Iranian Food Science and Technology
Research Journal
Homepage: https://ifstrj.um.ac.ir

Review Article
Vol. 20, No. 3, Aug.-Sep. 2024, p. 81-103

Exploring the Potential of Cultured Meat: Technological Advancements, Sustainability Prospects, and Challenges

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Received: 28.04.2024
Revised: 16.06.2024
Accepted: 29.06.2024
Available Online: 29.06.2024

How to cite this article:
Ramezani, P., & Motamedzadegan, A. (2024). Exploring the potential of cultured meat: Technological advancements, sustainability prospects, and challenges. *Iranian Food Science and Technology Research Journal, 20*(4), 81-103. https://doi.org/10.22067/ifstrj.2024.87796.1329

Abstract

The effects of traditional livestock farming on the environment and its limited scalability contribute to the persistent worldwide dilemma of food insecurity. Growing animal cells under regulated conditions has given rise to cultured meat, which might be a more ethical and ecological option. The potential of cultured meat to solve issues with food security is critically examined in this review article, which does so by thoroughly analyzing its effects on global food systems, sustainability prospects, technical breakthroughs, and related obstacles. Life cycle analyses show that the environmental impact of producing cultured meat is much lower than that of producing traditional meat. Significant scientific advancements have moved the production of cultured meat closer to commercial viability, including scaffold advances, tissue engineering, bioreactor design, and cell line optimization. There are still a number of formidable obstacles to overcome, including establishing large-scale manufacturing at a reasonable cost, negotiating intricate regulatory environments, guaranteeing product safety, and cultivating customer acceptability. To overcome these challenges and realize the promise of cultured meat to improve food and nutrition security while promoting environmental sustainability and animal welfare, an interdisciplinary strategy incorporating scientific, technical, regulatory, and social views is essential.

Keywords: Bioreactor design, Cultured meat, Food security, Environmental sustainability, Scaffolding

Introduction

A significant problem facing the world today is food insecurity since millions of people lack access to enough food that is safe and nourished. The conventional livestock production industry, which plays a vital role in the world's food systems, is confronted with many issues such as resource depletion, environmental degradation, and ethical concerns over animal care. Cultured meat has gained a lot of interest as a possible more ethical and sustainable meat substitute for conventional meat production. Cultured meat is produced by cultivating animal cells in carefully regulated lab settings to create products that resemble meat.

In 2013, the first cultured meat burger patty was developed, leading to the establishment of many firms dedicated to marketing cultured meat products. These enterprises are geographically dispersed and specialize in distinct meat products (Choudhury *et al.*, 2020). Memphis Meats, now known as Upside Foods, is a pioneering firm that successfully created the world's first cultured meatball and chicken strip. Eat Just Company introduced the first

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https://doi.org/10.22067/ifstrj.2024.87796.1329

cultured chicken nuggets and obtained authorization to market cultured chicken meat in Singapore. In 2013, Mosa Meat, a company that emerged from research conducted at Maastricht University, successfully created the first-ever cultured beef burger. This groundbreaking achievement came at a significant expense of $330,000 (Stephens *et al*., 2018).

We critically evaluate cultured meat's ability to solve issues with food security in this review. We examine the implications of producing cultured meat for the world's food systems, sustainability, and related possibilities and problems. The means of an extensive assessment of the literature.

The World's Food Systems and Sustainability

A viable substitute for conventional cattle farming, cultured meat, also referred to as lab-grown or in vitro meat, has the ability to address a number of the environmental problems related to conventional meat production. Growing meat from animal cells in a controlled environment is the process of producing cultured meat, which has the potential to significantly lower greenhouse gas emissions as well as land and water usage.

Compared to traditional animal farming, cultured meat production drastically reduces water and land use by as much as 90% and 99%, respectively (Penn, 2018). According to Munteanu *et al*. (2021) cultured meat also can lessen greenhouse gas emissions, which are a significant problem since cattle production is primarily to blame. Cultured meat production, however, may use more energy than usual since technological processes are supplanting biological ones. Cultured meat can potentially reduce soil erosion and water pollution, two of the main environmental problems caused by cattle farming. Another advantage of cultured meat is that it may be produced in places where conventional cattle would not thrive.

According to a life cycle assessment (LCA) research, compared to traditional European meat production, producing 1000 kg of cultured meat uses a lot less land and water and produces a lot less greenhouse gas emissions. According to Tuomisto and Teixeira de Mattos (2011), cultured meat may specifically lead to 78–96% reductions in greenhouse gas emissions, 99% reductions in land usage, and 82–96% reductions in water use. Energy consumption, on the other hand, maybe comparable to or slightly lower, except chicken which has a lower energy use.

A multidisciplinary assessment of the research on cultured meat reveals that it has the potential to reduce pollution and the amount of agricultural area used for farming, both of which might be beneficial to human health. The assessment also notes that when certain biological activities are replaced by artificial processes, there is a possibility that the energy required for the creation of cultured meat might be more significant. To completely comprehend the sustainability and effectiveness of cultured meat production, further experimental research is needed (Munteanu *et al*., 2021).

Spirulina, a type of microalgae, is renowned for its substantial protein content, ranging from 46% to 63% of its dry weight. This protein concentration is comparable to meat and soybeans (Lupatini *et al*., 2017). Additionally, it has indispensable amino acids, rendering it a protein source with a high biological value. Spirulina is regarded as a sustainable protein source since it grows rapidly and utilizes resources efficiently. Compared to conventional protein sources, it necessitates a smaller amount of land and water (Manzocchi *et al*., 2020). Additionally, its cultivation can help reduce nitrogen waste, making it environmentally friendly (Mullenix *et al*., 2021).

Proteins obtained from yeasts and other microorganisms, known as single-cell proteins, are also rich in protein content. Yeast-based SCPs can yield a significant quantity of protein, however the exact proportions may differ depending on the specific microorganism employed. SCPs are produced using fermentation techniques that can effectively utilize agricultural and industrial by-products, making them a viable and environmentally friendly choice. Vertical farming necessitates smaller amounts of land and water in contrast to conventional agriculture and can be cultivated in controlled surroundings, hence minimizing the influence on natural ecosystems. (Aragão *et al*., 2022).

Proteins derived from legumes, grains, and seeds, which are acquired from plants, exhibit varying protein content. Soybeans are a well-known source of plant-based protein, known for their high protein concentration and sometimes used as a benchmark for comparing other plant proteins. Plant-based proteins often have a lower environmental footprint compared to animal-based proteins. They possess a reduced need for water, land, energy and produce a smaller amount of greenhouse emissions. The uptake of plant-based proteins is driven by the imperative to develop more sustainable food systems (López-Martínez *et al*., 2022).

Mealworms (*Tenebrio molitor*) and lesser mealworms (*Alphitobius diaperinus*) have high protein content and a favorable amino acid profile, making them suitable for human and animal consumption (Kröncke & Benning, 2023; Roncolini *et al*., 2020). Earthworms (*Eisenia fetida*) also offer high protein levels and a proper amino acid profile. Using worms as protein sources can reduce the environmental impact associated with traditional livestock feed, contributing to more sustainable production processes (Musyoka *et al*., 2019). Despite challenges related to biosafety, consumer acceptance, and market price, there is promising potential for large-scale manufacturing of this type of products. Snacks can be enhanced with lesser mealworm powder to significantly boost their protein and mineral content, while maintaining the enjoyable sensory characteristics of the snacks (Roncolini *et al*., 2020). Moreover, the hydrolysates derived from these worms can be employed as a growth factor in the production of cultured meat.

Comparative investigation has shown that Spirulina and cultured beef have the highest land use efficiency per unit of protein and calories, outperforming other protein sources. Cultured meat exhibits comparable energy consumption levels to conventional animal products, while showcasing lower greenhouse gas emissions. In contrast, crops demonstrate optimal energy utilization and minimal greenhouse gas emissions per unit of energy and protein. They can serve as feedstock for cultured meat production or as ingredients for plant-based meat. Additionally, crops supply essential nutrients and proteins for cellular growth and development (Newton & Blaustein-Rejto, 2021). Substituting animal products with cultured meat can improve food security and yield positive environmental results (Chriki & Hocquette, 2020; Tzachor *et al*., 2022).

Last but not least, the production of cattle contributes significantly to the utilization of land, water, and greenhouse gas emissions. As an alternative, cultured beef has the potential to mitigate several environmental impacts associated with animal production. It uses 99% less land, 90% less water, and 45% less energy (Penn, 2018).

Due to its novelty, obtaining regulatory permission for the production and sale of cultured meat is a crucial hurdle that must be tackled. The European Union has incorporated cultured beef into its Novel Foods Regulation, establishing a lawful framework for its future development and commercialization. The manufacturing of cultured meat in the United States is being regulated by both the FDA and USDA in collaboration. In 2020, Singapore achieved the distinction of becoming the first jurisdiction to provide regulatory approval for a cultured beef product. Nevertheless, there is currently a global absence of a comprehensive regulatory framework that encompasses all aspects, including safety review of media components, scaffolds, prospective use of gene editing techniques, as well as guidelines for assessing food safety concerns, toxicity, and correct labeling (Guan *et al*., 2021).

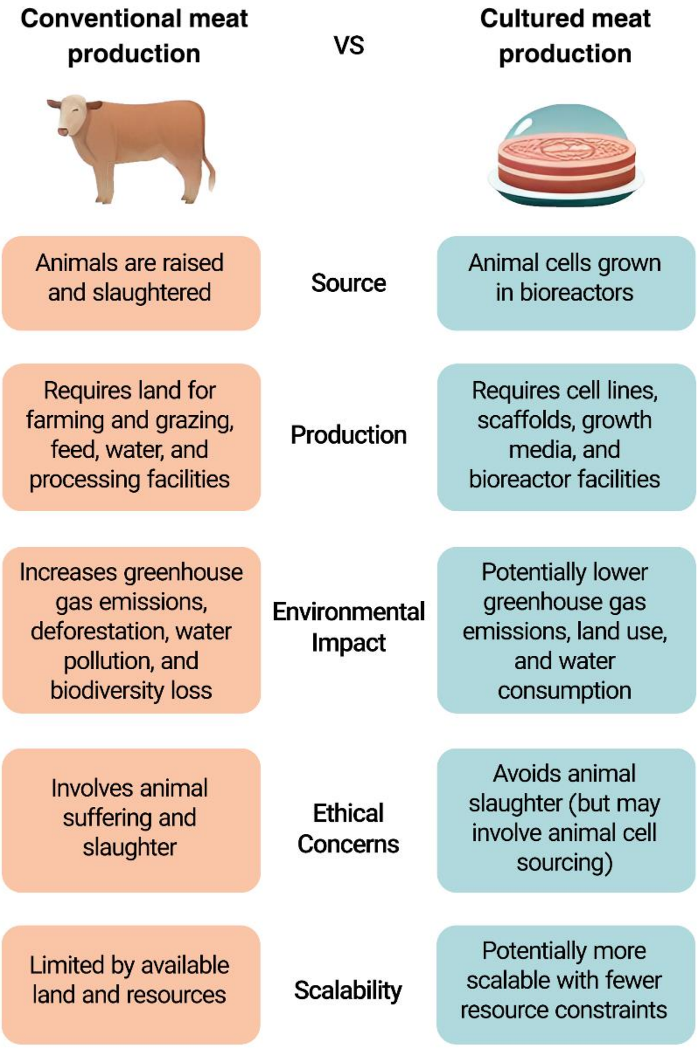

Fig. 1. Comparison between conventional and cultured meat production

In conclusion, producing meat using cultured means offers a practical way to lessen the environmental effect of meat consumption. It provides a significant reduction in land, water, and greenhouse gas use, all of which are essential for the sustainability of food production systems. However, in order to fully reap the advantages of cultured meat, further investigation is required, along with changes to regulations.

A comparison of the resource efficiency of traditional livestock production to cultured meat may be made by looking at metrics like feed conversion ratios and water footprint. The water footprint (WF) of animal products is a crucial resource usage indicator, with meat having a greater WF than milk or eggs, according to the literature. In particular, compared to other animals like sheep, goats, pigs, and chickens, beef has a far higher WF. The leading cause of this variance is the different feed conversion ratios between monogastric species like poultry and swine and ruminants like cattle, sheep, and goats, which have lower feed conversion ratios (Ibidhi & Ben Salem, 2020). Additionally, since more water is needed for feed and animal upkeep, the water footprint of livestock products is often more significant than that of plant-based diets (Mekonnen & Hoekstra, 2012).

The emergence of cultured meat signals a profound change in the way humans may grow and prepare meat in the future. This invention may help to resolve a number of moral issues related to conventional cattle production methods.

The way animals are treated in traditional livestock production is one of the main issues with animal welfare. Animals raised in traditional agricultural ways may be subjected to cruel handling techniques, cramped quarters, and painful methods of killing. These problems may be resolved by using cultured meat, which does away with the need of raising and killing animals for nourishment. Because cultured meat is made from animal cells in a lab, it has the potential to significantly minimize the animal suffering involved in the meat industry (Penn, 2018).

Furthermore, animal dignity is a factor in the ethical discussion surrounding cultured meat. Similar to vegetarianism, some claim that cultured meat might cause farm animals to become extinct, which could be seen as an insult to their dignity. The argument that created meat does not inherently diminish animal dignity any more than existing techniques does, however, cast doubt on this viewpoint. Alternatively, Chauvet (2018) suggests that it may be seen as a means of averting the agony and sacrificing of nonhuman creatures.

Culture, religion, health, and epidemiology concerns may all play a role in determining whether or not cultured meat is seen as an acceptable alternative to regular beef. As an example, Muslims hold the ceremonial slaughter of animals in high regard. Due to the steadfast nature of specific religious directives, the commercialization of cultured meat could not entirely eradicate current practices. A possible marketable alternative might be cultured beef that abides by Shariah rules (Hamdan *et al.*, 2021). Another example is that cultured meat, as opposed to traditional meat from killed animals, may lower the risk of transmissible spongiform encephalopathies (TSEs), such as mad cow disease (bovine spongiform encephalopathy, BSE). Cultured meat is made by cultivating cells of animals in a controlled lab setting, without using any parts of the animal's neurological system. The brain and other organs of afflicted animals' neurological systems are the primary sites of improperly folded prion proteins, which cause TSEs such as mad cow disease. Additionally, contamination from other sources is minimized in the controlled laboratory setting where cultured beef is produced (Schaefer & Savulescu, 2014).

Furthermore, since cultured meat production is not constrained by land availability or the biological limitations of animal reproduction, it can be scaled up more effectively than conventional livestock farming. This scaling potential may make it possible to more sustainably supply the rising demand for beef products worldwide. However, according to Stephens *et al.* (2018), the development of cultured meat permits the possibility of modifying the nutritional makeup, texture, and taste of meat products.

Although the manufacturing of cultured meat exhibits promises for environmental sustainability, several obstacles need to be overcome to fulfill its potential fully: (1) The energy source used has a significant influence on the environmental effects of producing cultured meat. When compared to fossil fuel-based energy sources, renewable energy sources like solar, wind, or hydroelectric electricity would dramatically lower the carbon footprint (Smetana *et al.*, 2015), (2) Reducing environmental effects and reaching sustainability objectives depend on obtaining economies of scale and increasing the effectiveness of cultured meat production procedures (Mattick *et al.*, 2015), (3) For cultured meat products to be widely adopted and sustainably produced, suitable regulatory frameworks must be developed and public concerns about their acceptability and safety must be addressed (Bryant & Barnett, 2018; Stephens *et al.*, 2018). (4) To reduce environmental effects and increase sustainability, ongoing research and optimization of the whole life cycle of cultured beef production, from cell line generation to bioreactor design and waste management, are required (Mattick *et al*., 2015).

Cultured meat production has the potential to greatly aid in the attainment of sustainability objectives and the reduction of the environmental effects linked to traditional livestock production systems by effectively tackling the obstacles and capitalizing on the available prospects.

Technological Advancements in the Production of Cultured Meat

Cell Line Development

An essential part of producing cultured meat is the creation and refinement of cell lines. For this reason, stem cells from a variety of origins have been investigated:

Animal-derived stem cells, such as muscle satellite cells or embryonic stem cells from cattle, have been used in early studies on the generation of cultured meat (Post, 2012). These cells may divide and specialize into numerous types of muscle fibers. The use of iPSCs, somatic cells that have been reprogrammed to a pluripotent state, as a result of advancements in stem cell technology also presents a viable and moral alternative for the scalable and ethical creation of cultured meat, as opposed to using stem cells sourced from animals (Lee *et al*., 2023). The use of immortalized cell lines, which can proliferate continuously and be kept in culture for long periods, has also been investigated by other researchers (Wang *et al*., 2024). These cell lines may provide a reliable and scalable source for the creation of cultured meat.

The utilization of pluripotent cells in cultured meat entails the conversion of these cells into distinct muscle and adipose cells that are necessary for meat generation. This procedure is essential for the development of sustainable and practical techniques to manufacture cultured meat, which has the potential to overcome the limits of conventional meat production.

Porcine induced pluripotent stem cells (piPSCs) can be effectively transformed into skeletal muscle cells by employing a combination of a GSK3B inhibitor (glycogen synthase kinase-3β) and a DNA methylation inhibitor (5-aza-cytidine), followed by the activation of MYOD1. Within a span of 11 days, this technique leads to the development of myotubes that possess the functional attributes of muscle cells (Genovese *et al*., 2017).

Stem cells, such as progenitor stem cells derived from muscle tissues, mesenchymal stem cells, and induced pluripotent stem cells (iPSCs), are very suitable for producing muscle cells for cultured meat. These cells possess the ability to renew themselves and differentiate into numerous cell types, making them well-suited for extensive growth in a laboratory setting while keeping their stem cell characteristics. Stem cells show great potential for the production of lab-grown meat, but they encounter difficulties associated with the cultivation process, including the need to retain a large number of cells while ensuring their excellent quality. Methods to address these constraints involve improving the environment in which the culture takes place and utilizing specialized inhibitors and activators to direct the process of differentiation (Ozhava *et al*., 2022).

Pluripotent stem cells, specifically piPSCs, can be efficiently transformed into muscle cells by the use of specific inhibitors and activators. These cells, in addition to other types of stem cells, possess substantial potential for the generation of grown meat. Nevertheless, the obstacles in preserving the quality and quantity of cells during in vitro culturing must be resolved by the use of optimum procedures.

For dependable and effective cultured meat production, cell lines must be stable and behave consistently. To evaluate the stability and usefulness of cell lines, characterization approaches such as metabolic profiling, karyotyping, and gene expression analysis are used (Lee *et al*., 2023)

One of the main obstacles in the development of cultured meat is optimizing the proliferation and differentiation of stem cells into muscle fibers. Numerous methods and approaches have been investigated. In order to facilitate efficient cell proliferation and differentiation, researchers have concentrated on creating specialized culture media formulations. In addition, sophisticated bioreactor systems have been developed to offer controlled environments for cell growth, nutrient delivery, and waste removal, allowing for scalable production (Edelman *et al*., 2005). To imitate the texture and organoleptic qualities of conventional meat, researchers have looked into using three-dimensional scaffolds and tissue engineering techniques to direct the organization and structure of cultured muscle fibers (Ben-Arye & Levenberg, 2019; Stephens *et al*., 2018).

It is essential to understand that cultured meat currently has distinct organoleptic features compared to regular meat. Due to its lack of postmortem changes, it has different sensory and nutritional qualities than regular meat. The texture of uncooked cultured meat can be challenging to achieve and may need co-cultivation of various cell types and electrical or mechanical stimulation. However, processed meat products may need ingredients as additives to improve texture. Without myoglobin, chemical colorants may be required to produce the right red. Postmortem metabolism lacks crucial flavor precursors, hence artificial flavors like plant-based meat replacements are used. Without appropriate supplementation, meat may lack vitamins, minerals, fatty acids, and bioactive compounds, lowering consumer satisfaction. Without adding exogenous chemicals, cultured meat cannot match the sensory experience and nutritional content of regular meat (Fraeye *et al*., 2020).

Ong *et al*. (2023) have identified genetic drift in the cell lines used for cultured meat production as a potential food safety hazard. During prolonged culture periods, cells have the potential to a mass genetic mutations and experience phenotypic alterations as a result of several stimuli such as physical pressures, biochemical exposures, excessive cell division, or contamination events like mycoplasma infection. It is crucial to monitor the stability of cell lines and analyze any changes in gene expression or metabolite profiles to guarantee safety and maintain product consistency. In addition, regulators have expressed concerns about the potential risk of tumor formation from consuming immortalized or continuously reproducing cell lines. Expert panels have determined that the likelihood of immortalized cells surviving digestion and developing tumors is exceedingly low according to existing scientific knowledge. However, the authors suggest further studies to confirm these assumptions experimentally. It may be necessary to communicate the risks carefully in order to address any remaining consumer beliefs that connect uncontrolled cell growth to concerns about cancer. Identifying primary research goals includes creating reliable techniques to identify and manage genetic drift, as well as defining safe thresholds for the maximum number of times, cells can be passed.

The discovery, characterization, and optimization of cell lines via ongoing research and technical breakthroughs are essential for enhancing the commercial viability, scalability, and efficiency of cultured meat production.

Bioreactor Design

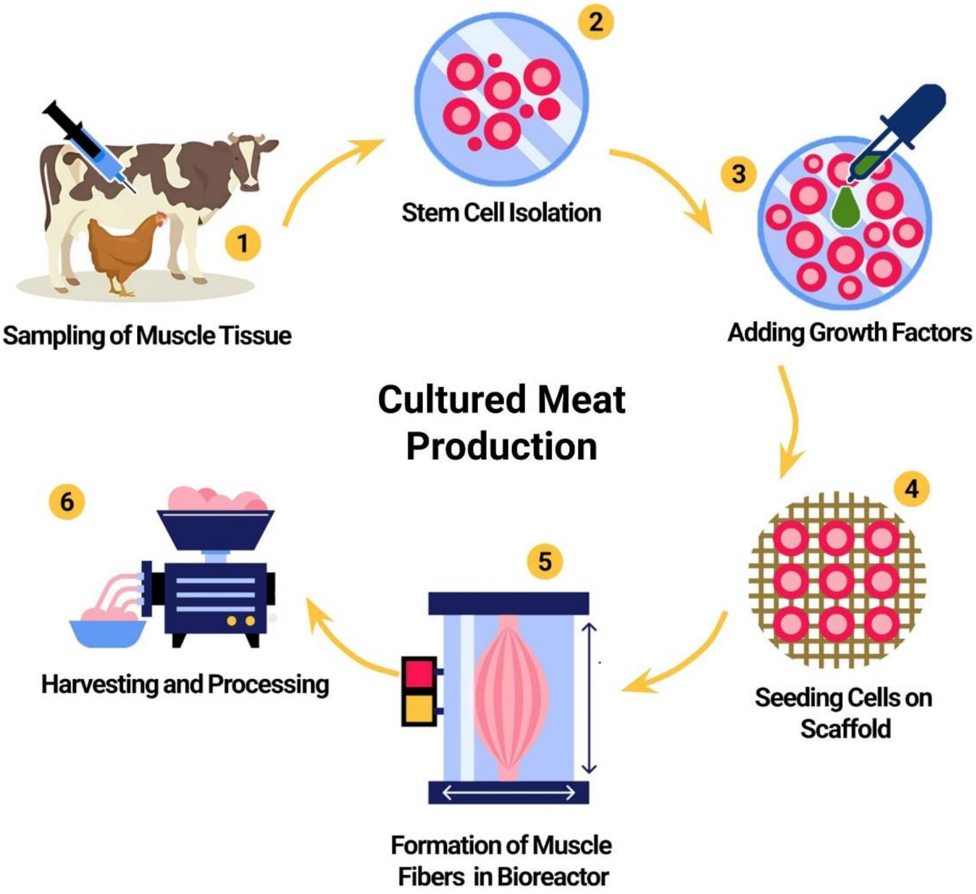

Fig. 2. A schematic showing the steps used to make cultured meat

The progress of cultured meat production heavily depends on developing scalable bioreactor systems. Animal stem cells are multiplied and differentiated in bioreactors to make cultured meat, which offers a sustainable substitute for conventional livestock production.

Bioreactors provide a regulated and adequate substitute for animal husbandry by improving efficiency and scalability in cell treatment and the production of cultured meat (Ge *et al*., 2023).

The potential of stirred tank bioreactors (STRs) for large-scale cultured meat production has been assessed. Larger reactors may lower the cost of goods sold (COGS), according to research that analyzed facilities with various STR sizes. A ~211,000 L STR, for example, might reduce the COGS to $25/kg, but a ~42,000 L STR had a base case COGS of $35/kg. Moreover, a ~262,000 L airlift reactor (ALR) would lower the COGS to $17/kg, suggesting that more expansive and unconventional bioreactor designs might be more economical (Negulescu *et al*., 2023)

In the context of cell expansion, whereby bovine adipose-derived stem cells (bASCs) were grown on microcarriers in spinner flasks, the scalability of bioreactors is also investigated. The results of the research showed that an 80% medium exchange in conjunction with decreased cell seeding densities led to a 28-fold growth without affecting the cells' capacity to differentiate into distinct lineages (Hanga *et al*., 2020). This shows that using microcarrier-based methods to scale up cell culture to produce cultured meat may be a feasible alternative.

Microcarriers are matrices that provide support for adherent cells in bioreactor systems. They have a high surface area-to-volume ratio, which allows for efficient cell growth and expansion. This feature also makes cell manufacturing more cost-effective (Chen *et al*., 2020). Within the realm of cultured meat production, they have a vital function in expanding muscle cell culture, perhaps acting as a temporary surface for cell growth and as a consumable material integrated into the end result (Bodiou *et al*., 2020).

In contrast to conventional fermentation procedures, the design of expansion bioreactors for producing cultured meat presents particular difficulties. A review highlights how crucial it is to take into account essential elements and basic cell biology characteristics when creating a procedure that is both economically competitive and practical. It emphasizes how vital details that are essential to the process' success are often overlooked in the design of cultured meat bioreactors (Allan *et al*., 2019).

The possibility for effective large-scale production of cultured beef using alternatives to typical bioreactor technologies, such as microcarrier cultures in suspension or packed bed bioreactors, is highlighted. It is expected that these systems' optimization would result in resource- and money-efficient manufacturing techniques (Moritz *et al*., 2015).

Perfusion bioreactors, like hollow fiber bioreactors (HFBs), are designed to create cultured meat with perfectly aligned, densely packed muscle fibers at the centimeter scale. The HFB method makes use of semipermeable hollow fibers to evenly distribute nutrients and oxygen, two essential elements for tissue growth and development. The texture and taste of conventional beef may be almost perfectly replicated with this technique (Nie *et al*., 2023).

Even with these developments, there are still issues and constraints to be resolved. Significant barriers include the high cost of cell culture medium, the difficulty of scaling up bioreactors, and the need to preserve cell quality throughout expansion (Allan *et al*., 2019; Hanga *et al*., 2020; Negulescu *et al*., 2023). In addition, the adaption of bioreactor technologies for industrial-sized cell culture is driven by the requirement for automation, strict management of production conditions, and increased productivity potential.

There are still obstacles to be solved even if scalable bioreactor technologies like STRs, microcarrier-based systems, and HFBs can support large-scale cell and tissue growth for the production of cultured meat. These include media costs, scaling up technological obstacles, and making sure the bioprocess design is both economical and efficient. In order to optimize these systems for the commercial-scale production of cultured meat, further investigation and development are required.

For the purpose of producing cultured meat, it is crucial to optimize the growth conditions in bioreactors to maximize cell proliferation, differentiation, and tissue creation.

The design of the bioreactor and the way mass transfer and fluid flow interact are crucial for establishing a consistent environment for tissue development. Specific geometries, like the radial-flow-type bioreactor, provide a more consistent environment for parenchymal cells to develop and differentiate ex vivo, according to the research performed on several bioreactor designs. This is because areas with slow-flowing conditions that are unfavorable to uniform cell proliferation may result from the lack of barriers parallel to the flow routes (Peng & Palsson, 2000).

The practical and scalable production of cultured meat is another use for bioreactors. They provide the oxygen and nutrients and the regulated environments required for cell division, maturation, and proliferation. The assessment of bioreactor technologies in cell treatment and the production of cultured meat emphasizes the significance of bioreactor types and their uses, highlighting the need for further study to go beyond present constraints and difficulties (Ge *et al*., 2023).

The last topic discussed is the growth of embryonic stem cells (ESCs) in bioreactors, emphasizing the effects of metabolic stress brought on by ineffective feeding. Perfusion cultures were shown to be able to sustain metabolite concentrations below hazardous limits, leading to an intense proliferation of high-quality 'naive' ESCs in research that used a perfusion bioreactor and a mathematical model. According to Yeo *et al.* (2013), this work emphasizes how crucial it is to regulate cellular metabolism in order to preserve pluripotency and enhance ESC bioprocesses.

An encouraging substitute for conventional cattle farming is the production of cultured meat in bioreactors, which has the potential to both lessen environmental effects and meet the world's expanding food need. However, the capacity to sustain ideal growth circumstances is what will determine this technology's success, and that means putting in place efficient monitoring and control mechanisms.

Controlled process conditions may considerably limit variability in product output and quality, which is especially important for the production of cultured meat, as shown by bioreactors developed for plant cell and tissue cultures (Eibl & Eibl, 2008). Similar to this, micro-bioreactors equipped with microfluidic devices and integrated online monitoring have shown the capacity to monitor biomass and regulate pH, improving the results of fermentation (Buchenauer *et al.*, 2009). The application of these ideas to cultured meat bioreactors may guarantee a consistent and repeatable production process.

Sensor monitoring is crucial for preserving the most crucial parameters in the context of cultured meat production (Djisalov *et al.*, 2021). To cultivate adherent cells in closed bioreactors, innovative process control systems that integrate monitoring and control technologies for ideal environmental conditions have been created (Das *et al.*, 2014). This method may be modified to improve quality and repeatability in cultured meat bioreactors.

Last but not least, the use of a single-use pneumatic bioreactor system for mammalian cells highlights the significance of reducing the creation of nutritional gradients and hydrodynamic shear, while allowing real-time monitoring and modification of culture conditions (Obom *et al.*, 2014). The uniform proliferation of meat cells might be ensured by using this technique in the manufacturing of cultured meat.

To sum up, the precise control of growth conditions, which is necessary to ensure the quality, safety, and scalability of cultured meat products, is made possible by the integration of advanced sensors, monitoring devices, and automated control systems, all of which are essential for the efficient operation of bioreactors in the production of cultured meat.

Growth Factors

The utilization of growth factors (GFs), which are necessary for cell proliferation and differentiation in culture conditions, is a key part of cultured meat production. The unique composition of fetal bovine serum (FBS) and the difficulty in replicating its effects with serum-free media has made its replacement in cultured meat production challenging. FBS contains a complex mixture of proteins, growth factors, and other nutrients essential for cell growth (Lee *et al.*, 2022). It is crucial to optimize the content of FBS or an alternative in the media for cultured meat production, since it directly affects cell development. Higher concentrations of FBS promote increased cell proliferation (Ikasari *et al.*, 2022).

The utilization of fetal bovine serum (FBS) throughout the manufacturing procedure gives rise to ethical apprehensions and possible health hazards, specifically the transfer of zoonotic diseases. Fetal bovine serum (FBS) is obtained by performing a cardiac puncture on bovine fetuses, without the use of anesthetic. This procedure has the potential to cause agony and anguish to the fetuses, rendering the technique cruel (Jochems *et al.*, 2002).

Bovine viral diarrhea virus (BVDV) is a prominent pathogen in the cattle industry, recognized for its ability to induce many reproductive and developmental complications in afflicted animals. Recent research has brought attention to the possibility of fetal bovine serum (FBS) being contaminated with BVDV, which has raised concerns regarding its impact on the health of both animals and humans. A recent investigation examined commercially accessible FBS samples gathered from 2017 to 2021 to assess the presence of BVDV contamination. The results were concerning, since 82.9% of the samples tested positive for pestivirus-specific RT-PCR, and a considerable number exhibited seropositivity for BVDV1 and BVDV2 (Nakamura *et al*., 2022). The significant level of contamination emphasizes the necessity for rigorous quality control protocols in the manufacturing of FBS to minimize the hazards linked to BVDV.

Although BVDV mainly affects cattle, its existence in FBS utilized in many biotechnological and pharmacological applications, including its role as a growth factor in cultured meat production, poses significant zoonotic risks. Theoretically, if FBS is contaminated, it could transfer BVDV into cell cultures and biological products, which could potentially endanger human health.

Protein hydrolysates as a cost-efficient substitute for fetal bovine serum in cultured meat media shows great potential. Taheri *et al*. (2011) demonstrated that protein hydrolysates obtained from fish waste have an appropriate amino acid composition. These hydrolysates can be used as a nitrogen source in fish diets and also as functional additives in the food industry. Thus, protein hydrolysates could serve as a cost-effective alternative to replace fetal bovine serum in the manufacturing of cultured meat.

The research conducted by Hamzeh *et al*. (2018) investigated the bioactive properties of protein hydrolysates derived from the mantle of cuttlefish (*Sepia pharaonis*), with a specific emphasis on their antioxidant and antiproliferative activities. They found that cuttlefish protein hydrolysates with degrees of hydrolysis (DH) of 20%, 30%, and 40% exhibited the highest levels of DPPH radical scavenging activity, reducing power, and overall antioxidant capacity. The observed values in the cuttlefish mantle protein isolate were markedly inferior compared to these values. Moreover, the protein hydrolysate with a degree of hydrolysis (DH) of 20% had the most pronounced inhibitory impact on the proliferation of MDA-231 and T47D cancer cell lines. The predominant amino acids in the cuttlefish protein hydrolysates were glutamine, constituting 15.7% of the total, and asparagine, comprising 10.9%. The findings suggest that protein hydrolysates derived from marine sources, particularly cuttlefish can serve as functional constituents in the production medium of cultured meat. This utilization would enhance the stability of antioxidants and promote cellular proliferation, thereby diminishing the requirement for mammalian serum or growth factors. Mirzakhani *et al*. (2018) investigated the apparent protein digestibility (APD) and degree of protein hydrolysis (DPH) of several feed ingredients for Siberian sturgeon (*Acipenser baeri*) in both a live animal context and a laboratory setting, respectively. A strong correlation was found between the length of action potential in living organisms and the use of enzyme extracts taken from the digestive system of the fish to study diphenyl hydrazine in a laboratory setting. The study demonstrates that the *in vitro* DPH method, which employs species-specific enzymes, can be a valuable tool for assessing protein digestibility in feed materials. This method can determine the suitability of various protein hydrolysates and growth factors derived from different sources for incorporation into the production media of cultured meat. It takes into account the particular requirements of the cell lines being cultivated.

According to Ahmad *et al*. (2023), growth factors, including FGF-2, IGF-1, PDGF, and TGF-β1, as well as hormones like insulin and testosterone, are vital for the proliferation and differentiation of MSCs, which are essential for the generation of cultured meat. Research conducted by Yu *et al*. (2023) found that muscle satellite cell proliferation was enhanced in commercial serum-free medium containing high concentrations of FGF2. This finding highlights the significance of FGF2 and its receptor FGFR1 in advancing effective cell-cultivated meat production. Stout *et al*. (2024) found that engineering muscle satellite cells to make their own FGF2 via autocrine signaling is a feasible technique to reduce the cost of cultured meat production by eliminating the requirement for this expensive growth factor in the medium. Epidermal growth factor (EGF) may be helpful to cultured meat production medium because it improves the cleavage and development rates of cow embryos *in vitro* when added to media (Prasad *et al*., 2018).

Lugworms, which are frequently encountered in marine habitats, offer a unique and encouraging reservoir of protein hydrolysates that can be utilized to facilitate the production of cultured meat. In a recent study conducted by Batish *et al*. (2022), the researchers investigated the ability of lugworm protein hydrolysates to decrease or substitute fetal bovine serum (FBS) in cell culture conditions used for fish cell lines. Surprisingly, lugworm hydrolysates at low concentrations of 0.001-0.1 mg/mL achieved a significant 90% decrease in FBS levels. This reduction was achieved without compromising the proliferation, survival, and morphology of zebrafish embryonic stem cells, which remained comparable to those under conventional conditions with 10% serum. The hydrolysates derived from lugworms demonstrated significant yields (30.05%) and productivity (100.16 mg/mL), indicating their feasibility for large-scale production. Furthermore, lactate dehydrogenase experiments verified that these hydrolysates did not damage the integrity of the cell membrane. Lugworm protein hydrolysates are a viable option for creating cost-effective and sustainable media formulations for cultured aquatic meat products. They have the ability to support serum-free or low-serum cell culture conditions, making them an attractive contender for this purpose.

Ashizawa *et al*. (2022) proposed a method to reduce the costs of cultured meat production by using insect cell lines. This requires including growth factors obtained from insects in the culture media. The cost of the culture media significantly rises when standard mammalian cell culture employs expensive recombinant growth agents like FGF-2 and TGF-β. To assess the potential cost reduction of generating meat from insect cells, the scientists conducted a simulation using IDGF-2, a growth factor present in *Drosophila* species that promotes the development of imaginal discs. Although the exact cost is still uncertain, the simulation indicates that including IDGF-2 into the mixture might potentially reduce the cost to $7.78 per kilogram. This highlights the possibility of using insect-derived macromolecules as more affordable alternatives to expensive mammalian growth factors in cultured meat production systems.

In addition to this discovery, research conducted by Kim *et al*. (2023) examined the possibility of using edible hydrolysates obtained from fermented soybean meals and edible insects (mealworm and cricket) as substitutes for fetal bovine serum (FBS) in the growth of pig muscle stem cells. The hydrolysates exhibited antioxidant activity and created an appropriate cell culture environment, maintaining the medium pH within an acceptable range. Cell proliferation was enhanced by supplementing the medium containing 10% FBS with hydrolysates (0.01-5% FAB-H (Fermented soybean meal with *Aspergillus oryzae* and *Bacillus subtilis* hydrolysate) and FB-H (Fermented soybean meal with *Bacillus licheniformis* hydrolysate), 0.01-1% TM-H (*Tenebrio molitor* larvae hydrolysate), or 0.01-0.1% GB-H (*Gryllus bimaculatus* imago hydrolysate)). Significantly, concentrations of 0.01% and 0.1% of FAB-H, FB-H, and TM-H demonstrated the ability to substitute for up to 50% of FBS while preserving the ability to proliferate and differentiate. Occasionally, the presence of 0.1% FB-H and TM-H in 50% FBS-reduced medium resulted in even greater differentiation than 10% FBS media. Although more research is required to understand the long-term effects fully, this study indicates that substituting a portion of fetal bovine serum (FBS) with three edible and affordable natural substances (FAB-H, FB-H, and TM-H) might substantially decrease the expenses associated with producing cultured meat.

Scaffolding Technology

In order to produce cultured meat that tastes, feels, and is nutritionally similar to regular meat, biomaterials and scaffold design play a critical part in the process. To create cultured meat, cells must grow, proliferate, and differentiate into muscle tissue. Scaffolds provide these processes the support they need.

Collagen and gelatin, mainly derived from animals, are the predominant components used in scaffolds for cultured meat research. Gelatin is a biopolymer protein that can form a gel and is used for its functional properties. Tabarestani *et al.* (2010) conducted a study that demonstrated the efficient extraction of gelatin from rainbow trout skin and confirmed its desirable physico-chemical properties. The extracted gelatin had a favorable molecular weight distribution, characterized by a high ratio of α1/α2 chains and a significant number of β chains. Additionally, it displayed exceptional gel strength, viscosity, and melting point. In the context of cultured meat production, fish-derived gelatin, namely from rainbow trout skin, is an ideal biomaterial. This is because it has the capacity to form a gel and has molecular properties that make it suitable for providing structural support for muscle cell adhesion, proliferation, and differentiation.

Moreover, the utilization of scaffold biomaterials derived from fish waste has potential in aligning cultured meat production with the objectives of animal welfare and sustainability. In their study, Shaviklo *et al.*, (2016) investigated the use of protein derived from tuna red flesh as a substitute raw material in the production of silver carp fish burgers. The researchers discovered that adding 20% tuna protein isolate to minced silver carp enhanced the sensory characteristics and overall approval of the product. The results indicated that proteins derived from discarded fish parts have the potential to be used as alternative ingredients for building the structure of cultured fish meat. This could lead to enhanced sustainability and quality of the end product.

Furthermore, the characteristics of biomaterials may be enhanced for the manufacturing of cultured meat by the process of crosslinking. Crosslinking methods play a crucial role in the creation of scaffolds for cultured meat and tissue engineering. These techniques are essential for providing the required support for cell survival, proliferation, and differentiation. The mechanical characteristics of alginate hydrogels can be improved and muscle cell development can be supported by dual-crosslinking employing visible light and covalent bonding. This suggests that these hydrogels have the potential to be used as scaffolds for cultured meat (Tahir & Floreani, 2022). The combination of physical gelation and chemical crosslinking in gelatin methacryloyl (GelMA) hydrogels leads to a variety of mechanical characteristics, which have an impact on cellular behavior and enable accurate photopatterning of structures containing cells (Young *et al.*, 2020). The process of radiation crosslinking gelatin scaffolds provides excellent transparency and effective crosslinking, which helps maintain cell adhesion motifs and amino acid content. This is advantageous for tissue engineering (Kimura *et al.*, 2021).

However, there is rising interest in plant-derived biomaterials for scaffolding to better fit with the objectives of animal welfare and environmental conservation. Better tissue formation, differentiation, and cell proliferation are possible with these materials (Seah *et al.*, 2022).

The difficulties in designing scaffolds for generating cultured meat are distinct from those encountered in biomedical tissue engineering. Critical factors include the size and expense of the manufacturing process as well as the characteristics of the finished product, such as food safety and texture. For a cultured meat product to be successful, the scaffold has to mimic the characteristics of vertebrate skeletal muscle. Future research is focused on scaffolds that enable high-quality meat development while reducing production costs. The farmed meat business is seeing promising advances in scaffolding technology at this time (Bomkamp *et al*., 2022).

For the development of cultured meat, combining biomaterials with food biopolymers is another strategy under consideration. The goal of this integration is to solve limitations related to scalability, sustainability, and edibility. Ng and Kurisawa (2020) conducted a study of existing biomaterial methodologies for the engineering of muscle and adipose tissue, highlighting the need for solutions that address these new limitations.

Biomaterials for decellularized scaffolds are a highly biocompatible and biodegradable substitute for synthetic scaffolds. Research on the use of decellularized scaffolds produced from plants and animals in the production of cultured meat is ongoing, and it has the potential to have a major impact on cellular agriculture and future food applications (Lu *et al*., 2022).

The development of biomaterials and technologies that facilitate the organization and culture of muscle stem cells in a way that emulates the normal tissue structure of animals has dominated recent advancements in the engineering of three-dimensional scaffolds. This is essential to produce cultured meat that tastes and feels like real animal flesh (Wang *et al*., 2023).

It has been shown that textured soy protein works well as a scaffold to create three-dimensional skeletal muscle tissue in cows. This biomaterial is edible and rich in nutrients, which promotes cell adhesion and proliferation to produce a meat-like product with desirable sensory qualities (Ben-Arye *et al*., 2020).

To sum up, the effective development of cultured meat depends on the design and material composition of the scaffolds. With a significant emphasis on sustainability, scalability, and the capacity to mimic the taste and nutritional attributes of traditional meat, innovations in this sector are developing quickly.

The production of cultured meat with the texture and organoleptic qualities of real meat is a difficult task that calls for a variety of methods and strategies. In order to achieve the necessary texture features and sensory properties that meet customer expectations, scaffold design plays a critical role.

Technological advancements in scaffolding are necessary to overcome the particular challenges associated with producing grown meat, including scale, affordability, and quality aspects, including texture and food safety (Bomkamp *et al*., 2022). Promising scaffold materials and methods that may be used for cultivated meat development are revealed by a study of recent advancements in scaffolding within the cultivated meat sector. These include a range of tissue engineering techniques, including cell sheet engineering, molding, bioprinting, textured scaffolds, and 3D bioprinting (Wang *et al*., 2022). The fact that the materials used in these tactics must be appropriate for food production and consumption makes them another vital factor to consider.

Tissue engineering methods, which were first performed for biomedical applications, provide new ways to modify the characteristics of meat when it comes to cultured meat production. The architecture of the scaffold, for example, may be precisely controlled by 3D bioprinting and can be tailored to resemble the fibrous structure of muscle tissue, which will affect the final product's texture (Wang *et al*., 2022). Textured scaffolds may be designed to mimic the mouthfeel and chewiness of regular meat while still providing the required mechanical support.

To sum up, in order to replicate the texture and organoleptic qualities of traditional meat, scaffold design plays a crucial role in the manufacturing of cultured meat. Achieving the desired textural and sensory attributes may be facilitated by using suitable materials and sophisticated tissue engineering techniques. It is advised that further study be done in this area to develop scaffolds that can assist the development of premium meat while lowering manufacturing costs.

Challenges and Prospects for Future Development

There are many issues surrounding the commercialization of cultured meat in science, law, and society. Achieving large-scale manufacturing at a reasonable cost, negotiating intricate regulatory environments, guaranteeing safety, and promoting customer acceptability are the main obstacles.

Large-scale manufacturing, significant progress in cell culture techniques, biomanufacturing techniques, and culture medium optimization are needed to produce economically cultured meat at a commercially feasible scale (Post *et al*., 2020). The efficiency and robustness of current technologies are insufficient to rival traditional meat production. To increase output while cutting expenses, advancements in tissue and bioreactor engineering are essential (Zhang *et al*., 2020). To make cultured meat a viable alternative, it is also necessary to produce affordable culture medium and bioreactor designs (Lee *et al*., 2023). Moreover, to address these issues, it is suggested that interdisciplinary research be integrated, including sophisticated bioreactor engineering and synthetic biology (Zhang *et al*., 2020).

There are a lot of regulatory obstacles to overcome, including uncertainty over how cultured meat will be regulated under current laws. The implementation of a well-defined regulatory framework is vital to guarantee both consumer trust and safety. Furthermore, for regulatory compliance and customer acceptability, developing sensitive and specialized analytical instruments is essential, such as sensors for food safety monitoring (Djisalov *et al*., 2021). The social and political environment must also be navigated by technology, considering issues like ethics, media coverage, religious beliefs, and possible economic effects (Bryant, 2020).

The flavor and sensory assessment of cultured meat, as well as education and addressing ethical and environmental issues, are all critical factors in the complicated problem of consumer acceptability (Hong *et al*., 2021). Neophobia, technophobia, and the idea that cultured meat is healthier all have an impact on public acceptability (Gaydhane *et al*., 2018). Transparent information and instruction on the advantages of cultured meat, such as its ability to prevent illness, preserve the environment, and improve animal welfare, are to allay these worries (Hong *et al*., 2021). Consumer acceptability also depends on developing scaffolding materials and 3D printing techniques that can create muscle cells with a texture and flavor more like to that of traditional meat (Lee *et al*., 2023).

The multidisciplinary character of these problems emphasizes how different stakeholders, such as scientists, engineers, legislators, and social scientists, must work together. For cultured meat production to be viable and widely accepted, a comprehensive strategy that takes into account the technological, socio-political, and economic components of the process is necessary (Jairath *et al*., 2021). The intricate problems of producing cultured meat need the fusion of many scientific fields, including tissue engineering, food science, material science, and sensor technology.

The commercialization of cultured meat is a lofty objective that calls for coordinated efforts from many academic fields. The successful integration of cultured meat into the food system will depend heavily on addressing the issues of cost-effective manufacturing, regulatory compliance, safety, and customer acceptability. Research and development in cultured meat is promising because of its potential advantages for environmental sustainability, animal welfare, and food and nutrition security.

Conclusion

Cultured meat has great promise for addressing issues related to global food security and environmental sustainability. Cultured meat provides a solution to satisfy the increasing need for protein while reducing the harmful effects of traditional animal agriculture by separating the production of meat from regular livestock husbandry.

Achieving this promise will require overcoming several scientific, technical, social, and regulatory obstacles. Developments in scaffold engineering, bioreactor design, cell line creation, and culture medium optimization are necessary to achieve large-scale manufacturing at a reasonable cost. Gaining the confidence of consumers and facilitating the commercialization of cultured meat products requires navigating complicated regulatory environments and putting in place robust safety procedures.

Promoting customer acceptability is perhaps the biggest obstacle. Concerns about cultured meat's perceived naturalness, safety, and sensory appeal will need to be addressed by open communication, education, and ongoing product development. To address these complex issues holistically, interdisciplinary cooperation between scientists, engineers, politicians, and social scientists is crucial.

Prioritizing sustainability, scalability, and the capacity to mimic the sensory and nutritional attributes of traditional meat is essential as research in this area advances. Tissue engineering, biomaterials, and bioreactor technological innovations are critical to producing cultured meat products that satisfy consumers and have the least negative environmental effects.

In conclusion, the development of cultured meat offers a viable solution to the problems of environmental sustainability and global food security. Even if there are still many obstacles to overcome, the potential advantages of this cutting-edge technology make it worthwhile to carry out further study, make investments, and work together to realize its full potential.

Author contributions

P. Ramezani: Writing–original draft, writing–editing, visualization. **A. Motamedzadegan:** Supervision, validation, writing–review and editing.

Funding Sources

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit.

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مقاله مروری

جلد ۲۰، شماره ۳، مرداد-شهریور ۱۴۰۳، ص. ۸۱-۱۰۳

بررسی پتانسیل گوشت کشت شده: پیشرفت‌های فناورانه، چشم‌انداز پایداری و چالش‌ها

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تاریخ دریافت: ۱۴۰۳/۰۲/۰۹
تاریخ پذیرش: ۱۴۰۳/۰۴/۰۹

چکیده

دامپروری سنتی به‌دلیل اثرات زیانبار بر محیطزیست و محدودیت در امکان توسعه مقیاس تولید، یکی از عوامل اصلی چالش جهانی عدم امنیت غذایی محسوب می‌شود. کشت سلول‌های جانوری در شرایط کنترل شده، منجر به تولید گوشت کشت داده شده یا گوشت مصنوعی گردیده که می‌تواند گزینه‌ای اخلاقی‌تر و سازگارتر با محیطزیست برای تأمین امنیت غذایی باشد. این مقاله مروری، پتانسیل گوشت مصنوعی را با تحلیل دقیق تأثیرات آن بر سیستم‌های جهانی تولید و توزیع مواد غذایی، چشم‌انداز پایداری آن، پیشرفت‌های تکنولوژیکی حاصل شده و موانع پیش رو، برای رفع معضل امنیت غذایی مورد ارزیابی قرار می‌دهد. تحلیل چرخه حیات نشان می‌دهد تولید گوشت مصنوعی، اثرات زیست‌محیطی به مراتب کمتری نسبت به گوشت سنتی دارد. پیشرفت‌های علمی مهم در زمینه‌های فناوری داربست‌ها، مهندسی بافت و طراحی بیوراکتورها، تولید گوشت مصنوعی را به تجاری‌سازی نزدیک‌تر کرده است. با این حال، موانع قابل توجهی نیز وجود دارد که باید مرتفع شوند؛ از جمله امکان تولید انبوه در مقیاس بزرگ با هزینه مقرون به صرفه، تطبیق با چارچوب‌های پیچیده قانون‌گذاری و نظارتی، تضمین ایمنی و سلامت محصول و افزایش پذیرش آن از سوی مصرف‌کنندگان. برای غلبه بر این چالش‌ها و تحقق وعده گوشت مصنوعی در راستای بهبود امنیت غذایی و تغذیه، حفظ پایداری محیطزیست و رعایت رفاه حیوانات، اتخاذ رویکردی میان‌رشته‌ای که ابعاد علمی، فنی، قانونی و اجتماعی را در نظر می‌گیرد، امری ضروری است.

واژه‌های کلیدی: امنیت غذایی، پایداری، داربست‌سازی، طراحی بیوراکتور، گوشت کشت‌شده

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https://doi.org/10.22067/ifstrj.2024.87796.1329