The Public Health Perspective of Cell-Cultivated Meat Technology in Mitigating Antimicrobial Resistance

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Abstract. The abuse of antibiotics in animal husbandry leads to the widespread diffusion of antibiotic-resistant bacteria through food chains, environmental contamination, and occupational exposure, exacerbating global public health challenges. According to World Health Organization forecast, antimicrobial resistance could cause 10 million annual deaths by 2050 if left uncontrolled. Cell-cultivated meat (CM) technology has achieved antibiotic-free meat production through closed-system bioreactors, developments in serum-free culture medium, and germless control protocols. However, current researches predominantly focuse on nutritional optimization and environmental impact assessments of cultured meat, while systematic investigations into its potential for reducing antimicrobial resistance transmission are obviously insufficient. This study analyses the CM technology's potential to interrupt antibiotic usage chains at their source. By avoiding pollution pathways in traditional meat production, the industry has realized antibiotic-free manufacturing protocols. Nevertheless, technological promotion confronts many challenges including regulatory fragmentation, consumer skepticism, and economic viability constraints in low- to middle-income nations. The research's significance is providing new pathways for alternative protein technologies to fight against antimicrobial resistance, fostering synergistic development of sustainable food systems and public health infrastructure. In the future, it is necessary to optimize the cost of the culture medium and improve the taste to enhance the product's competitiveness. At the same time, we should strengthen interdisciplinary cooperation to coordinate the global regulatory framework, turing cultured meat from a laboratory innovation into a public commodity.

Keywords: Cell-Cultivated Meat, Antimicrobial Resistance, Antibiotic Misuse in Animal Husbandry, Transmission of Drug-resistant Bacteria, Public Health.

1. Introduction

The application of antibiotics in livestock started in the 1940s with the initial use of penicillin for treating farm animal infections. Since then, the utilization of antibiotics in animal production had expanded constantly, and preventive medication and growth promotion had gradually become popular in poultry farming. [1].

Nowadays, the global spread of antimicrobial resistance (AMR) has been a severe public health challenge. According to World Health Organization (WHO) projections, continued antibiotic misuse could result in 10 million annual deaths from drug-resistant infections by 2050, accompanied by economic losses exceeding US$100 trillion [2]. This crisis is mainly caused by antibiotic overuse in animal agriculture, which accounts for approximately half of global antibiotic consumption. Antibiotic resistance genes (ARGs) persistently endanger human health through food chain contamination and environmental movement pathways [3]. Although international regulatory measures (e.g., the EU's 2006 ban on antibiotic growth promoters) have limited the antibiotics use in agriculture, persistent regulatory absebce in low- and middle-income countries (LMICs) like India, with continued antibiotic residue inputs, making high levels of resistant pathogens in environmental and food still [4].

More critically, most LMICs confront dual challenges of high disease burdens in livestock populations and inadequate veterinary services, leading to increased frequency of zoonotic disease outbreaks. Epidemiological surveillance data reveal endemic circulation of highly transmissible viral and bacterial pathogens across Africa, Asia, and Latin America, characterized by cyclical epidemic patterns [5].

Recent advancements in cell-cultivated meat (CM) technology have demonstrated unique public health value through its manufacturing paradigm. This innovation harnesses pluripotent animal stem cells that undergo controlled expansion into tissue mass, with contemporary techniques enabling fibroblasts to simultaneously promote myogenesis and modulate meat tenderness through extracellular matrix regulation [6]. By decoupling meat production from conventional livestock systems, this technology fundamentally eliminates antibiotic application at the production source.

Nevertheless, current scholarship predominantly emphasizes CM's nutritional profiles and environmental footprints, leaving its AMR mitigation potential insufficiently explored. This review systematically investigates three intervention pathways: 1) disruption of antibiotic misuse chains, 2) implementation of streamlined biomanufacturing protocols, and 3) synergistic integration with public health governance frameworks. The analysis aims to establish theoretical foundations for synergizing alternative protein innovation with global AMR governance, ultimately advancing the co-realization of sustainable food systems and public health objectives.

2. Current Status of Antibiotic Use in Conventional Animal Husbandry

2.1. Global Antibiotic Usage Patterns

As a cornerstone of global agricultural economies, the sustainable development of animal husbandry directly impacts food security and public health infrastructure. Current estimates indicate that 50–80% of global antibiotic production is deployed in food animal systems, with applications spanning routine feed supplementation to disease management [7]. Antimicrobials are administered not only for therapeutic purposes but also routinely incorporated into disease prevention regimens for healthy herds [8].

Mulchandani's projections on global antimicrobial use (AMU) reveal a concentrated geographic distribution, with China, Brazil, India, the United States, and Australia collectively accounting for 58% of total consumption in 2020 (Figure 1A). These nations are projected to maintain their positions as the top five antimicrobial consumers through 2030 [9].

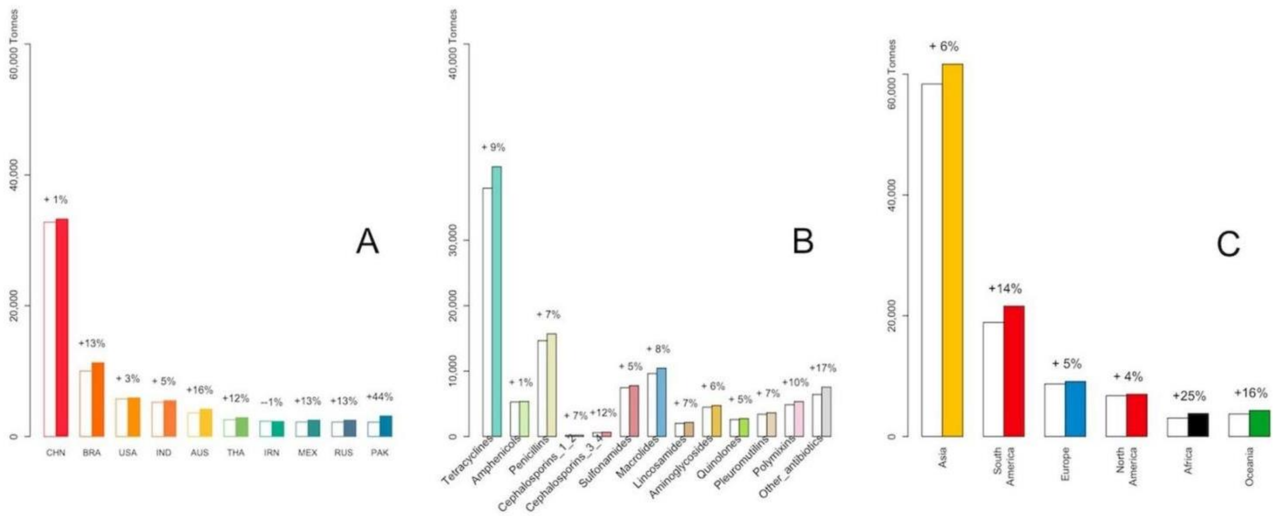

Figure 1. Consumption patterns of veterinary antimicrobial agents in 2020 and projected 2030 across three classification systems [9].

A) National rankings (Top 10 consumers): CHN (China), BRA (Brazil), IND (India), USA (United States), AUS (Australia), IRN (Iran), THA (Thailand), PAK (Pakistan), JPN (Japan), MEX (Mexico). B) Category-based analysis of antimicrobial agents. C) Continent-level distribution of consumption.

2.2. Regulatory Challenges in Antibiotic Governance

Global efforts to combat antimicrobial resistance have prompted significant regulatory reforms. Developed nations including the United States have prohibited non-therapeutic antibiotic use for growth promotion in livestock. China established its National Action Plan to Contain Bacterial Resistance in 2016, integrating antibiotic stewardship into comprehensive public health governance systems. However, persistent regulatory gaps persist in developing economies.

EU food safety audits have persistently detected extended-spectrum β-lactamase (ESBL)-producing bacteria in Brazilian poultry imports, yet Brazil maintains no categorized antibiotic management system for veterinary applications [1]. Similarly, an investigation by India's Centre for Science and Environment (CSE) revealed widespread incorporation of antimicrobial growth promoters (AGPs) in commercial livestock feeds, despite the absence of national regulatory standards governing antibiotic use in animal production [1]. These regulatory deficiencies perpetuate high-risk practices that facilitate antimicrobial resistance transmission through global food supply chains.

3. Transmission of Drug-Resistant Pathogens and Zoonotic Risks

The dissemination of drug-resistant bacteria within animal husbandry operates through three interconnected pathways—food chain transmission, direct contact exposure, and environmental dispersion—collectively compromising public health security.

Food chain transmission serves as the principal vector. Hansen's investigation of a mink farm outbreak traced the pathogen to swine slaughter byproducts in feed, demonstrating cross-species transmission via pork-mink production chains [10]. Animal-derived foods directly endanger human health, with dairy and meat products serving as vehicles for transmitting methicillin-resistant *Staphylococcus aureus* (MRSA) from livestock to humans, substantially complicating clinical management of resistant infections [11].

Occupational exposure poses elevated risks for animal handlers. Longitudinal monitoring of swine farm personnel revealed that veterinary students developed significantly enriched gut resistomes after three months of farm exposure. Metagenomic analyses confirmed microbial composition convergence between workers, students, and environmental samples, suggesting occupational exposure-mediated transmission of resistance determinants may engender protracted health risks [12].

Environmental dispersion establishes a clandestine transmission network. Antibiotic residues and resistant bacteria in livestock waste infiltrate ecosystems through manure fertilization. Comparative studies detected 28,000-fold higher resistance gene concentrations in manure-amended soils versus control sites [13]. This contamination exhibits pronounced bioaccumulation potential—lettuce cultivated in manure-treated soil harbored 144 resistance genes in rhizosphere microbiomes, confirming plants as intermediate vectors for resistance gene entry into food chains [14].

Aquatic systems constitute critical secondary transmission routes. Swine wastewater systems maintain high-abundance resistomes, where phage-mediated transduction mechanisms accelerate horizontal gene transfer in aquatic environments [15]. The resultant environmental resistome reservoirs not only reshape microbial ecosystems but also create novel interspecies transmission opportunities, fundamentally altering the evolutionary trajectory of antimicrobial resistance.

4. Zero-Antibiotic Production Pathways in CM

4.1. Technical Principles and Manufacturing Workflow

CM diverges fundamentally from conventional meat production paradigms through its establishment of antibiotic-minimized cell proliferation systems. The standardized biomanufacturing process comprises five sequential phases: 1) Isolation and characterization of cell lines from healthy donor animals, 2) Biomass expansion in controlled bioreactors, 3) Guided cellular differentiation, 4) Harvesting of mature cellular aggregates, and 5) Post-processing into consumer products [16]. This closed-loop bioproduction architecture, implemented in closed stainless-steel systems, achieves pharmaceutical-grade aseptic standards—effectively eliminating microbial contamination risks inherent in slaughterhouse processing.

Unlike conventional meat production, cellular cultivation maintains complete environmental isolation during critical phases (stages 1-3). Even post-harvest processing (stages 4-5) occurs without exposure to zoonotic contaminants. This paradigm circumvents multiple contamination vectors plaguing traditional systems: fecal pathogen transmission in livestock facilities, cross-contamination in abattoirs, and biofilm colonization on processing equipment. The technical framework thus establishes inherent barriers against both antibiotic requirement and resistance transmission throughout the production continuum.

4.2. Breakthroughs in Serum-Free Media Development

Innovations in culture media composition represent the pivotal challenge for achieving antibiotic-free CM. Conventional basal media formulations—comprising glucose, amino acids, mineral salts, and vitamins—have historically relied on animal serum supplementation to provide critical growth factors. This dependency creates dual dilemmas: 1) biosafety risks from potential prion pathogens or undefined contaminants, and 2) ethical conflicts with the technology's animal-use reduction objectives.

Serum substitute development has thus emerged as a critical research frontier. Recent advances demonstrate that plant-derived or synthetic alternatives can effectively sustain cell proliferation. Notably, a breakthrough study revealed that conditioned media from rat liver epithelial cells (RL34) under specific culture parameters promoted muscle cell expansion with efficacy comparable to serum-containing formulations [17]. This discovery establishes a theoretical pathway for complete serum elimination while enabling media cost reduction and compositional standardization.

Industrial validation confirms technical feasibility. Mosa Meat achieved an 88-fold cost reduction in 2020 by eliminating fetal bovine serum (FBS) from their production media. Concurrently, Future Meat Technologies developed animal component-free media utilizing plant-based protein matrices [18]. These advancements simultaneously address multiple challenges: standardizing media components, controlling production costs, and eradicating viral contamination risks—collectively advancing the commercial viability of serum-free CM systems.

4.3. Implementation of Aseptic Control Systems

The contamination prevention protocols established in biopharmaceutical manufacturing demonstrate technical superiority when adapted to CM. With biopharmaceutical contamination rates approximating 2% under stringent controls, this track record validates the feasibility of antibiotic-free animal cell cultivation at commercial scales. Regulatory approvals for pioneering products confirm this advantage: GOOD Meat and UPSIDE Foods have successfully implemented antibiotic-free bioprocesses certified by the U.S. Food and Drug Administration (FDA), while Vow Foods' production system complies with equivalent standards under Food Standards Australia New Zealand (FSANZ) oversight [19].

A tripartite aseptic control architecture ensures production safety:

1) Primary containment**:** Rigorous pathogen screening of master cell banks eliminates endogenous microbial risks.

2) Secondary isolation: Closed bioreactor systems maintain physical separation throughout biomass expansion phases.

3) Tertiary protection: Processing exclusively employs non-animal-derived scaffolding materials to prevent exogenous contamination [20].

5. Prospects, Challenges, and Controversies in CM

5.1. Market Development and Commercialization Trajectory

The past five years have witnessed remarkable progress in CM commercialization and technological innovation. The industry achieved its inaugural market entry in 2020 through U.S.-based Eat Just's commercial sale of cultivated chicken at Singapore's "1880" restaurant. Currently, over 100 enterprises worldwide are engaged in cellular meat development, with U.S., EU, Israeli, and Asian companies driving market expansion. Markets and Markets projects the global cultivated meat market will reach US$593 million by 2032, reflecting a 15.7% compound annual growth rate from 2025 to 2032 [21].

Technological breakthroughs in antibiotic avoidance have been institutionally validated. The Good Food Institute (GFI) confirms that commercial-scale production systems inherently exclude routine antibiotic use. A 2023 analysis of 23 industry leaders revealed: 9 companies restrict antibiotic/antifungal applications exclusively to cell line development or banking phases, while 11 implement fully antibiotic-free protocols [22]. Empirical validation comes from technical disclosures by 13 major producers including GOOD Meat and Aleph Farms [23].

Notably, residual antibiotic use during R&D phases demonstrates orders-of-magnitude lower intensity compared to conventional livestock systems. Confined to controlled laboratory processes at limited scales, such applications present negligible AMR risks. While current pricing positions cultivated meat as a premium product, ongoing technological refinement and cost reduction strategies are expected to facilitate gradual market democratization, ultimately establishing CM as a pillar alongside conventional and plant-based proteins in global food systems.

5.2. Technical Challenges and Cost Optimization

While select enterprises have established antibiotic-free production pathways, complete elimination of antimicrobials across the industry remains incomplete. Antimicrobial usage introduces regulatory complexities—Singapore's Food Agency mandates that cultivated meat producers submit antimicrobial usage documentation [23]. As of October 2022, international regulatory frameworks remain under development, though emerging guidelines such as Good Cell Culture Practice recommendations explicitly advocate antibiotic avoidance where feasible [23].

Cost containment presents a parallel challenge, with culture media constituting 55–95% of total production expenses. Growth factor procurement remains the primary cost barrier. Strategic solutions include growth factor substitution through metabolic byproduct utilization or synthetic signaling proteins, potentially reducing costs to commercially viable thresholds [24]. Notably, production costs for cultured meat patties have plummeted from US$325,000 to US$11 per unit, demonstrating accelerating commercial feasibility [25].

5.3. Consumer Acceptance and Societal Debates

Consumer acceptance constitutes a pivotal determinant for market penetration of cultivated meat technologies. A Super Meat survey of 250 culinary professionals revealed that 86% expressed interest in cultivated meat products, with 22% demonstrating strong enthusiasm. Notably, 77% indicated willingness to pay premium pricing, accepting 11–15% cost increments over conventional meats [21]. Resistance persists among certain demographics, primarily stemming from perceived artificiality, food safety concerns, and religious proscriptions governing lab-grown products. Certain religious traditions impose dietary restrictions on cultured meat consumption, thereby constricting market demographics [26]. U.S. consumer research paradoxically shows lower adoption intent among vegetarians compared to omnivores, despite their recognition of environmental advantages [27]. Producers with verifiable antibiotic-free production claims may gain competitive advantages in food safety positioning.

Organoleptic limitations further challenge consumer adoption. Current prototypes suffer from flavor profile deficiencies due to absent lipid marbling and vascularization. Technological innovations in adipocyte-myocyte coculture systems show promise for replicating conventional meat's sensory characteristics.

5.4. Divergence in Global Regulatory Frameworks

The commercialization of cultivated meat hinges on the establishment of robust national regulatory systems. Countries with active CM industries have developed distinct legal frameworks to ensure product safety and market legitimacy. The European Union mandates rigorous pre-market assessments by the European Food Safety Authority (EFSA), with member states formulating supplementary management protocols. In the United States, regulatory oversight is bifurcated: the FDA governs cell cultivation and harvesting phases, while the United States Department of Agriculture(USDA) supervises processing and labeling. In 2020, Singapore approved the sale of cultured chicken by Eat Just and released the world's first food safety assessment guidelines for novel foods. Japan accelerates regulatory processes through collaborative governance via the Japanese Association of Cellular Agriculture (JACA), integrating governmental, industrial, and academic stakeholders [21].

Persistent regulatory fragmentation nevertheless poses global challenges. The absence of harmonized international standards and specialized legislation in numerous jurisdictions risks delaying market access while amplifying public health uncertainties through inconsistent safety governance practices.

6. Conclusion

This article reveals the severe current situation where the abuse of antibiotics in traditional animal husbandry leads to the spread of drug-resistant bacteria through three major pathways, and explores the potential of cultured meat technology to achieve antibiotic-free production through a closed production system, serum-free culture medium, and a sterile control system. This discovery addresses the urgent need for the governance of the antibiotic resistance crisis and provides a new approach for CM technology to participate in the prevention and control of AMR. By eliminating antibiotic application at the source, this technology may drive livestock industry transformation and promote the coordinated development of the food industry and public health. The limitation of the current research lies in the lack of in-depth analysis of the obstacles to the promotion of the technology (e.g.,the impact of differences in regulatory standards on the global market, consumers' concerns about taste and safety, and the economic feasibility issues of implementing the technology in LMICs) . Most of the existing studies focus on the technical principles and lack discussions from the policy and economic dimensions.

Future research should optimize the cost of the culture medium and improve the taste to enhance the product's competitiveness, and strengthen interdisciplinary cooperation to unify the global regulatory framework. By integrating bioengineering and public health research, CM is expected to become an effective tool to curb the antibiotic resistance crisis and provide a practical paradigm for sustainable food innovation.

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