistance genes，ARGs)的产生。ARGs 在环境中的扩散和传播，使病原菌获得耐药性，对生态环境和人类健康造成威胁[4]。联合国世界卫生组织(WHO)已将 ARGs 列为新型三大污染问题之一[5]。如何有效消减畜禽粪便中的 ARGs，已成为保障畜禽养殖业健康发展、保护人民生命安全亟需解决的问题。

鉴于此，本文在总结了近年研究基础上，综述了畜禽粪便中 ARGs 的种类、分布和影响因素，以及 ARGs 消减技术的研究进展，旨在为进一步开展畜禽粪便中 ARGs 的相关研究提供一定思路，对控制 ARGs 水平、解决 ARGs 污染问题提供科学依据和建议。

1 ARGs 在畜禽养殖环境中的产生、传播及危害

畜禽养殖环境中 ARGs 的产生和主要传播途径如图 1 所示。抗生素在规模化畜禽养殖业中的滥用，主要通过如下 2 种方式诱导微生物

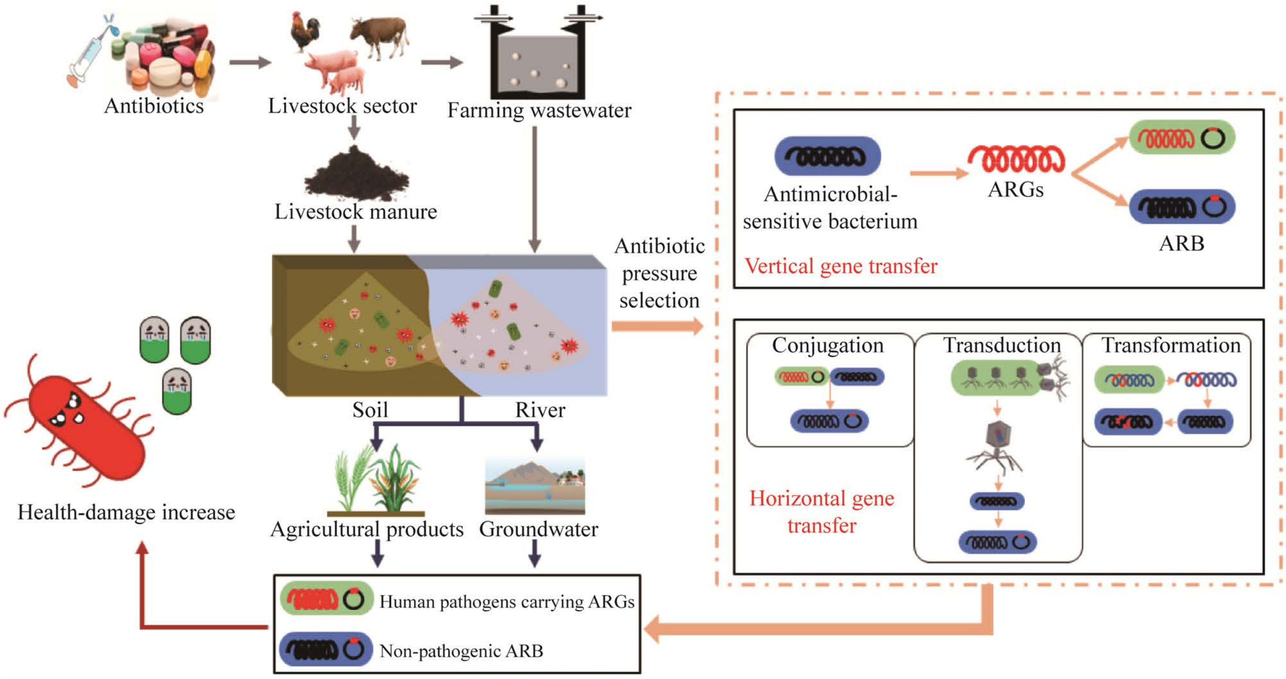

图 1　畜禽养殖环境中 ARGs 的产生及传播

Figure 1　Generation and dissemination of ARGs in livestock farming. ARGs: antibiotic resistance genes; ARB: antibiotic resistant bacteria.

产生 ARGs：(1) 过量抗生素在畜禽胃肠道内诱导出大量携带 ARGs 的微生物，随排泄物进入环境中[6–7]；(2) 畜禽体内约 30%–90%的抗生素不能被完全吸收，以原样或代谢物的形式通过排泄物排出体外，对环境中的微生物产生选择性压力，进而选择和诱导微生物产生 ARGs[7–8]。作为世界上最大的畜禽生产国之一，我国每年生产和排放的畜禽粪便超过 20 亿 t[9]，增加了环境中 ARGs 的产生和传播风险。

畜禽粪便是传统农业中常用的有机肥料[10–11]，ARGs 可随粪肥应用和养殖废水排放进入土壤、地下水等自然环境，破坏生态环境[12–13]。ARGs 还能进一步随食物链富集和转移进入人体，从而对人类健康构成潜在威胁[13–14]。此外，ARGs 可以通过垂直基因转移(vertical gene transfer, VGT)和水平基因转移(horizontal gene transfer, HGT) 2 种方式在微生物间传播[15]。其中，VGT 主要是指 ARGs 以细胞分裂为主，在亲代间通过宿主菌的自我繁殖进行传递。HGT 是 ARGs 借助基因遗传元件(mobile genetic elements, MGEs)，作为重要媒介在不同微生物(包括同一物种的不同个体和不同物种的不同个体)之间转移，也是 ARGs 获得和传播的主要途径[16]。如图 1 所示，ARGs 水平基因转移的分子传播机制主要有接合、转导和转化 3 种方式。通过 HGT，ARGs 不仅可以使某些病原微生物产生耐药性，还能够使 ARB 逐步发展成多重耐药性细菌，导致大量药物失去治疗作用。由此可知，相比抗生素的残留，畜禽粪便中 ARGs 的产生、迁移和转化更具有危险性。因此，亟需探究畜禽粪便中 ARGs 的分布特征以及影响因素，开发经济高效的 ARGs 消减技术。

2 畜禽粪便中 ARGs 的种类和分布

畜禽养殖业中常见的抗生素种类及作用如表 1 所示。其中，四环素类、磺胺类、喹诺酮类、大环内酯类是主要的抗生素类型，针对痢疾、伤寒、呼吸道感染、经常性腹泻等疾病具有一定疗效。不同的抗生素种类也会诱导产生不同的 ARGs (表 1)[17–18]。Li 等[25]考察了包括水、土壤、沉积物、污泥、生物膜和粪便等在内的 10 种典型环境中 50 个样本的 ARGs 广谱分布规律，调查结果表明，畜禽粪便中 ARGs 含量比沉积物、土壤、河水、饮用水中 ARGs 含量高 1–3 个数量级，其中检出比例高于 10^{-3} 的 ARGs 高达 15 种，进一步证实了畜禽粪便是 ARGs 的主要储蓄池。对我国不同地区规模化养猪场的猪粪管理全过程(粪便、粪便堆肥产品以及接受粪肥的土壤环境)进行样品采集和检测分析，共检测出 46 种四环素类抗性基因、5 种磺胺类抗性基因、51 种大环内酯-林可酰胺-链球菌素抗性基因、55 种 β-内酰胺类抗性基因和 35 种氨基糖苷类抗性基因等上百种 ARGs[26]。随着科学的不断进步，新型抗生素的应用也会诱导新型 ARB 和 ARGs 的产生，在未来 ARGs 消减工艺的研发中，应根据抗生素的使用种类，充分考虑可能存在的各种 ARGs，以评估 ARGs 消减工艺的有效性。

本文综述了我国几个规模化畜禽养殖场中粪便 ARGs 的分布情况，如表 2 所示。畜禽粪便中常见抗生素的 ARGs 主要以四环素类、大环内酯类、喹诺酮类、磺胺类为主[21]。由于不同畜禽种类(主要包括猪、鸡、牛)的生理生活特性、工人养殖习惯不同，导致抗生素种类及用量不同，使畜禽粪便中 ARGs 多样性和丰度也存在着显著差异[31]。Qian 等[19]从 12 个规模化养殖场采集了猪、鸡、牛等 3 种畜禽粪便，对其中 ARGs 种类和丰度进行了考察，在猪、鸡、牛 3 种畜禽粪便中检测到一百余种 ARGs，而且鸡粪和猪粪的 ARGs 丰度和多样性高于牛粪。同样，Mu 等[21]调查了我国北方多个畜禽养殖场畜禽粪便中 ARGs 的种类和丰度，发现不同畜禽粪便中 ARGs 含量的总体趋势为鸡粪>猪粪>牛粪。分析认为，相比于牛肉，我国生产生活对鸡肉和猪肉的需求量较高，家禽和生猪的养殖密度也较高，这使得在家禽和生猪养殖过程中抗生素的残留量也远高于生牛养殖[32]，诱导产生了更多的 ARGs。不同养殖场的同种

表 1　畜禽养殖业中常用抗生素类别和作用及常见抗生素抗性基因

Table 1　Common antibiotics in livestock breeding and their functions, and there lated antibiotic resistance genes

Antibiotic category	Antibiotics	Efficacy of antibiotics	Common antibiotic resistance genes	References
Tetracyclines	Tetracycline	(1) For treating chlamydia infection, mycoplasma pneumonia, rickettsial disease, cholera, tularemia, rat bite fever, tetanus, plague, gas gangrene, etc.	*tet*A, *tet*B, *tet*C, *tet*E, *tet*G, *tet*H, *tet*Z, *tet*K, *tet*L, *tet*M, *tet*O, *tet*S, *tet*W, *tet*Q, *tet*T, *tet*PB, *tet*X, *tet*PA, *tet*U, *tet*R, *tet*(33), *tet*(32), *otr*A, *tet*(36), *tet*(40), *otr*C, *otr*B	[12,19–20]
	Oxytetracycline	(2) For treating white scour and lamb dysentery caused by *Escherichia coli* or *Salmonella*, hemorrhagic septicemia, swine pneumonia and fowl cholera caused by *Pasteurella multocida*, bovine pneumonia, swine enzootic pneumonia and chronic respiratory disease of chickens caused by mycoplasma, etc.		

(待续)

(续表 1)

	Chlortetracycline	(3) For promoting the growth of livestock and poultry, improving the feed conversion rate, and preventing pullorum, typhoid, paratyphoid, cholera, coccidiosis, pneumonia, enteritis, etc.		
	Doxycycline	(4) For treating suppuration, vibrosis and tail-rot disease caused by halophilic bacteria, mycoplasmosis, psittacosis, mixed infection of bacteria and fungi, etc.		
Sulfonamides	Sulfadiazine	(1) For treating sensitive bacterial infection and toxoplasma infection.	*sul*1, *sul*2, *sul*3, *dfr*A1	[19,21]
	Sulfamethoxazole	(2) For treating the infection of respiratory tract, digestive tract and urinary tract caused by sensitive bacteria.		
	Sulfamethazine	(3) For treating staphylococcal infection, poultry typhoid and chicken coccidiosis.		
Fluoroquinolones	Norfloxacin	(1) For treating pullorum typhoid and paratyphoid, inactivating *Staphylococcus aureus*, mainly focusing on dysentery, edema disease and toxic chronic diarrhea in pigs.	*acrA*, *acrB*, *mex*A, *mex*F, *gyr*A, *par*C, *qnr*A, *qnr*B, *qnr*D, *qnr*S, *flo*R, *oqx*B, *qep*A, *cfr*	[19,21–22]
	Ciprofloxacin	(2) For inhibiting *Vibrio cholerae*, *Staphylococcus aureus*, *Pseudomonas aeruginosa*.		
	Enrofloxacin	(3) For treating bacterial and mycoplasma infection caused by sensitive bacteria.		
Macrolides	Erythromycin	(1) For treating various infections caused by penicillin-resistant *Staphylococcus aureus* and other sensitive bacteria, such as pneumonia.	*erm*R, *erm*F, *erm*B, *erm*X, *erm*T, *erm*Y, *erm*A, *erm*C, *mph*A, *mef*A, *erm*A, *lnu*B, *erm*G, *vat*B, *vat*E, *ere*A	[19–20]
	Roxithromycin	(2) For treating chronic respiratory disease in livestock and poultry, infectious coryza, staphylococcosis, swine enzootic pneumonia, streptococcosis, etc.		
	Tilmicosin	(3) For inhibiting mycoplasma and spirochete, and inactivating *Haemophilus parasuis*, *Actinobacillus pleuropneumoniae* and *Pasteurella multocida*.		
β-lactams	Penicillin	(1) Showing a good curative effect on most diseases caused by G^+, and for treating coccidiosis combined with sulfonamides.	*cph*A, *bla*PER, *bla*VEB, *pen*A, *bla*MP, *blaO*A10, *cfi*A, *bla*TEM, *bla*PSE, *amp*C, *bla*SFO, *bla*CMY, *bla*CTX-M, *bla*CMY2, *bla*OXA1_*bla*OXA30	[19]
	Amcarbcillin	(2) Showing a significant inhibition on *Enterococcus*.		
	amoxicillin	(3) Improving sow immunity, treating diarrhea of piglets and *Streptococcus suis* infection.		
Aminoglycosides	Streptomycin	(1) Inhibiting *Mycobacterium tuberculosis* and *Arcanobacterium pyogenes* in intestine.	*str*, *str*A, *str*B, *aad*A1, *aph*A1, *aad*A, *aad*A2, *aad*E, *aad*A5, *aad*A9, *aad*D, *acc*C	[19]
	Kanamycin	(2) For treating pullorum disease, and enteritis caused by *Escherichia coli*, *Salmonella*, *Riemerella anatipestifer*, etc.		
	Gentamicin	(3) For treating septicemia, respiratory, gastrointestinal, and urinary tract infections caused by sensitive bacteria.		
Glycopeptides	Vancomycin	For treating drug-resistant bacterial infections, pseudomembranous enteritis, intestinal inflammation, etc.	*van*A, *van*B, *van*C, *van*D, *van*HB	[19,23]
Peptides	Polymyxin E	For treating diarrheal diseases of livestock and poultry.	*mcr*-1, *mcr*-2, *mcr*-3, *mcr*-4, *mcr*-5, *arn*A	[20,24]

表 2　我国不同地区规模化养殖场畜禽粪便中 ARGs 分布情况

Table 2　Distribution of ARGs in livestock manure at large-scale farm in different regions of China

Farm location	Livestock species	Detected ARGs type and content	Comparison of ARGs in different livestock manures	References
Liaoning province, Tianjin city	Pig	SRGs[a]>QRGs[b]>TRGs[c]>MRGs[d]	Chicken>pig>cattle	[21]
	Chicken	QRGs>>SRGs>>TRGs>MRGs		
	Cattle	SRGs>>QRGs>TRGs>QRGs		
Tianjin city	Finishing pigs	TRGs>SRGs>MRGs>QRGs	Chicken>sow>piglet>finishing pigs>cattle (pig manure has higher QRGs than chicken manure and cow manure)	[27]
	Piglet	TRGs>SRGs>MRGs>QRGs		
	Sow	SRGs>TRGs>MRGs>QRGs		
	Chicken	SRGs>TRGs>MRGs>QRGs		
	Cattle	TRGs>SRGs>MRGs>QRGs		
Hebei province	Pig	TRGs>MRGs>SRGs	Chicken>pig	[28]
	Chicken	MRGs>SRGs>TRGs		
Taian, Shandong provice	Pig	TRGs>SRGs>MRGs>QRGs	Chicken>pig>cattle	[29]
	Chicken	SRGs>>TRGs>MRGs>QRGs		
	Cattle	TRGs>>SRGs>MRGs>QRGs		
Hangzhou, Zhejiang provice	Pig	TRGs>>SRGs	Duck>chicken>pig	[12]
	Chicken	TRGs>SRGs		
	Duck	SRGs>TRGs		
Yunnan province	Pig	TRGs>SRGs>MRGs>QRGs	Chicken>pig>cattle	[23]
	Chicken	SRGs>TRGs>MRGs>QRGs		
	Cattle	TRGs>SRGs>MRGs>QRGs		
Hexi, Heshan, Guangdong province	Sow	QRGs>TRGs>MRGs>SRGs	Piglet>boar>sow	[30]
	Boar	TRGs>QRGs>MRGs>SRGs		
	Piglet	QRGs>TRGs>MRGs>SRGs		
Hedong, Heshan, Guangdong province	Sow	TRGs>QRGs>MRGs>SRGs	Sow>boar>piglet	[30]
	Boar	TRGs>QRGs>MRGs>SRGs		
	Piglet	TRGs>QRGs>MRGs>SRGs		
Kaiping, Guangdong province	Sow	TRGs>MRGs>QRGs>SRGs	Boar>sow>piglet	[30]
	Boar	TRGs>QRGs>MRGs>SRGs		
	Piglet	TRGs>QRGs>MRGs>SRGs		

a: SRGs, sulfonamides resistance genes; b: QRGs, quinolones resistance genes; c: TRGs, tetracyclines resistance genes; d: MRGs, macrolides resistance genes.

类畜禽粪便中 ARGs 的种类和丰度也存在一定差异[33]，这可能与喂养方式、抗生素使用、畜禽年龄和体型差异等有关。可见，我国畜禽粪便中 ARGs 的分布并无明显规律，ARGs 的分布受多种因素共同影响，既包括畜禽养殖种类、抗生素使用等人为原因，也包括地理位置、气候条件等自然原因。

3　畜禽粪便中ARGs分布的影响因素

如上所述，不同地区不同种类畜禽粪便中

ARGs 的种类和丰度存在一定差异。影响畜禽粪便中 ARGs 分布的原因主要可以分为人为原因和自然原因两类。

3.1 人为原因

3.1.1 畜禽管理和养殖模式

研究发现，猪粪和鸡粪中 ARGs 含量明显高于牛粪中 ARGs 含量，其传播风险也较高[29]。一方面，不同用途畜禽、不同饲养阶段动物所使用的抗生素种类与剂量也有所不同，进而导致诱导产生的 ARGs 也存在明显差异；另一方面，养殖方式和养殖规模也是影响畜禽粪便中 ARGs 分布的重要因素之一。相比于种牛和肉牛养殖，生猪和家禽的养殖更易采用圈养方式，圈养模式下动物流动性较差、粪便经常性堆积，封闭式环境也不利于畜禽粪便中抗生素的降解，从而形成抗生素和 ARGs 的积累，这也是导致其粪便中 ARGs 含量较高的原因之一[34]。邹威等[28]考察了华北地区(河北省和天津市)不同规模畜禽养殖场粪便中 ARGs 分布规律，研究发现，养殖规模显著影响了猪粪中 ARGs 含量(中型>大型>小型)，但不同规模养鸡场粪便中 ARGs 的含量无显著性差异。上述研究表明，畜禽粪便中 ARGs 的分布受养殖类型和养殖规模等多方面因素共同影响。

3.1.2 畜禽养殖场与周边环境的互相作用

畜禽养殖场周边环境也会影响畜禽粪便中 ARGs 的分布和传播。例如，当规模化畜禽养殖场与制药厂、化工厂等工业区相邻时，制药废水废渣和化工废水与养殖场废弃物将共同作用于周边环境，同时，来自制药厂废弃物中的 ARGs 和化工废水中的重金属离子可以通过协同作用影响畜禽粪便中 ARGs 的水平基因转移和垂直基因转移[31,35]。

3.2 自然原因

地势、气候条件等影响因素使不同地区畜禽粪便中 ARGs 的分布情况存在较大差异。研究发现，在我国北方畜禽养殖场粪便中检测出的喹诺酮类抗性基因和磺胺类抗性基因要高于南方养殖场的畜禽粪便[21,23]。畜禽粪便中 ARGs 的丰度也会随季节性变化(降雨强度和温度差异等)而改变。Wang 等[36]研究发现，猪粪中四环素类 ARGs 和磺胺类 ARGs 在冬季的检出频率和相对丰度均高于夏季。此外，自然环境中的有机物、氮、磷、氧浓度，以及水分含量和 pH 值等也会影响 ARGs 的丰度[6,37–38]。如总氮和总磷浓度与粪便中编码核糖体保护蛋白的四环素抗性基因含量有显著相关性[36]。

综上所述，影响畜禽粪便中 ARGs 分布的因素十分复杂，可能是人为因素与自然因素的共同作用，抗生素含量、微生物群落结构、重金属含量以及其他环境因素都会影响 ARGs 的分布。正因如此，全面分析畜禽粪便中 ARGs 的分布及影响因素，有针对性地开发 ARGs 消减工艺，对营造健康的畜禽养殖环境、促进畜禽养殖业可持续发展具有重要意义。

4 畜禽粪便中ARGs消减技术的研究进展

目前，已开发出多种畜禽粪便处理工艺，其中，生物处理工艺因具有可回收资源、能耗少、操作简单、运行成本低等优点而被广泛应用，以实现畜禽粪便的资源化和减量化。在此基础上，本文总结了畜禽粪便 ARGs 的消减技术及研究进展。常用的生物处理技术主要包括好氧堆肥和厌氧消化技术，对畜禽粪便中的 ARGs 均具有一定的消减效果，可保障畜禽养殖业的可持续发展[39–40]。

4.1 好氧堆肥及其强化工艺

4.1.1 好氧堆肥

好氧堆肥是畜禽粪便稳定化、无害化、资

源化的主要途径之一[41],也是一种重要的ARGs消减手段[42]，同时，堆肥温度是影响好氧堆肥ARGs 消减效能的主要因素[43]。郑宁国等[44]研究发现,高温堆肥对猪粪中*qnr*S、*erm*C、*bla*TEM和 *bla*SHV 的消减效率达到了 98%以上，对*erm*A 和 *erm*B 的消减效率超过 80%，对 *qnr*A和 *bla*CTX 的消减效率也能达到 60%左右，然而堆肥后 *erm*F 的含量却增加了 28.7%，这说明高温堆肥对不同种类 ARGs 的消减效果也有较大差异。Selvam 等[45]的研究也表明，低温和高温堆肥对猪粪中大部分四环素类、磺胺类以及氟喹诺酮类 ARGs 均有一定的消减效果。Qian等[46]的研究进一步表明，连续高温堆肥工艺对ARGs 的消减效能，显著优于常规的高温和中温堆肥，这说明堆肥工艺的运行参数和运行方式也会影响其对 ARGs 的消减效果。

在好氧堆肥过程中，高温期和腐熟期对降低 ARGs 丰度起主要作用，具体机制可以归纳为以下 4 点：(1) 堆肥过程中产生的高温可以破坏抗生素结构，削弱抗生素对 ARGs 形成的选择性压力[47]；(2) 大多数ARGs的宿主菌和ARB不耐受高温，在堆肥过程中被灭活，降低了ARGs 含量[48]；(3) 高温导致细胞自溶、蛋白质和核酸降解，迅速破坏 ARGs；(4) 高温降低了整合子和转座子等移动遗传元件的丰度，减少细菌间的接触和转导，抑制 ARGs 的水平基因转移[48–49]。好氧堆肥虽然在一定程度上降低了ARGs 的丰度，但不能完全消减 ARGs，且对于某些特定的 ARGs 消减效果较差，需进一步强化好氧堆肥的 ARGs 消减效能。

4.1.2　微生物菌剂强化好氧堆肥 ARGs 消减效能

单一的好氧堆肥工艺存在温室气体排放量高、氮损失率高以及某些 ARGs 消减效率低等问题[44,50–51]。微生物菌剂能够重复使用，可以根据污染物特性灵活调整微生物菌剂的复配比例，从而实现多种污染物的同步去除。因此，投加微生物菌剂被认为是一种经济高效的强化措施。已有研究表明，在堆肥过程中添加微生物菌剂可以减少氮流失、提高堆肥效能和 ARGs消减效率[52]。Liu 等[52]发现，黄孢原毛平革菌、黑曲霉、地衣芽孢杆菌的复配混合菌剂可以有效降低猪粪堆肥过程中 ARGs 的相对丰度。Guo等[53]考察了巨大芽孢杆菌对鸡粪堆肥系统ARGs 消减效能的影响，结果表明，在添加 5%的巨大芽孢杆菌条件下，ARGs 和 MGEs (主要为 Tn916/1545)的消减效率分别提高了 64.6%和67.9%。Li 等[54]向猪粪堆肥系统中添加复合微生物菌剂(枯草芽孢杆菌:地衣芽孢杆菌:巨大芽孢杆菌:酵母菌=1:1:1:2)，使 *tet*H、*tet*L、*tet*M、*tet*O、*tet*Q、*tet*W、*erm*B、*erm*Q、*bla*CTX、*bla*TEM等多个 ARGs 和 MGEs(Tn916)的消减效率得到了明显提升，提升率为 3.7%–23.8%。分析认为，添加微生物菌剂可以改变微生物群落结构，提高 ARGs 消减效率，同时也降低了抗生素对ARGs 的选择性诱导[27,53–54]。在实际应用中，应根据不同粪便中的抗生素和 ARGs 种类选择适当的微生物菌剂类型以及复配比例。

4.1.3　添加剂强化好氧堆肥 ARGs 消减效能

在好氧堆肥过程中添加调理剂、膨胀剂、营养调节剂等添加剂能够缩短堆肥进程、提高堆肥产物的腐殖化程度和 ARGs 的消减效能[55–58]。目前常用的添加剂有生物炭、木屑、稻壳、煤灰渣等具有表面多孔结构的物质，具有一定吸附作用，能够降低重金属的生物可利用性和迁移率，降低 ARGs 含量[57–59]。Cui 等[58]发现，蘑菇生物炭可以显著强化好氧堆肥 ARGs 的消减效率，但是稻草生物炭添加却产生了截然相反的效果。Li 等[60]研究发现，10%竹炭能够降低鸡粪堆肥中 ARGs 的丰度，其中 *tet*C、*tet*G、*tet*W、*tet*X、*sul*2、*drf*A1、*drf*A7、*erm*B、*erm*F、 *erm*Q 和 *erm*X 丰度下降了 21.6%–99.5%，但 *sul*1 的丰度稍有增加。分析认为，生物炭的添加改变了包括携带 ARGs 的致病菌在内的多种微生物的丰度，进而影响了堆肥系统的 ARGs 消减效能[58,60]。Wang 等[61]利用纳米零价铁(nZVI)作为添加剂强化猪粪堆肥效能，结果表明，当添加 100 mg/L 的 nZVI 时，ARGs (包括 *sul*1、*sul*2、*dfr*A7、*erm*F 和 *erm*X)的相对丰度下降了 33.26%–99.31%，MGEs 中 *int*I2 和 Tn916/1545 的相对丰度分别下降了 95.59%和 97.65%。这是因为 nZVI 具有杀菌特性，能够破坏 ARGs 和 MGEs 宿主菌的细胞结构进而使宿主菌死亡，但是 nZVI 浓度过高可能促使 HGT 的发生，因此需要添加适宜浓度的 nZVI[61]。Awasthi 等[62]考察了不同剂量粘土添加剂对畜禽粪便堆肥过程中 ARGs 的影响，研究发现，高剂量粘土添加剂在降低 ARGs 方面起着重要作用。分析认为，粘土中含有蒙脱石和高岭石的带电分子，能与金属离子形成复合物，降低有毒金属的生物可利用度，抑制 ARGs 的扩散，而且高浓度粘土的添加还会加速堆肥过程中有机物的活性矿化，降低抗生素浓度，进而降低了 ARGs 的相对丰度。

由上述分析可知，好氧堆肥及其强化工艺可有效消减畜禽粪便中的 ARGs，但消减效能还有望进一步提高，ARGs 的消减机制也有待进一步揭示，堆肥产物在农业应用中的环境风险，还需进一步评估。

4.2 厌氧消化及其强化工艺

4.2.1 厌氧消化

厌氧消化工艺能够在降解有机污染物的同时回收可再生能源甲烷，具有处理成本低、能耗低、效率高等优势[63]，广泛应用于畜禽粪便的处理。近期研究表明，厌氧消化工艺对 ARGs 也有一定的消减作用[64]。Sun 等[65]考察了 3 种温度(20、35 和 55 °C)条件下厌氧消化系统对牛粪中 ARGs 的消减效果，研究发现，高温条件下厌氧消化系统能够消减 80%的 ARGs，而中低温条件下仅对 50%的 ARGs 有明显的消减效果。同样，Zou 等[66]也证实了相比于 35 °C，55 °C 条件下厌氧消化系统对粪便中 ARGs 的消减效率更高。然而，也有研究呈现相反结果，如 Sun 等[67]发现中温牛粪厌氧消化的 ARGs 消减效果稍高于高温厌氧消化，但对 MGEs 消减效果却低于高温系统。Huang 等[68]发现温度并未显著影响猪粪厌氧消化系统 ARGs 的消减效能。温度对厌氧消化系统 ARGs 消减效能影响的不一致性，可能与微生物丰度、组成(微生物群落变化)以及 MGEs 和 HGT 有关[65,68]。此外，Chen 等[69]的研究发现，厌氧消化对猪粪中红霉素抗性基因和四环素抗性基因的消减没有明显效果。而 Tien 等[70]发现，牛粪中的 ARGs (如 *sul*1、*erm*F、*erm*B、*bla*oxa-20、*aad*A)浓度在厌氧消化后呈现升高趋势。这可能与厌氧消化系统对 ARGs 宿主菌的灭活效能有关。

由此可见，单一的厌氧消化工艺对 ARGs 的消减效果有限，无法有效控制质粒、整合子等 MGEs 的传播和扩散[67,71]。因此，优化厌氧消化系统的运行效能，强化其对 ARGs 的消减效率，深入研究 ARGs 和 MGEs 在厌氧消化过程中的消减机制，将丰富和发展厌氧消化理论，并为畜禽粪污的能源化资源化处理提供技术支撑。

4.2.2 预处理强化厌氧消化 ARGs 消减效能

碱水解、热水解、超声等预处理方式不仅可以通过破壁、溶胞作用，释放细胞内有机物，提高厌氧消化效能，还可以进一步降低 ARGs 丰度[72–75]。Lin 等[76]发现酸预处理能够强化猪粪中磺胺类 ARGs 的消减效率。一方面，酸预处理有利于磺胺类抗生素的降解，抑制磺胺类

ARB 的生长和 *int*I1 整合子的积累；另一方面，酸性条件有利于磺胺类抗生素降解菌(厚壁菌门)的富集，并影响 ARGs 宿主菌的生长。在上述因素的共同作用下，酸性预处理显著降低了猪粪中磺胺类 ARGs 的丰度，为进一步提高其厌氧消化效能奠定了基础。巴氏杀菌(67 °C, 1 h)预处理对畜禽粪便厌氧消化系统中 *sul*1 和 *sul*2 的消减也有一定的促进，其消减效率分别提高了 5%和 10%[77]。但巴氏杀菌预处理对 ARGs 的强化消减机制仍有待深入研究。近年来，游离亚硝酸(free nitrous acid，FNA)预处理已被认为是一种经济高效的预处理技术，用于强化剩余污泥厌氧消化产甲烷效能[78–79]。同时，游离亚硝酸作为一种杀菌剂，对病原菌的灭活十分有效[78–79]，能够有效灭活 ARB 和 ARGs、MGEs 的潜在宿主菌。最近的研究表明，FNA 预处理对胞外聚合物、磺胺甲恶唑等大分子化合物具有破坏作用[80–81]，说明 FNA 预处理可以降低抗生素浓度，进而减小 ARGs 的选择性压力。此外，低水平的 FNA 可以改变细胞内粒子，抑制 ARGs 的共轭转移[82]。上述研究表明，FNA 预处理在一定程度上能够提高畜禽粪便厌氧消化产甲烷效能，同时显著降低 ARB 水平以及 ARGs 和 MGEs 丰度，MGEs 丰度的降低也为控制 ARGs 的传播提供了保障。因此，有望利用游离亚硝酸预处理技术提高畜禽粪便厌氧消化工艺 ARGs 的消减效能，但是系统运行的最佳运行参数和 ARGs 的强化消减机制还需进一步研究。

4.2.3　添加剂强化厌氧消化 ARGs 消减效能

与好氧堆肥相似，添加剂同样可以强化厌氧消化系统的发酵效能和 ARGs 消减效率[83]。厌氧消化系统中常用的添加剂主要有煤气化渣(GS)[83]、nZVI[84]和活性炭[85]等。其中，GS 具有高度发达的孔隙结构，可以提供足够的位点容纳微生物以降低其移动性，微生物迁移率的降低有效减少 ARGs 的 HGT，从而降低了 ARGs 的传播机会，而且 GS 的添加能够抑制 MGEs 和 ARGs 潜在宿主菌的活性[83,86]。研究表明，在添加 10 g/L GS 的厌氧消化系统中，*dfr*A7、*sul*2、*tet*W、*erm*F 和 *erm*Q 的消减效率约为 24.81%–90.48%，MGEs (ISCR1)的消减效率更是高达 95.4%[83]。Ma 等[84]的研究发现，nZVI 的添加可以通过灭活 ARGs 宿主菌，有效提高厌氧消化的 ARGs 和 MGEs (Tn916/1545)消减效能，这与 nZVI 强化好氧堆肥 ARGs 消减效能的机制类似。Zhang 等[87]对比了 DNA 酶、天然沸石、零价铁 3 种添加剂对高温厌氧消化运行效能的影响，研究表明，零价铁和天然沸石都能强化厌氧消化系统 ARGs 的消减效率，提高率分别为 33.3%和 138.5%，但 DNA 酶却抑制了厌氧消化系统 ARGs 的消减效能。该研究认为添加剂引起的微生物群落改变和重金属抗性基因水平是影响 ARGs 变化的主要因素。Zhang 等[88]考察了磁铁矿对猪粪厌氧消化过程 ARGs 变化规律的影响，发现磁铁矿主要影响厌氧消化中期的 ARGs 丰度，但对厌氧消化终产物 ARGs 丰度的影响并不显著。因此，在厌氧消化系统的实际运行中，应根据消化效能和目标 ARGs 消减效果选择合适的添加剂和浓度。

4.2.4　厌氧共消化

畜禽粪便中氨氮含量较高，在一定程度上限制了厌氧消化系统的发酵效能[86]。因此，在畜禽粪便厌氧消化系统中引入碳氮比较高、易降解的共消化底物可以缓解厌氧消化系统营养失衡问题，通过影响微生物群落结构，提高发酵效能和 ARGs 消减效率[89–90]。Song 等[91]探讨了猪粪与小麦秸秆在不同质量比条件下厌氧消化系统中 ARGs 含量和微生物群落结构，研究发现在粪便与小麦稻草的质量比为 7:3 时，系

统中 ARGs 丰度和 MGEs (*int*I1)丰度最低。Zhang 等[90]发现厌氧共消化系统有效降低了中药残留物和猪粪中的 ARGs (*erm*F、*qnr*A、*tet*W 等)和 MGEs (s*int*I1、*int*I2、Tn*916/1545*、ISCR1 等)含量。上述研究均证明了微生物群落变化是影响厌氧消化系统 ARGs 水平的主要因素，主要通过降低 ARGs 宿主菌水平实现 ARGs 丰度的降低。但是，厌氧共消化底物的配比要根据实际情况调整。

综上所述，单一好氧堆肥或厌氧消化处理工艺对畜禽粪便中 ARGs 的消减效果不佳，可以通过投加添加剂、预处理粪便等方法强化其 ARGs 的消减效能，但不可避免地增加了工艺流程和运行难度、基建投资以及运行成本。在畜禽粪便的工程处理中，应综合抗生素的投加种类、ARGs 类型等多种因素，选择适宜的处理工艺。

5 结论与展望

兽用抗生素的长期使用导致畜禽养殖环境中 ARGs 污染日益严重，破坏生态环境、威胁人类健康。研究发现，畜禽粪便是畜禽环境中 ARGs 的主要来源，粪便中 ARGs 分布与养殖模式、养殖场地理位置、气候条件、废物处置方式等多方面因素有关。有效消减畜禽粪便中 ARGs 含量是控制 ARGs 污染和传播风险的关键。好氧堆肥和厌氧消化等处理技术可以降低畜禽粪便中 ARGs 的含量，但不同处理工艺对 ARGs 的消减效果也不同。畜禽粪便处理系统仍然面临如何在保障其堆肥/消化效能的前提下高效消减 ARGs 的问题。因此，建议今后重点从以下几个方面开展研究：

(1) 系统分析畜禽粪便中 ARGs 的分布规律和在农业环境中的传播途径，降低抗生素的残留量、灭活 ARGs 潜在宿主菌，有效阻止 ARGs 的传播与扩散，以降低环境中多重耐药细菌的产生和迁移。

(2) 深入研究好氧堆肥/厌氧消化系统中 ARGs 的变化规律，结合 ARB 含量和抗生素迁移转化规律，分析 ARGs 的潜在宿主菌，阐明好氧堆肥/厌氧消化系统消减 ARGs 的微生物机制。

(3) 优化好氧堆肥/厌氧消化工艺的运行参数，强化其对畜禽粪便 ARGs 的消减效能；同时，开发经济、高效的 ARGs 消减技术，降低畜禽粪便的生物危害性，保障畜禽养殖业的健康发展。

(4) 基于生命周期评价方法，评估 ARGs 在环境中的迁移转化途径，在此基础上，提出和优化兽用抗生素的使用规范，加强对兽用抗生素使用的管控力度，致力于从源头降低抗生素相关污染的可能性。

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