ASP

自然科学学报 Chinese Journal of Natural Science, Vol. 1, No. 1
http://dx.doi.org/10.52810/CJNS.2024.001

ARTICLE

畜牧业来源的抗生素耐药大肠杆菌研究进展

李嘉[1,*], **孙世广**[2]

[1] 北京工商大学，大型仪器设备共享中心，北京 100048
[2] 北京工商大学，轻工科学与工程学院，北京 100048

学术编辑： 徐春明；**收稿日期：** 2024-02-18；**录用日期：** 2024-04-20；**发布日期：** 2024-04-25

***通讯作者：** ✉ 李嘉，20091101@btbu.edu.cn

文章引用

李嘉, 孙世广. 畜牧业来源的抗生素耐药大肠杆菌研究进展. 自然科学学报, 2024, **1**(1): 1–15.

Citation

Li, J., & Sun, S. (2024). Antibiotic-Resistant *Escherichia coli* from Farm Animal-Associated Sources. Chinese Journal of Natural Science, 1(1), 1–15.

摘　要

大肠杆菌是动物和人类胃肠道和肠道外疾病的最常见原因之一。由于抗生素的过度使用和误用，近年来抗生素耐药大肠杆菌在全球的流行率迅速上升；特别是来自农场动物相关来源的抗生素耐药大肠杆菌及其抗生素耐药基因 (ARGs) 正在成为全球关注的问题，并且在临床上对人类和动物的健康都具有负面的影响。本综述的目的是探讨来自畜牧业、废物处理和水生环境的抗生素耐药大肠杆菌的流行趋势。重点介绍了抗生素的消毒方法和可能的替代方法。同时发现来自食用动物、产品和动物粪便的过敏性大肠杆菌的流行率正在以惊人的速度增加，但在废物处理厂却有所减少。紫外线 (UV) 处理、表面等离子体氧化和生物炭通常用于有效消除抗生素耐药大肠杆菌。一些益生菌、植物提取物和抗菌肽作为抗生素的有希望的替代品正在引起人们的更大关注。目前的研究表明，来自畜牧业的抗生素耐药大肠杆菌普遍存在，并对全球公共卫生构成严重威胁。这一综述为进一步研究、开发和应用新的策略来减少农场动物源性大肠杆菌的抗生素耐药性提供了新的思路。

关键词: 抗生素耐药性，大肠杆菌，农场动物，选择，消毒

Antibiotic-Resistant *Escherichia coli* from Farm Animal-Associated Sources

Jia Li[1,*] **and Shiguang Sun**[2]

[1] Beijing Technology and Business University, Large-scale Instrument and Equipment Sharing Center, Beijing 100048, China

[2]Beijing Technology and Business University, School of Light Industry Science and Engineering, Beijing 100048, China

Academic Editor: Chunming Xu; **Submitted:** 2024-02-18; **Accepted:** 2024-04-20; **Published:** 2024-04-25

***Correspondence Author:** ✉Jia Li, 20091101@btbu.edu.cn

Abstract

Escherichia coli is one of the most frequent causes of gastro-intestinal and extra-intestinal diseases in animals and humans. Due to overuse and misuse of antibiotics, recent years have seen a rapidly increasing prevalence of antibiotic-resistant (AR) *Escherichia coli* globally; particularly, AR *E. coli* from farm animal-associated sources and its antibiotic resistance genes (ARGs) are becoming a global concern, with clinical negative effects on both human and animal health. The aim of this review was to explore the prevalence trends of AR *E. coli* from farm animals, waste treatment, and aquatic environments. The disinfection methods of AR *E. coli* and possible alternatives to antibiotics were also highlighted. The current review highlights that the prevalence of AR *E. coli* from food animals, products, and animal waste is increasing at an alarming rate, but is reduced at waste treatment plants. Ultraviolet (UV) treatment, surface plasma oxidation, and biochar are commonly used to effectively eliminate AR *E. coli*. Some probiotics, plant extracts, and antimicrobial peptides are arousing interest as promising alternatives to antibiotics to fight against AR *E. coli*. The current review suggests that AR *E. coli* from farm animal-associated sources is prevalent and poses a serious global threat to public health. This review provides an avenue for further research, development, and application of novel strategies to minimize antibiotic resistance in E. coli of farm animal origin.

Keywords: Antibiotic resistance, *Escherichia coli*, Farm Animals, Alternatives, Disinfection

1 引言

大肠杆菌存在于环境、食物以及动物和人类的肠道中。它是一种机会致病菌，可引起动物和人的腹泻、肠炎、菌血症、尿路感染等胃肠道和肠外疾病[1–5]。大肠杆菌也存在于大部分动物粪便中[6,7]。由于抗生素的过度使用和误用，动物源性大肠杆菌对多种抗生素产生耐药性，包括四环素类、氨基糖苷类、β-内酰胺类、氟喹诺酮类、第三代头孢菌素类等[8–11]。研究表明，2010-2020 年间，从韩国食用动物 (包括健康肉鸡、牛和猪) 中分离出的大肠杆菌中，90% 以上对喹诺酮类药物和头孢菌素具有高耐药性[12]。同时，携带抗生素耐药基因 (ARGs) 的抗生素耐药大肠杆菌存在于多个宿主和环境空间中，并可在动物和人类之间传播[13]。在一些废物处理厂和水生环境中，抗生素耐药大肠杆菌浓度高达 $10–10^5$ CFU/mL，高于灌溉用水要求 (10 CFU/100 mL)[14–16]，对公众健康构成严重威胁[3,4,17–19]。

抗生素耐药大肠杆菌及其抗生素耐药基因的传播经常发生在农场动物之间[20,21]。动物和畜产品是抗生素耐药大肠杆菌传播的潜在宿主和媒介。牲畜养殖场携带抗生素耐药基因 (如 blaCTX-M、sul1、tetA、tetB 等) 的抗生素耐药大肠杆菌可转移到周围环境，如水体、土壤等[1,20,22,23]。此外，抗生素耐药大肠杆菌及其动物源性抗生素耐药基因还可以通过水平基因转移 (horizontal gene transfer, HGT) 转移到其他细菌中，这在细菌中抗生素耐药基因的获取、积累和传播中起着关键作用[24–27]。从肉鸡和猪等食用动物中分离的共生大肠杆菌菌株中提取的一些抗生素耐药基因 (包括 sul3、cmLA、aadA1、aadA2、tetR、tetA 和 dhrfI) 可转移给人类[28,29]。值得注意的是，来自牲畜的多重耐药 (MDR) 大肠杆菌分离株与来自人类的分离株相同，表明抗生素耐药大肠杆

菌具有高度可转移性[26]。抗生素耐药大肠杆菌及其抗生素耐药基因对动物和人类健康构成严重风险[5]，需要有效的应对策略。

为了对抗动物源抗生素耐药大肠杆菌，一些传统和新颖的策略已被报道，包括紫外线 (UV) 处理、质膜氧化和生物炭法等，通过抑制 DNA 复制和破坏细胞膜来有效杀死抗生素耐药大肠杆菌[30–32]。经质膜氧化或生物炭氧化处理后，动物源性大肠杆菌中少数 ARGs(包括 tetC、tetW、blaTEM-1、AmpC 等) 被显著去除或还原，ARGs(如整合子基因-intI1) 的共轭转移被显著抑制[31,33]。这些方法的优点是效率高，设备简单，无或低外源化学残留[30,33,34]。值得一提的是，近年来，一些潜在的抗生素替代品用来处理抗生素耐药大肠杆菌的传播，如益生菌、植物提取物、抗菌肽等，其具有强大的生物学功能而且对健康有益[35–38]。尤其是抗菌肽，这种少于 100 个氨基酸残基的效应分子几乎存在于所有生物体中，对抗生素耐药细菌具有较强的抗菌活性，且耐药风险低[39,40]。迄今为止，几种抗菌肽 (如 microcin、magainin、cathelicidin 等) 被认为是一类很有前途的抗生素耐药大肠杆菌抗菌药物[41–44]。

在本综述中，我们简要介绍了畜牧业来源 (包括农场动物、污水/粪便处理和水生环境) 的抗生素耐药大肠杆菌的现状，以及对抗抗生素耐药大肠杆菌的策略。通过对目前动物源性抗生素耐药大肠杆菌的研究，我们希望更多的人能够清楚地了解其不良影响，这可能有助于制定更有效的策略来对抗农场动物相关来源的细菌耐药性。

2 畜牧业来源的过敏性大肠杆菌患病率

2.1 来自农场动物的抗生素耐药大肠杆菌

食用动物可能是抗生素耐药菌传播的潜在宿主和媒介, 包括大肠杆菌, 这是全世界日益关注的问题。监测食用动物及其产品中的抗生素耐药大肠杆菌对于确定抗生素耐药性的出现及其对人类的相关风险至关重要[20,45–47]。

禽致病性大肠杆菌可引起禽大肠杆菌病，常见于德国、埃及、巴基斯坦等国家，对氨苄西林、四环素、环丙沙星等抗生素具有较高的耐药性[48–50]。在德国的肉鸡中发现了耐粘菌素的大肠杆菌和 mcr-1 基因[49]，通过潜在的人畜共患病对人类健康构成威胁[51]。在不同的家禽产品和来自不同类型零售商的禽肉中，观察到过敏性大肠杆菌的高流行率 (100%)，特别是针对四环素、庆大霉素、粘菌素和 β-内酰胺类；耐药基因以 tetA 和 blaTEM 为主[10]。Aklilu 等人分析了马来西亚食用动物中的肉鸡和零售鸡，发现 37.5%(27/72) 的大肠杆菌至少一种抗生素耐药基因呈阳性[52]。这种情况在越南更为严重，在大约一半的鸡肉样本中发现了耐粘菌素的大肠杆菌，大多数抗生素耐药大肠杆菌含有 mcr-1 基因[53]。Abdallah 等人分析了埃及 Zagazig 的零售羊肉样本，在近五分之一的样本中发现了抗生素耐药大肠杆菌[54]。在埃及，从 78%(51/65) 的生牛肉和 53%(24/45) 的即食牛肉产品中分离出了耐粘菌素大肠杆菌，存在牛的个体传播[55]。Ahmad 等人调查了来自巴基斯坦白沙瓦地区农场、牛奶供应商和商店的原料奶样本，以检测耐多药大肠杆菌。在 28 株分离的大肠杆菌中，6 株为耐多种抗生素大肠杆菌，且均鉴定出 blaCTX-M 耐药基因[56]。此外，近年来小型和路边门店的即食街头食品中也发现了抗生素耐药大肠杆菌，对人类健康构成重大风险[4,57]。街头即食食品 (含鸡肉) 中大肠杆菌对头孢吡肟、头孢噻肟、亚胺培南、美罗培南耐药的比例为 16.9-72.9%；最常见的 ARGs 包括 blaTEM(40.68%)、blaCTX(32.20%)、blaSHV(10.17%) 和 blaNDM，表明存在从食物传播给人类的潜在风险[4]。

同时，在印度孟买零售市场销售的鱼类和贝类等新鲜海鲜中发现了抗生素耐药大肠杆菌[3]。约 71.58-95% 的大肠杆菌分离株对 β-内酰胺类和头孢菌素 (包括头孢噻肟、头孢多肟和头孢他啶) 耐药，其中 blaCTX-M 耐药率为 62.37%，blaSHV 耐药率为 23.35%，blaTEM 耐药率为 2.6%，blaOXA 耐药率为 7.06%，blaNDM 耐药率为 4.42%，blaVIM 耐药率为 0.88%，表明耐多种抗生素大肠杆菌在海鲜消费者和处理者中传播的风险较高[3]。这说明海洋环境中的贝类受到河流、生活污水和污水处理厂等含有抗生素耐药大肠杆菌的污水的影响[58]。

因此，在食用动物中使用抗生素导致了从农场到餐桌的整个过程中耐药细菌的选择。必须改善卫生条件，并采取由有关不同组织协调的部门间行动。

2.2 动物粪便

动物粪便是含有大肠杆菌及其 ARGs 的大量抗生素耐药菌池，导致抗生素耐药大肠杆菌及其 ARGs 传播到环境中，是一种重要且危险的环境污染物[59]。研究人员从南非本土食草动物 (包括角马、斑马和长颈鹿)、宠物和农场猪的粪便中分离出大肠杆菌，以分析耐药性的传播模式[61]。结果表明，南非本土食草动物可能是抗生素耐药大肠杆菌传播的重要载体[61]。Rehman 等人从中国散养的食用动物 (如鸡、仔猪和牦牛) 中分离的抗生素耐药大肠杆菌菌株中整合子[62]。从中国散养食用动物中分离到的大肠杆菌共 432 株，对氨苄西林、头孢曲松、氯霉素、庆大霉素、链霉素、磺胺、四环素等至少一类抗生素耐药。在 6% 的抗生素耐药大肠杆菌菌株中检测到整合子，表明必须要采取有效的预防措施来防止抗生素耐药大肠杆菌的转移[62]。Weiss 等人分析了来自乌干达西部家畜、人类和野生灵长类动物的 1685 份大肠杆菌粪便样本，发现 499 株大肠杆菌对所测试的 11 种抗生素具有耐药性[66]。人、家畜和野生灵长类分离株的耐药率分别为 57.4%、19.5% 和 16.3%。随着当地抗生素价格的提高，抗生素耐药型大肠杆菌的百分比下降。此外，33.2% 的 1 类整合子耐药菌株广泛分布于不同宿主的大肠杆菌菌株中[66]。在德国，研究人员分析了鸭、猪等多种动物的粪便，发现耐喹诺酮的大肠杆菌广泛存在于牲畜和食品中[64]。2010 年至 2020 年的一项调查显示，从韩国健康肉鸡、牛和猪的粪便中分离出的大肠杆菌 90% 以上对喹诺酮类药物和头孢菌素具有高耐药性[12]。此外，犬粪中还检出耐头孢唑林 (43.1%)、氟喹诺酮 (22.1%) 和 β-内酰胺耐药 (9.4%) 的抗生素耐药大肠杆菌，提示可能存在伴侣动物耐药传播[2]。

McIver 等[23] 对南非集约化养殖家禽中抗生素耐药大肠杆菌进行了流行病学研究。结果显示，67.3% 的家禽业大肠杆菌对氨苄西林 (48.1%)、四环素 (27.4%)、萘啶酸 (20.3%)、甲氧苄啶-磺胺甲恶唑 (13.9%) 和氯霉素 (11.7%) 耐药，与家禽业使用的抗生素相似。最常检出的 ARGs 为 blaCTX-M(100%)、sul1(80%)、tetA(77%) 和 tetB(71%)。这表明集约化家禽养殖可能是细菌抗生素耐药性传播的水库和潜在媒介，必须及时采取措施，减少细菌耐药性从家禽业传播给人类[23]。在卢旺达东部省的牛、山羊、猪和家禽粪便中检测到对第三代头孢菌素或喹诺酮类药物耐药的抗生素耐药大肠杆菌和沙门氏菌[11]，并发现在谨慎使用抗生素的农场，抗生素耐药大肠杆菌对周围野生动物和环境的影响较小。

成年牛和小牛肉屠宰场废水中抗生素耐药大肠杆菌的百分比为 5% 至 87.5%，每天约有 1010 株耐多种抗生素大肠杆菌被检测到排放到受污染的河流中[60]。Wandee 等[63] 分析了开放式养猪场系统中抗生素耐药大肠杆菌和抗生素残留的流行情况，他们观察到开放式养猪场系统中存在高水平的过敏性大肠杆菌种群，这可能是由于供水中的抗生素污染以及新霉素或粘菌素等抗生素的额外应用，对猪粪中过敏性大肠杆菌的流行产生了重大影响[63]。这表明应提出更适当的废物管理指南，可减少致病性耐多药大肠杆菌及其 ARGs 的传播。

此外，管理不善，如在饲料中持续使用抗生素或抗生素在肉鸭垫草中积累，也可能是细菌耐药性演变的原因[8]。从鸭场垫草中分离出的大肠杆菌对多种抗生素耐药，包括四环素、氨苄西林、强力霉素、氧氟沙星、庆大霉素等，表明大肠杆菌对多种抗生素的耐药率较高。禽类垫草被认为是细菌耐药性进化的理想环境[8]。

2.3 水生环境中的抗生素耐药大肠杆菌

目前，抗生素耐药和 MDR 大肠杆菌在水生环境中不断涌现，对动物和人类的健康造成了极大的威胁[74]。其中，HGT 的转移效应对抗生素耐药性的传播有显著影响[75]。Hamelin 等人利用 DNA 微阵列法检测了圣克莱尔河和底特律河不同地表水区大肠杆菌分离株中的 ARGs[76]，结果发现，位于城市站点的废水出水口下游 48% 的水样携带至少一种 ARG 的大肠杆菌分离株，高于其他站点 (24%)。这表明来自城市污水的抗生素耐药大肠杆菌可能在水生生态系统中广泛传播[76]。多种抗生素耐药大肠杆菌在溪流等小水体中的水平传播主要是由径流和淋滤引起的，影响邻近水体或大水体。在雨季放牧期间，抗生素耐药大肠杆菌的百分比增加到 30-35%，高于干旱期放牧 (<7%)。氯霉素和四环素最常见于水中。此外，耐多种抗生素大肠杆菌，即使对 8 种不同的抗生素具有耐药性，也占总耐药分离株的 23%，它们起源于动物和人类。这表明农村喀斯特地区的地下水饮用

水容易受到抗生素耐药菌污染[77]。Zhang 等发现文玉河流域有 61 种抗生素 (包括喹诺酮类、四环素类、磺胺类) 残留与耐喹诺酮类大肠杆菌相关[78]。在新西兰，城市和农村河流中的抗生素耐药大肠杆菌浓度在 10 至 100 CFU/mL 之间，耐氨苄西林大肠杆菌在两条河流中最为常见[15]。Malema 等人利用 PCR 和圆盘扩散法研究了南非收集的雨水中致病性大肠杆菌菌株的流行情况和耐药性[79]。结果显示，大肠杆菌对头孢菌素的耐药性最高 (76%)，52% 的菌株存在多重耐药; 所有检测的致病性大肠杆菌分离株均对庆大霉素敏感，说明收集的雨水在处理前不宜供人饮用。

Laroche 等在法国农村喀斯特水系统具有代表性的相互关联地点 (包括溪流、燕子洞、泉水和水井) 的水中，共发现 436 株对 17 种抗生素具有耐药性的大肠杆菌[77]。Fakhr 等调查了埃及东北部扎加齐格市饮用水中致泻性抗生素耐药大肠杆菌的污染情况[80]，结果表明，从 300 份饮用水样品中分离出 16 株大肠杆菌，所有大肠杆菌分离株至少对一种抗生素耐药，62.5% 的大肠杆菌对三种或三种以上抗生素耐药，大肠杆菌对头孢噻肟、四环素和氨苄西林的耐药率为 50-62.5%，饮用水中粪便污染的高频率表明由抗生素耐药大肠杆菌引起腹泻的高风险[80]。Bong 等调查了拉鲁特河受人为影响的抗生素耐药大肠杆菌的流行率和多样性，发现携带 tet 和 sul 基因的抗生素耐药大肠杆菌在废水中的浓度为4.1×10^3-4.7×10^3 CFU/mL，高于河水；这表明大肠杆菌是淡水河流环境中 ARGs 的主要载体[74]。应采取更有效的措施，预防和控制抗生素耐药大肠杆菌的流行和传播风险。

2.4 抗生素耐药大肠杆菌中垂直基因转移的模式

垂直基因转移 (Vertical gene transfer, VGT) 和水平基因转移 (HGT) 是 AGRs 在大肠杆菌中传播的两种主要机制[25]。VGT 被定义为基因从父母转移到他们的后代。相比之下，水平基因转移，即生物体将遗传物质传递给其他细胞而不是其后代的过程，使得基因转移更加复杂。HGT 被认为是最常见的作用机制，在动物源性大肠杆菌中抗生素耐药性的快速传播中起着重要作用，导致 ARGs 在大肠杆菌与其他细菌之间迅速而广泛地传播[29]。通过 HGT 传播抗生素耐药大肠杆菌主要取决于耐药质粒可以在不同环境和宿主之间传播[27,82,83]。HGT 主要涉及 MGEs 中携带的 ARGs，如转座子、质粒和整合子[84,85]。动物源性大肠杆菌与其他细菌群体之间 ARGs 的 HGT 转移主要受三种机制模式控制，包括偶联、转化和转导[84,86,87]。其中，接合是 HGT 的主要方式，质粒通过菌毛孔在相互接触的供体细胞和受体细胞之间传递。食用动物大肠杆菌中携带 ARGs(如 mcr-1 基因) 的质粒通过接合转移到人类大肠杆菌和沙门氏菌的受体中，使其对多粘菌素、阿帕霉素、氯霉素等产生耐药性[88,89]。转化是指从环境中转移短的游离 DNA，不需要活的供体细胞，并纳入受体细胞。转导是 DNA 通过噬菌体转移的过程[84,85]。亚最低抑制浓度 (MIC) 四环素可促进大肠杆菌质粒 (PR4) 的偶联转移，加速 HGT 效应[90]。这些机制可能导致大肠杆菌的快速进化，因为 HGT 可以在抗生素存在下增加其适应性[91]。

3 抗生素耐药大肠杆菌及其 ARGs 的处理

3.1 紫外线处理

传统的紫外线处理系统可以通过破坏 DNA 分子中的碱基对和抑制 DNA 复制来有效地消灭抗生素耐药大肠杆菌[92]。紫外线处理不产生任何化学副产物, 在处理废水和饮用水中的过敏性大肠杆菌及其 ARGs 方面越来越普遍。Rizzo 等人评估了紫外线辐射对来自城市污水处理厂的抗生素耐药大肠杆菌的影响[93]。经$1.25 \times 10^4 \mu Ws/cm^2$剂量的紫外线照射 1 h 后，抗生素耐药型大肠杆菌灭活，而传统的氯化消毒工艺 (浓度为 2 mg/L) 对所研究的大肠杆菌的耐药性没有影响。此外，紫外线处理没有改变大肠杆菌对阿莫西林和磺胺甲恶唑的耐药性 (MIC>256 或 >1024μg/mL)，但影响了对环丙沙星的耐药性 (MIC 降低了 33-50%)。常规消毒可能对抗生素耐药菌失活无效，这可能与紫外线水平有关[93]。使用合适的紫外线水平来消除过敏性大肠杆菌是至关重要的。Pang 等人发现，40 mJ/cm^2的紫外线剂量导致耐氨苄西林大肠杆菌减少 5.5 log，但较低紫外线剂量 (5-20 mJ/cm^2) 的大肠杆菌耐药性更强[94]。Zhang 等从污水处理厂分离出抗生素耐药大肠杆菌，并评估了紫外线照射对细菌及其

ARGs 的影响[34]。发现耐多药大肠杆菌对紫外线的抵抗力更强。

3.2 表面等离子体氧化

表面等离子体氧化可以破坏细菌细胞膜，改变蛋白质的构象结构，破坏 DNA 的核苷酸碱基[73]。近年来，表面等离子体氧化法因其效率高、设备简单、无外源化学残留等优点在各种细菌灭活中受到越来越多的关注[95]。Li 等研究了表面等离子体氧化对消除水环境中抗生素耐药大肠杆菌及其 ARGs 的影响[73]。结果表明，表面等离子体氧化处理 10 min 后，6.6 log 大肠杆菌被灭活，大肠杆菌对四环素、庆大霉素和阿莫西林的耐药性显著降低，这可能与活性氧和活性氮有关。表面等离子体氧化处理后，大肠杆菌的部分 ARGs(包括 tet(C)、tet(W)、blaTEM-1 和 aac(3)-II) 被显著去除，整合子基因 intI1 等 ARGs 的共轭转移被显著抑制。这一结果表明，表面等离子体氧化在去除水环境中的抗生素耐药大肠杆菌及其 ARGs 方面具有潜在的应用前景[73]。Song 等人 (2021) 发现，表面等离子体处理 10 分钟后，7.0 log 抗生素耐药大肠杆菌灭活，其相关 ARGs(包括 tetC、tetW、blaTEM-1、aac(3)-II 和 intI1) 减少了 1.04-2.3 log 拷贝，这可能是氧化性物质 (如 H_2O_2、O_3、NO_2^- 等) 的作用[31]。等离子体处理后，大肠杆菌对四环素、阿莫西林、庆大霉素的耐药性降低了 96.9% - 98.4%，ARGs 的 HGT 抑制了 63%。总的来说，表面等离子体处理可能是去除水环境中抗生素耐药大肠杆菌和相关 ARGs 的有效方法[31]。

3.3 其他方法

其他方法如生物炭、噬菌体、氧化剂等也已被开发用于灭活抗生素耐药大肠杆菌并从水中去除其相关的 ARGs[30,31]。Ye 等利用复合生物炭和多价噬菌体 (phage) 灭活土壤-植物系统中的抗生素耐药大肠杆菌及其 ARGs[30]，联合处理 63 d 后，土壤和生菜组织中抗生素耐药大肠杆菌 K-12 及其 ARGs(如 tetM、tetQ、tetW、AmpC 等) 的丰度显著下降。该研究中使用的一种新型生物技术为抗生素耐药大肠杆菌及其 ARGs 的靶向失活提供了新的思路，从而降低了它们在土壤-植物-人体系统中的分散风险[30]。Zhao 等研究了三种渔业氧化剂 (溴、氯和 $KMnO_4$) 在消毒过的池塘水中对抗生素耐药大肠杆菌和抗磺胺基因 sul1 的消毒效果[32] 发现 3 种氧化剂在 5-15 mg/L 的剂量下处理后，抗生素耐药大肠杆菌被完全灭活，sul1 被有效去除，且氯对抗生素耐药大肠杆菌的清除能力高于溴和 $KMnO_4$; 氯和溴对硫的去除率中等。由此可知，氧化处理可能有助于实际消毒，以防止抗生素耐药菌及其 ARGs 在水产养殖环境中的传播[32]。此外，其他生物或化学方法 (如过氧乙酸) 也能有效去除废水中的抗生素耐药大肠杆菌 ($<1 \times 10^2$ CFU/mL)[14,71]。

4 对抗畜牧源的抗生素耐药大肠杆菌的抗生素替代品

目前，包括欧洲 (如 1986 年的瑞典、1995 年的丹麦和挪威、1996 年的德国等)、亚洲 (如 2008 年的日本、2011 年的韩国、2017 年的越南、2020 年的中国等) 和美国在内的 128 个国家已经采取行动，通过禁止、限制和减少动物饲料中促生长抗生素的用量来规范食用动物中抗生素的使用[99,100]。此外，一些益生菌、中草药和抗菌药物已经被开发出来，以取代抗生素的使用。

4.1 益生菌

益生菌是抗生素的潜在替代品之一，因为它们可以调节肠道菌群，提高动物的生长性能。如枯草芽孢杆菌能增强免疫反应，维持肠道菌群平衡，增加乳酸菌和双歧杆菌的丰度，减少大肠杆菌和产气荚膜梭菌。此外，枯草芽孢杆菌产生的短链脂肪酸可以促进肠道健康[101]。其它如 *B.velezensis* 菌株 ZBG17 对动物肠道内的肠胃液具有很高的稳定性[102]，*B.velezensis* ZBG17 完全抑制肠道内的大肠杆菌和肠炎沙门氏菌等致病菌 6- 8 h，显著提高了肉仔鸡的饲料效率和体液免疫应答。这表明 *B.velezensis* ZBG17 是肉鸡生产中抗生素的潜在替代品[102]。

Bilal 等人发现，饲喂 1.5 g/kg 酿酒酵母 ($<2\times10^6$ CFU/g) 和发酵乳杆菌 ($<1\times10^7$ CFU/g) 作为益生元和益生菌，可抑制大肠杆菌 O78 的生长[103]。在动物饲料中添加益生元和益生菌可以促进和保护绒毛结构，减少病原体定植，如大肠杆菌在家禽肠道中的定植，从而提高动物健康和生产性能[103]。这些数据为肉鸡饲料工业提供了一种商业上可行的抗生素替代品的新思路。

4.2 DNA 条形码候选序列鉴定效率评价

植物提取物在抑菌方面发挥着重要作用，由于其对由抗生素耐药 *E. coli* 引起的大肠菌群腹泻具有积极作用，正被考虑作为抗生素的替代品[37]。Dell 'Anno 等人研究了核桃/栗子单宁 (0.75%) 提取物、龙纳迪酸 (0.25%) 和三丁酸甘油酯 (0.2%) 对猪大肠杆菌病的影响[104]。研究发现，植物提取物联合使用可提高断奶仔猪粪便中乳酸杆菌与大肠菌群的比例，降低仔猪腹泻的发生率[104]。这表明植物提取物被认为是抗生素的潜在替代品，可以维持猪的健康和生产性能。植物提取物浓缩单宁对禽抗生素耐药大肠杆菌具有良好的体外抗菌活性[105]。最近的研究表明，各种植物精油 (包括萜类和苯丙烯) 具有强大的抗菌活性，可以有效地减少大肠杆菌等病原体[106–108]。在饲粮中添加 300 – 600 mg/kg 肉桂皮油后，肉鸡盲肠前大肠杆菌数量显著降低[109]。同时，精油可以维持肠道健康并促进生长，这表明精油可以在动物生产中作为抗生素的绿色替代品来对抗抗生素耐药大肠杆菌[108]。

4.3 抗菌肽

在针对抗生素耐药菌的不同临床试验阶段 (I-III 期)，有研究表明，少数抗菌肽 (如 plectasin、AA139、LL-37、hLF1-11、ZY4 等) 由于耐药低，比传统抗生素更有效[110–113]。抗菌肽具有较强的抗菌活性，可增加细菌内外膜的通透性，破坏细胞膜，促进细胞内物质的渗漏，从而导致低耐药性[114]。细菌素是一种对大肠杆菌具有较强抗菌活性的肽或前体肽[115]。多个 Ib-M 肽 (长度为 20 个氨基酸) 对耐氨基糖苷型大肠杆菌 O157:H7 AC188 表现出较强的活性，MIC 值为 1.6 – 6.3μM; 暴露于 1 × MIC Ib-M 肽 4 小时后，大肠杆菌的数量减少了 95% 以上，这表明开发新的抗生素替代品来对抗抗生素耐药大肠杆菌具有潜在的前景[116]。革兰氏阴性菌产生的微球蛋白被认为是抗生素的潜在替代品[117]。Lu 等证实，大肠杆菌产生的微霉素 PDI (mcpdi) 可通过破坏细菌膜来抑制耐多药大肠杆菌和志贺氏菌分离株，表明其作为抗生素替代品的潜力[118]。其他抗菌肽，如 dermaseptin、cathelicidin-OH-CATH30 和 magainin-PGLa，为耐多药细菌 (包括大肠杆菌) 提供了替代疗法[41–43]。一般来说，尽管几种抗菌肽提供了减少抗生素耐药菌的有希望的收入，但由于生产成本高，体内稳定性差以及其他副作用，前面的路仍然很长[119,120]。

5 结论

畜牧业抗生素使用的增加导致了抗生素耐药大肠杆菌及其 ARGs 的传播。在这里，我们回顾了农场动物源性抗生素耐药大肠杆菌的流行情况。消毒方法 (如紫外线处理、表面等离子体氧化、生物炭、氧化剂)，强调了一些抗生素的替代品 (包括益生菌，植物提取物和抗菌肽) 来对抗抗生素耐药大肠杆菌，这可能有助于我们解决畜牧业来源的细菌抗生素耐药性问题。

创新说明

本综述的目的是探讨来自畜牧业、废物处理和水生环境的抗生素耐药大肠杆菌的流行趋势。

重点介绍了抗生素抗性基因的消除方法和可能的替代方法。如紫外线 (UV) 处理、表面等离子体氧化和生物炭等用于有效消除抗生素耐药大肠杆菌。另外一些益生菌、植物提取物和抗菌肽作为抗生素的有希望的替代品。

本综述为进一步研究、开发和应用新的策略来减少农场动物源性大肠杆菌的抗生素耐药性提供了新的思路。

参考文献

[1] Rugumisa T B, Call R D, Mwanyika O G, et al. Comparison of the prevalence of antibiotic-resistant Escherichia coli isolates from commercial-layer and free-range chickens in Arusha district, Tanzania[J]. African Journal of Microbiology Research,2016,10(34):1422-1429.

[2] Chen J W, Huang H H, Chang S M, et al. Antibiotic-Resistant Escherichia coli and Sequence Type 131 in Fecal Colonization in Dogs in Taiwan [J]. Microorganisms, 2020, 8(9): 1439.

[3] Singh A S, Nayak B B, Kumar S H. High Prevalence of Multiple Antibiotic-Resistant, Extended-Spectrum β-Lactamase (ESBL)-Producing Escherichia coli in Fresh Seafood Sold in Retail Markets of Mumbai, India [J]. Veterinary Sciences, 2020, 7(2): 46.

[4] Giri S, Kudva V, Shetty K, et al. Prevalence and Characterization of Extended-Spectrum β-Lactamase-Producing Antibiotic-Resistant Escherichia coli and Klebsiella pneumoniae in Ready-to-Eat Street Foods [J]. Antibiotics-Basel, 2021, 10(7): 850.

[5] Ewers C, Antao E M, Diehl I, et al. Intestine and Environment of the Chicken as Reservoirs for Extraintestinal Pathogenic Escherichia coli Strains with Zoonotic Potential [J]. Applied and Environmental Microbiology, 2009, 75(1): 184-92.

[6] Knutson K. Chapter 8-Nobody is talking about environmental monitoring [M] KNUTSON K. Food Safety Lessons for Cannabis-Infused Edibles. Academic Press. 2020: 111-37.

[7] Lim J Y, Yoon J W, Hovde C J. A Brief Overview of Escherichia coli O157:H7 and Its Plasmid O157 [J]. Journal of Microbiology and Biotechnology, 2010, 20(1): 5-14.

[8] Lin Y, Zhao W, Shi Z D, et al. Accumulation of antibiotics and heavy metals in meat duck deep litter and their role in persistence of antibiotic-resistant Escherichia coli in different flocks on one duck farm [J]. Poultry Science, 2017, 96(4): 997-1006.

[9] Sorbara M T, Dubin K, Littmann E R, et al. Inhibiting antibiotic-resistant Enterobacteriaceae by microbiota-mediated intracellular acidification [J]. Journal of Experimental Medicine, 2019, 216(1): 84-98.

[10] García-béjar B, Martín I G D, Arévalo-villena M, et al. High Prevalence of Antibiotic-Resistant Escherichia coli Isolates from Retail Poultry Products in Spain [J]. Animals, 2021, 11(11): 3197.

[11] Manishimwe R, Moncada P M, Musanayire V, et al. Antibiotic-Resistant Escherichia coli and Salmonella from the Feces of Food Animals in the East Province of Rwanda [J]. Animals, 2021, 11(4): 1013.

[12] Song H J, Kim S J, Moon D C, et al. Antimicrobial Resistance in Escherichia coli Isolates from Healthy Food Animals in South Korea, 2010-2020 [J]. Microorganisms, 2022, 10(3): 524..

[13] Levy S B, Marshall B. Antibacterial resistance worldwide: causes, challenges and responses [J]. Nature Medicine, 2004, 10(12): S122-S9.

[14] Reinthaler F F, Posch J, Feierl G, et al. Antibiotic resistance of E-coli in sewage and sludge [J]. Water Research, 2003, 37(8): 1685-90.

[15] Van Hamelsveld S, Adewale M E, Kurenbach B, et al. Prevalence of antibiotic-resistant Escherichia coli isolated from urban and agricultural streams in Canterbury, New Zealand [J]. Fems Microbiology Letters, 2019, 366(8): fnz104.

[16] Administration, D. Standards for Growing, Harvesting, Packing, and Holding of Produce for Human Consumption; Department of Health and Human Services, Food and Drug Administration: College Park [J]. MD, USA, 2015.

[17] Van Driel A A, Notermans D W, Meima A, et al. Antibiotic resistance of Escherichia coli isolated from uncomplicated UTI in general practice patients over a 10-year period [J]. European Journal of Clinical Microbiology & Infectious

Diseases, 2019, 38(11): 2151-2158.

[18] Bhardwaj D K, Taneja N K, Shivaprasad D P, et al. Phenotypic and genotypic characterization of biofilm forming, antimicrobial resistant, pathogenic Escherichia coli isolated from Indian dairy and meat products [J]. International Journal of Food Microbiology, 2021, 336: 108899.

[19] Bean D C, Livermore D M, Papa I, et al. Resistance among Escherichia coli to sulphonamides and other antimicrobials now little used in man [J]. Journal of Antimicrobial Chemotherapy, 2005, 56(5): 962-964.

[20] Brynildsen M P, Winkler J A, Spina C S, et al. Potentiating antibacterial activity by predictably enhancing endogenous microbial ROS production [J]. Nature Biotechnology, 2013, 31(2): 160-165.

[21] Yang H C, Chen S, White D G, et al. Characterization of multiple-antimicrobial-resistant Escherichia coli isolates from diseased chickens and swine in China [J]. Journal of Clinical Microbiology, 2004, 42(8): 3483-3489.

[22] Zhang X L, Li Y X, Liu B, et al. Prevalence of Veterinary Antibiotics and Antibiotic-Resistant Escherichia coli in the Surface Water of a Livestock Production Region in Northern China [J]. Plos One, 2014, 9(11): e111026.

[23] Mciver K S, Amoako D G, Abia A L K, et al. Molecular Epidemiology of Antibiotic-Resistant Escherichia coli from Farm-to-Fork in Intensive Poultry Production in KwaZulu-Natal, South Africa [J]. Antibiotics-Basel, 2020, 9(12): 850.

[24] Schink A K, Kadlec K, Kaspar H, et al. Analysis of extended-spectrum-lactamase-producing Escherichia coli isolates collected in the GERM-Vet monitoring programme [J]. Journal of Antimicrobial Chemotherapy, 2013, 68(8): 1741-1749.

[25] Messerer M, Fischer W, Schubert S. Investigation of horizontal gene transfer of pathogenicity islands in Escherichia coli using next-generation sequencing [J]. Plos One, 2017, 12(7): e0179880.

[26] Poole T L, Callaway T R, Norman K N, et al. Transferability of antimicrobial resistance from multidrug-resistant Escherichia coli isolated from cattle in the USA to E.coli and SalmonellaNewport recipients [J]. Journal of Global Antimicrobial Resistance, 2017, 11: 123-132.

[27] Blahna M T, Zalewski C A, Reuer J, et al. The role of horizontal gene transfer in the spread of trimethoprim–sulfamethoxazole resistance among uropathogenic Escherichia coli in Europe and Canada [J]. Journal of Antimicrobial Chemotherapy, 2006, 57(4): 666-672.

[28] Lambrecht E, Van C E, Boon N, et al. Transfer of Antibiotic Resistance Plasmid from Commensal E. coli towards Human Intestinal Microbiota in the M-SHIME: Effect of E. coli dosis, Human Individual and Antibiotic Use [J]. Life-Basel, 2021, 11(3): 192.

[29] Viñes J, Cuscó A, Napp S, et al. Transmission of Similar Mcr-1 Carrying Plasmids among Different Escherichia coli Lineages Isolated from Livestock and the Farmer [J]. Antibiotics-Basel, 2021, 10(3): 313.

[30] Ye M, Sun M M, Zhao Y C, et al. Targeted inactivation of antibiotic-resistant Escherichia coli and Pseudomonas aeruginosa in a soil-lettuce system by combined polyvalent bacteriophage and biochar treatment [J]. Environmental Pollution, 2018, 241: 978-987.

[31] Song R Y, Li H, Kang Z, et al. Surface plasma induced elimination of antibiotic-resistant Escherichia coli and resistance genes: Antibiotic resistance, horizontal gene transfer, and mechanisms [J]. Separation and Purification Technology, 2021, 275: 119185.

[32] Zhao X, Su H, Xu W, et al. Removal of antibiotic resistance genes and inactivation of antibiotic-resistant bacteria by oxidative treatments[J]. Science of the Total Environment, 2021, 778: 146348.

[33] Li H, Kang Z, Jiang E, et al. Plasma induced efficient removal of antibiotic-resistant Escherichia coli and antibiotic resistance genes, and inhibition of gene transfer by conjugation[J]. Journal of Hazardous Materials, 2021, 419: 126465.

[34] Zhang C M, Xu L M, Wang X C, et al. Effects of ultraviolet disinfection on antibiotic-resistant Escherichia coli from wastewater: inactivation, antibiotic resistance profiles and antibiotic resistance genes [J]. Journal of Applied Microbiology, 2017, 123(1): 295-306.

[35] De Mandal S, Panda A K, Murugan C, et al. Antimicrobial peptides: novel source and biological function with a special focus on entomopathogenic nematode/bacterium symbiotic complex[J]. Frontiers in Microbiology, 2021, 12: 555022.

[36] Jiang C, Ding L, Dong Q, et al. Effects of root extracts of three traditional Chinese herbs as dietary supplements on dry matter intake, average daily gain, rumen fermentation and ruminal microbiota in early weaned yak calves[J]. Animal Feed Science and Technology, 2021, 278: 115002.

[37] Rabelo-Ruiz M, Ariza-Romero J J, et al. Allium-based phytobiotic enhances egg production in laying hens through microbial composition changes in ileum and cecum[J]. Animals, 2021, 11(2): 448.

[38] Ramirez S Y, Peñuela L M, Ospina M A. Effects of oregano (Lippia origanoides) essential oil supplementation on the performance, egg quality, and intestinal morphometry of Isa Brown laying hens [J]. Veterinary World, 2021, 14(3): 595-602.

[39] Rima M, Rima M, Fajloun Z, et al. Antimicrobial Peptides: A Potent Alternative to Antibiotics [J]. Antibiotics, 2021, 10(9): 1095.

[40] Xia J, Ge C, Yao H. Antimicrobial peptides from black soldier fly (Hermetia illucens) as potential antimicrobial factors representing an alternative to antibiotics in livestock farming[J]. Animals, 2021, 11(7): 1937.

[41] Li S A, Lee W H, Zhang Y. Efficacy of OH-CATH30 and Its Analogs against Drug-Resistant Bacteria In Vitro and in Mouse Models [J]. Antimicrobial Agents and Chemotherapy, 2012, 56(6): 3309-3317.

[42] Zaïri A, Ferrières L, Latour P, et al. In Vitro Activities of Dermaseptins K4S4 and K4K20S4 against Escherichia coli, Staphylococcus aureus, and Pseudomonas aeruginosa Planktonic Growth and Biofilm Formation [J]. Antimicrobial Agents and Chemotherapy, 2014, 58(4): 2221-2228.

[43] Bechinger B, Juhl D W, Glattard E, et al. Revealing the mechanisms of synergistic action of two magainin antimicrobial peptides[J]. Frontiers in Medical Technology, 2020, 2: 615494.

[44] Büyükkiraz M E, Kesmen Z. Antimicrobial peptides (AMPs): A promising class of antimicrobial compounds [J]. Journal of Applied Microbiology, 2022, 132(3): 1573-1596.

[45] Krizman M, Avgustin J A, Zdovc I, et al. Antimicrobial Resistance and Molecular Characterization of Extended-Spectrum β-Lactamases and Other Escherichia coli Isolated from Food of Animal Origin and Human Intestinal Isolates [J]. Journal of Food Protection, 2017, 80(1): 113-120.

[46] Davis G S, Waits K, Nordstrom L, et al. Antibiotic-resistant Escherichia coli from retail poultry meat with different antibiotic use claims[J]. BMC microbiology, 2018, 18: 1-7.

[47] Balcázar J L. How do bacteriophages promote antibiotic resistance in the environment? [J]. Clinical Microbiology and Infection, 2018, 24(5): 447-449.

[48] Azam M, Mohsin M, Sajjad U R, et al. Virulence-associated genes and antimicrobial resistance among avian pathogenic Escherichia coli from colibacillosis affected broilers in Pakistan [J]. Tropical Animal Health and Production, 2019, 51(5): 1259-1265.

[49] Hornsey M, Betts J W, Mehat J W, et al. Characterization of a colistin-resistant Avian Pathogenic Escherichia coli ST69 isolate recovered from a broiler chicken in Germany [J]. Journal of Medical Microbiology, 2019, 68(1): 111-114.

[50] Awad A M, El-Shall N A, Khalil D S, et al. Incidence, pathotyping, and antibiotic susceptibility of avian pathogenic Escherichia coli among diseased broiler chicks[J]. Pathogens, 2020, 9(2): 114.

[51] Wang P, Zhang J, Chen Y, et al. ClbG in avian pathogenic Escherichia coli contributes to meningitis development

in a mouse model[J]. Toxins, 2021, 13(8): 546.

[52] Aklilu E, Harun A, Singh K K B. Molecular characterization of bla NDM, bla OXA-48, mcr-1 and bla TEM-52 positive and concurrently carbapenem and colistin resistant and extended spectrum beta-lactamase producing Escherichia coli in chicken in Malaysia[J]. BMC Veterinary Research, 2022, 18(1): 190.

[53] Nakayama T, Thi H L, Thanh P N, et al. Abundance of colistin-resistant Escherichia coli harbouring mcr-1 and extended-spectrum β-lactamase-producing E. coli co-harbouring blaCTX-M-55or-65with blaTEM isolates from chicken meat in Vietnam [J]. Archives of Microbiology, 2022, 204(2): 137.

[54] Abdallah H M, Al Naiemi N, Elsohaby I, et al. Prevalence of extended-spectrum β-lactamase-producing Enterobacterales in retail sheep meat from Zagazig city, Egypt[J]. BMC veterinary research, 2022, 18(1): 191.

[55] Sabala R F, Usui M, Tamura Y, et al. Prevalence of colistin-resistant Escherichia coli harbouring mcr-1 in raw beef and ready-to-eat beef products in Egypt[J]. Food Control, 2021, 119: 107436.

[56] Ahmad I, Khattak S, Ali R, et al. Prevalence and molecular characterization of multidrug-resistant Escherichia coli O157: H7 from dairy milk in the Peshawar region of Pakistan [J]. Journal of Food Safety, 2021, 41(6): e12941.

[57] O'flaherty e, Borrego C M, Balcázar J L, et al. Human exposure assessment to antibiotic-resistant Escherichia coli through drinking water [J]. Science of the Total Environment, 2018, 616: 1356-1364.

[58] Jeong S H, Kwon J Y, Shin S B, et al. Antibiotic resistance in shellfish and major inland pollution sources in the drainage basin of Kamak Bay, Republic of Korea[J]. Environmental Monitoring and Assessment, 2021, 193: 1-19.

[59] Checcucci A, Trevisi P, Luise D, et al. Exploring the animal waste resistome: the spread of antimicrobial resistance genes through the use of livestock manure[J]. Frontiers in Microbiology, 2020, 11: 536406.

[60] Um M M, Barraud O, Kérourédan M, et al. Comparison of the incidence of pathogenic and antibiotic-resistant Escherichia coli strains in adult cattle and veal calf slaughterhouse effluents highlighted different risks for public health[J]. Water research, 2016, 88: 30-38.

[61] King T L B, Schmidt S. Assessment of three indigenous South African herbivores as potential reservoirs and vectors of antibiotic-resistant Escherichia coli[J]. European Journal of Wildlife Research, 2017, 63: 1-8.

[62] Rehman M U, Zhang H, Huang S C, et al. Characteristics of Integrons and Associated Gene Cassettes in Antibiotic-Resistant Escherichia coli Isolated from Free-Ranging Food Animals in China [J]. Journal of Food Science, 2017, 82(8): 1902-1907.

[63] Wandee S, Chan R, Chiemchaisri W, et al. Alteration of antibiotic-resistant phenotypes and minimal inhibitory concentration of Escherichia coli in pig farming: Comparison between closed and open farming systems[J]. Science of The Total Environment, 2021, 781: 146743.

[64] Juraschek K, Deneke C, Schmoger S, et al. Phenotypic and genotypic properties of fluoroquinolone-resistant, qnr-carrying Escherichia coli isolated from the German food chain in 2017[J]. Microorganisms, 2021, 9(6): 1308.

[65] Suzuki Y, Hiroki H, Xie H, et al. Antibiotic-resistant Escherichia coli isolated from dairy cows and their surrounding environment on a livestock farm practicing prudent antimicrobial use[J]. International Journal of Hygiene and Environmental Health, 2022, 240: 113930.

[66] Weiss D, Wallace R M, Rwego I B, et al. Antibiotic-resistant Escherichia coli and class 1 integrons in humans, domestic animals, and wild primates in rural Uganda[J]. Applied and environmental microbiology, 2018, 84(21): e01632-18.

[67] Schwermer C U, Krzeminski P, Wennberg A C, et al. Removal of antibiotic resistant E-coli in two Norwegian wastewater treatment plants and by nano- and ultra-filtration processes [J]. Water Science and Technology, 2018, 77(4): 1115-1126.

[68] Osińska A, Korzeniewska E, Harnisz M, et al. The occurrence of antibiotic-resistant bacteria, including Escherichia

coli, in municipal wastewater and river water [J]. E3S Web of Conferences, 2019, 100: 00061.

[69] Bojar B, Sheridan J, Beattie R, et al. Antibiotic resistance patterns of Escherichia coli isolates from the clinic through the wastewater pathway [J]. International Journal of Hygiene and Environmental Health, 2021, 238: 113863.

[70] Gregova G, Kmet V, Szaboova T. New Insight on Antibiotic Resistance and Virulence of Escherichia coli from Municipal and Animal Wastewater[J]. Antibiotics 2021, 10: 1111.

[71] Zanotto C, Bissa M, Illiano E, et al. Identification of antibiotic-resistant Escherichia coli isolated from a municipal wastewater treatment plant [J]. Chemosphere, 2016, 164: 627-633.

[72] Yuan W, Tian T, Yang Q, et al. Transfer potentials of antibiotic resistance genes in Escherichia spp. strains from different sources[J]. Chemosphere, 2020, 246: 125736.

[73] Summerlin H N, Pola C C, Mclamore E S, et al. Prevalence of Escherichia coli and Antibiotic-Resistant Bacteria During Fresh Produce Production (Romaine Lettuce) Using Municipal Wastewater Effluents [J]. Frontiers in Microbiology, 2021, 12: 660047.

[74] Bong C W, Low K Y, Chai L C, et al. Prevalence and diversity of antibiotic resistant Escherichia coli from anthropogenic-impacted Larut River[J]. Frontiers in Public Health, 2022, 10: 794513.

[75] Shao S C, Hu Y Y, Cheng J H, et al. Research progress on distribution, migration, transformation of antibiotics and antibiotic resistance genes (ARGs) in aquatic environment [J]. Critical Reviews in Biotechnology, 2018, 38(8): 1195-208.

[76] Hamelin K, Bruant G, El A, et al. Occurrence of virulence and antimicrobial resistance genes in Escherichia coli isolates from different aquatic ecosystems within the St. Clair River and Detroit River areas [J]. Applied and Environmental Microbiology, 2007, 73(2): 477-484.

[77] Laroche E, Petit F, Fournier M, et al. Transport of antibiotic-resistant Escherichia coli in a public rural karst water supply [J]. Journal of Hydrology, 2010, 392(1-2): 12-21.

[78] Zhang Q Q, Jia A, Wan Y, et al. Occurrences of Three Classes of Antibiotics in a Natural River Basin: Association with Antibiotic-Resistant Escherichia coli [J]. Environmental Science & Technology, 2014, 48(24): 14317-14325.

[79] Malema M S, Abia A L K, Tandlich R, et al. Antibiotic-resistant pathogenic Escherichia coli isolated from rooftop rainwater-harvesting tanks in the Eastern Cape, South Africa[J]. International journal of environmental research and public health, 2018, 15(5): 892.

[80] Fakhr A E, Gohar M K, Atta A H. Impact of Some Ecological Factors on Fecal Contamination of Drinking Water by Diarrheagenic Antibiotic-Resistant Escherichia coli in Zagazig City, Egypt [J]. International Journal of Microbiology, 2016: 6240703.

[81] Ahmed W, Hodgers L, Masters N, et al. Occurrence of Intestinal and Extraintestinal Virulence Genes in Escherichia coli Isolates from Rainwater Tanks in Southeast Queensland, Australia [J]. Applied and Environmental Microbiology, 2011, 77(20): 7394-7400.

[82] Zhou Z C, Shuai X Y, Lin Z J, et al. Prevalence of multi-resistant plasmids in hospital inhalable particulate matter (PM) and its impact on horizontal gene transfer[J]. Environmental Pollution, 2021, 270: 116296.

[83] Yang D, Wang J F, Qiu Z G, et al. Horizontal transfer of antibiotic resistance genes in a membrane bioreactor [J]. Journal of Biotechnology, 2013, 167(4): 441-447.

[84] Liu G, Thomsen L E, Olsen J E. Antimicrobial-induced horizontal transfer of antimicrobial resistance genes in bacteria: a mini-review [J]. Journal of Antimicrobial Chemotherapy, 2022, 77(3): 556-567.

[85] Vinayamohan P G, Pellissery A J, Venkitanarayanan K. Role of horizontal gene transfer in the dissemination of antimicrobial resistance in food animal production[J]. Current Opinion in Food Science, 2022, 47: 100882.

[86] Loayza F, Graham J P, Trueba G. Factors obscuring the role of E. coli from domestic animals in the global antimi-

crobial resistance crisis: an evidence-based review[J]. International journal of environmental research and public health, 2020, 17(9): 3061.

[87] Zhang S, Abbas M, Rehman M U, et al. Dissemination of antibiotic resistance genes (ARGs) via integrons in Escherichia coli: a risk to human health[J]. Environmental Pollution, 2020, 266: 115260.

[88] Liu Y Y, Wang Y, Walsh T R, et al. Emergence of plasmid-mediated colistin resistance mechanism MCR-1 in animals and human beings in China: a microbiological and molecular biological study [J]. Lancet Infectious Diseases, 2016, 16(2): 161-168.

[89] Blake D P, Hillman K, Fenlon D R, et al. Transfer of antibiotic resistance between commensal and pathogenic members of the Enterobacteriaceae under ileal conditions [J]. Journal of Applied Microbiology, 2003, 95(3): 428-436.

[90] Zhang Y H, Ma Q P, Su B M, et al. A study on the role that quorum sensing play in antibiotic-resistant plasmid conjugative transfer in Escherichia coli [J]. Ecotoxicology, 2018, 27(2): 209-216.

[91] Hiltunen T, Virta M, Laine A L. Antibiotic resistance in the wild: an eco-evolutionary perspective[J]. Philosophical Transactions of the Royal Society B: Biological Sciences, 2017, 372(1712): 20160039.

[92] Zimmer J L, Slawson R M. Potential repair of Escherichia coli DNA following exposure to UV radiation from both medium- and low-pressure UV sources used in drinking water treatment [J]. Applied and Environmental Microbiology, 2002, 68(7): 3293-3299.

[93] Rizzo L, Fiorentino A, Anselmo A. Advanced treatment of urban wastewater by UV radiation: Effect on antibiotics and antibiotic-resistant E. coli strains [J]. Chemosphere, 2013, 92(2): 171-176.

[94] Pang Y C, Huang J J, Xi J Y, et al. Effect of ultraviolet irradiation and chlorination on ampicillin-resistant Escherichia coli and its ampicillin resistance gene [J]. Frontiers of Environmental Science & Engineering, 2016, 10(3): 522-530.

[95] Li H, Song R, Wang Y, et al. Inhibited conjugative transfer of antibiotic resistance genes in antibiotic resistant bacteria by surface plasma[J]. Water research, 2021, 204: 117630.

[96] Lee C R, Cho I H, Jeong B C, et al. Strategies to Minimize Antibiotic Resistance [J]. International Journal of Environmental Research and Public Health, 2013, 10(9): 4274-4305.

[97] Lee C R, Lee J H, Kang L W, et al. Educational Effectiveness, Target, and Content for Prudent Antibiotic Use [J]. Biomed Research International, 2015, 2015.

[98] Uchil R R, Kohli G S, Katekhaye V M, et al. Strategies to combat antimicrobial resistance [J]. Journal of clinical and diagnostic research : JCDR, 2014, 8(7): ME01-4.

[99] Salim H M, Huque K S, Kamaruddin K M, et al. Global restriction of using antibiotic growth promoters and alternative strategies in poultry production [J]. Science Progress, 2018, 101(1): 52-75.

[100] Schoenmakers K. How China is getting its farmers to kick their antibiotics habit [J]. Nature, 2020, 586(7830): S60-S62.

[101] Qiu K, Li C, Wang J, et al. Effects of dietary supplementation with Bacillus subtilis, as an alternative to antibiotics, on growth performance, serum immunity, and intestinal health in broiler chickens[J]. Frontiers in Nutrition, 2021, 8: 786878.

[102] Soni R, Keharia H, Bose A, et al. Genome assisted probiotic characterization and application of Bacillus velezensis ZBG17 as an alternative to antibiotic growth promoters in broiler chickens [J]. Genomics, 2021, 113(6): 4061-4174.

[103] Bilal R M, Ul H F, Saeed M, et al. Role of Yeast and Yeast-Derived Products as Feed Additives in Broiler Nutrition [J]. Animal Biotechnology, 2023, 34(2): 392-401.

[104] Dell M, Reggi S, Caprarulo V, et al. Evaluation of Tannin Extracts, Leonardite and Tributyrin Supplementation on Diarrhoea Incidence and Gut Microbiota of Weaned Piglets [J]. Animals, 2021, 11(6): 1693..

[105] Dakheel M M, Alkandari F A, Mueller I, et al. Antimicrobial in vitro activities of condensed tannin extracts on

avian pathogenic Escherichia coli [J]. Letters in Applied Microbiology, 2020, 70(3): 165-172.

[106] Oussalah M, Caillet S, Saucier L, et al. Inhibitory effects of selected plant essential oils on the growth of four pathogenic bacteria: E-coli O157:H7, Salmonella Typhimurium, Staphylococcus aureus and Listeria monocytogenes [J]. Food Control, 2007, 18(5): 414-420.

[107] Abd E W, Ismail M. Tackling experimental colisepticaemia in broiler chickens using phytobiotic essential oils and antibiotic alone or in combination [J]. Iranian Journal of Veterinary Research, 2014, 15(2): 110-115.

[108] Abd E M, El M T, Saad A M, et al. Essential oils and their nanoemulsions as green alternatives to antibiotics in poultry nutrition: a comprehensive review [J]. Poultry Science, 2022, 101(2): 101584..

[109] Chowdhury S, Mandal G P, Patra A K, et al. Different essential oils in diets of broiler chickens: 2. Gut microbes and morphology, immune response, and some blood profile and antioxidant enzymes [J]. Animal Feed Science and Technology, 2018, 236: 39-47.

[110] Nibbering P H, Ravensbergen E, Welling M M, et al. Human lactoferrin and peptides derived from its N terminus are highly effective against infections with antibiotic-resistant bacteria [J]. Infection and Immunity, 2001, 69(3): 1469-1476.

[111] Mygind P H, Fischer R L, Schnorr K M, et al. Plectasin is a peptide antibiotic with therapeutic potential from a saprophytic fungus [J]. Nature, 2005, 437(7061): 975-980.

[112] Mwangi J, Yin Y Z, Wang G, et al. The antimicrobial peptide ZY4 combats multidrug-resistant Pseudomonas aeruginosa and Acinetobacter baumannii infection [J]. Proceedings of the National Academy of Sciences of the United States of America, 2019, 116(52): 26516-26522.

[113] Elliott A G, Huang J X, Neve S, et al. An amphipathic peptide with antibiotic activity against multidrug-resistant Gram-negative bacteria[J]. Nature communications, 2020, 11(1): 3184.

[114] Miao J Y, Liu G, Ke C, et al. Inhibitory effects of a novel antimicrobial peptide from kefir against Escherichia coli [J]. Food Control, 2016, 65: 63-72.

[115] Almeida-Santos A C, Novais C, Peixe L, et al. Enterococcus spp. as a producer and target of bacteriocins: a double-edged sword in the antimicrobial resistance crisis context[J]. Antibiotics, 2021, 10(10): 1215.

[116] Prada S, Flórez J, Farfán A, et al. Antimicrobial activity of Ib-M peptides against Escherichia coli O157: H7 [J]. Plos One, 2020, 15(2): e0229019..

[117] Yang S C, Lin C H, Sung C T, et al. Antibacterial activities of bacteriocins: application in foods and pharmaceuticals[J]. Frontiers in microbiology, 2014, 5: 91530.

[118] Lu S Y, Graça T, Avillan J J, et al. Microcin PDI inhibits antibiotic-resistant strains of Escherichia coli and Shigella through a mechanism of membrane disruption and protection by homotrimer self-immunity[J]. Applied and Environmental Microbiology, 2019, 85(11): e00371-19.

[119] Divyashree M, Mani M K, Reddy D, et al. Clinical Applications of Antimicrobial Peptides (AMPs): Where do We Stand Now? [J]. Protein and Peptide Letters, 2020, 27(2): 120-134.

[120] Zhang Q Y, Yan Z B, Meng Y M, et al. Antimicrobial peptides: mechanism of action, activity and clinical potential[J]. Military Medical Research, 2021, 8: 1-25.

李嘉 （1983-）男，北京市人，北京工商大学大型仪器管理中心, 研究方向：大型仪器开放共享、数据分析、维护、维修。

Jia Li From Beijing Beijing Technology and Business University Large scale instrument and equipment management center. His research focus includes open sharing of large-scale instruments, data analysis, maintenance, and repair.

孙世广 就读于北京工商大学生物工程专业。研究方向为机器学习预测蛋白质多肽结构与功能。

Shiguang Sun, affiliated with the Department of Bioengineering at Beijing Technology and Business University, specializes in machine learning techniques for predicting protein peptide structures and functions.