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Cellular Agriculture As A Novel Source Of Proteins

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Abstract

Introduced in 2015, cellular agriculture is a method of generating food in bioreactors utilizing cultured animal and plant cells or microbial cultures as an alternative to traditional livestock farming and agriculture. Dietary proteins, such as milk, eggs, fish, and meat, as well as lipids and flavourings, are the main foods produced by cellular agriculture. Numerous issues facing conventional crop or livestock farming, including water and land scarcity, the use of pesticides and veterinary drugs, climate change, environmental degradation, etc., are addressed by cellular agriculture. The produced food undoubtedly mimics the nutritional value and texture of conventional food, but it needs to be improved in terms of sensorial traits and quantity of micronutrients. This article outlines the various techniques used to produce cultivated foods in addition to their characteristics. Several multinational start-ups that produce cultured meat are also covered, along with the relevant regulatory environment. India is in the process of establishing the regulations about cellular food, while Singapore was the first to commercially approve cultured meat. Cellular agriculture is nonetheless in its infancy, but it has the potential to provide food in a sustainable and ethical manner.

Keywords: Cellular agriculture, cultivated meat, precision fermentation, safety and regulations, sustainability

Introduction

The term "*Cellular Agriculture*" is a recentandinitially used in 2015. It refers to the cultivation and manufacture of food using microorganisms or animal or plant cell cultures rather than livestock or agricultural plants. It is an alternative to conventional agriculture and food manufacturing usually occurs in bioreactors. Other names for cellular agriculture are "cell-based foods", "cell-grown foods", "clean food", "cell-cultured foods", and "lab-grown foods". Cellular agriculture can generate enormous quantities of dietary proteins (like eggs, milk, and cultured meat) as well as chemicals compounds responsible for fats, flavours, etc.It enables consumers to enjoy the same traditional foods such as burgers and dairy ice cream, but without the need to raise and kill farm animals. Precision fermentation, tissue engineering, cell culture, plant-based protein manipulation, and extrusion are some of the technologies used in cellular agriculture. This results in the delivery of protein products for human consumption in a more ethical, cost-effective, eco-friendlyand sustainable way.

Conventional agriculture is currently associated with several challenges, including soil erosion, eutrophication, excessive freshwater use, greenhouse gas (GHG) emissions, climate change, and a shortage of arable land and water. The world's fish supplies are overfished due to the rising seafood demand, endangering sensitive ecosystems and animal welfare. However, cellular agriculture offers ethical, compassionate, and sustainable substitutes for conventional farming, including raising fish and livestock.By cultivating agricultural or livestock products at the cellular level, it produces agricultural products that nearly resemble conventional ones, overcoming the difficulties of feeding the world's expanding population, which is expected to reach 10 billion people by 2050. Cellular agriculture has the potential to cut GHG emissions by 76%, water use by 94%,

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and land use by 80%. It entails growing tissue samples under controlled conditions using nutrient-rich media and bio-scaffolds. The manufacture of authentic animal products by cellular agriculture eliminates the need for animal breeding, rearing, and slaughter.

Animal-free dairy products, meat, eggs, and gelatin are a few examples of cellular agriculture products. Since proteins are among the most fundamental components of life, cellular agriculture is mostly used to produce proteins or foods high in proteins. Nowadays, enzymes that catalyze chemical reactions are produced commercially through the fermentation process. Cellular agriculture, on the other hand, seeks to create structural or storage proteinsthat provide structural qualities and store nutrients. Usually, these proteins don't show any enzymatic activity. Similarly, cellular agriculture techniques are also used to create ingredients like muscle fibre, which is a relatively new food production invention. To manufacture the desired tissue type, their production typically entails choosing cells (like muscle cells) from a target animal (like chicken) and cultivating them under carefully monitored circumstances. Like any other food ingredient, the resultant tissues are meant to be used (baked, grilled, etc.). Plant-derived proteins combined with cultured cells can lower cellular agriculture's expenses and improve its sensory qualities, allowing items to reach the market swifter. For further boosting such studies, a lot of research and business focus should begiven to plant-based and hybridized cell products.

Types of cellular agriculture

A range of proteins are produced by cellular agriculture using various techniques, such as fermenting microbes to make milk proteins or growing animal cells in a lab to produce meat.

Precision fermentation

Beer, wine, cheese, and other fermented foods are produced by microbial fermentation. Nowadays, several other compounds are made by microbial fermentation, such as citric acid (gives soft drinks their sour taste), monosodium glutamate (MSG, enhances savouryflavours) and chymosin (forms curds). Microbial fermentation has developed into precision fermentation because of recent advancements in synthetic biology and metabolic engineering technology.

Precision fermentation uses precise genetic perturbations to rewire metabolic pathways in microbes to manufacture food ingredients from economic and plentiful substrates. Precision fermentation can also result in fermented meals with more appealing qualities when conventional food-fermenting microorganisms are employed as hosts. Precision fermentation is accomplished by utilizing the precise genetic engineering instruments created for industrial biotechnology. Production in food-fermenting/Generally Regarded as Safe (GRAS) microorganisms can be maximized by introducing heterologous genes from GRAS microorganisms and/or deleting endogenous genes to reroute metabolic fluxes towards a desired product.Precision fermentation can also create fermented foods with better qualities by precisely modifying the genomes of the bacteria that ferment food. These genetic technologies enable the sustainable manufacture of costlier macronutrients, the nutraceuticals, and the modulation of flavours and nutritional content in fermented foods .

Products that use this technology include Perfect Day's ice cream, which contains bovine casein and whey proteins made in the fungus-*Trichoderma reseei*, and Impossible Foods' burgers, which contain leghemoglobin (from soybean) heterologous produced in the yeast-*Pichia pastoris*. But for commercialization of technology, lowering the production costs is still required.The ability to preserve both the high nutritional content of these proteins and the original animal-based food's functional qualities is their greatest benefit. As a result, the final producthas nutritional and sensory qualities similar to those of their animal-based equivalents but do not have the ethical or environmental problems associated with animal manufacturing.

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Cultivated meat or tissue-engineered cellular agriculture: Under this class, the main method employed is "tissue engineering," which entails cultivating live animal cells and then guiding them into a desired product (such as meat, sausage or mince patties). Cultivated meat technology is influenced by medical techniques such as employing a patient's own cells to repair injured muscle tissue or using mammalian cells to produce biopharmaceuticals on a big scale. To create muscle-like protein for astronauts and space station residents, efforts to synthesize food *in-vitro* were initiated. Because of the enormous potential for cell proliferation, meat produced from muscle satellite cells or fat cells is regarded as a novel meat product with promising futures. The fundamental technology used to produce cultivated meat is as:

1) harvesting and isolating muscle or adipose stem cells
2) growing the number of cells in a growth medium in bioreactors
3) employing edible scaffolds to mature the stem cells into muscle or fat cells and fibres
4) turning into a finished meat product through processing and assembly

Therefore, the creation of muscle or fat cells in a bioreactor away from the living animal holds promise as an innovative method of manufacturing animal protein that avoids animal production. Since there is currently no industrial technique, the estimated cost of producing one kg animal protein from a bioreactor is uncertain. According to a technical evaluation cost analysis, the cost of producing cultured meat is currently 100–10,000 times greater than that of producing normal meat products, and the costliest component is the cell culture medium. However, further cost reductions are anticipated as the sector grows, and the production of grown meat becomes more efficient beyond 2030.

Properties of cellular agriculture foods

Traditional meat products are nutrient-dense and provide necessary vitamins, minerals, and amino acids to humans. Additionally, myosin and actin - the structural muscle proteins, have a variety of functional qualities, like ability to produce gels, bind proteins and water, and generate emulsions. The marbling adds flavour and juiciness, and the lipids in the fat help to impart these qualities to the cooked meat. When using products from cellular agriculture to create novel food products, such characteristics mustbe considered.In 2013, the first cultivated meat burger was tasted and found to be dry and salty. Therefore, it is considered essential to improve the meat quality features of cultivated meat products. As demonstrated recently by Kang et al. (2021), who used 3D bioprinting to assemble differentiated muscle, adipose tissue, and blood capillary cell fibres to a steak-like meat, the mitigation strategies are as: cultivation of skeletal muscle cells and fat cells separately and then combine themfor making final product. In conventional methods, thenumerous volatiles can be introduced in meat primarily through Maillard reactions and lipid degradation during heating to improve meat's flavour. But in cultivated meat, theflavour components should be added, like in plant-based meat substitutes.

Colour is another essential quality trait and meat color is red due to myoglobin. Skeletal muscle cells generate a little quantity of myoglobin during the *in-vitro* development of muscle tissue. The myoglobin protein can be added to the growth media or cultivating cells in hypoxic environments to boost protein expression. Additionally, conventional beef is a great source of micronutrients like selenium, zinc, and iron. In traditional beef, iron is either kept in non-heme form in complexes with ferritin or is a component of the heme group in myoglobin. Increasing the myoglobin content of cultured beef is therefore essential for both colour and nutrition, as iron is most accessible in the heme form. The zinc and selenium need to be added which otherwise are missing from cell culture media.

Current start-ups

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Nowadays, several countries are working on cellular agriculture techniques and numerous start-ups from all over the world have entered this market, developing cutting-edge technologies ranging from precision-fermented dairy to bio-fabricated materials to cultivated meat and seafood (Table 1). By creating sustainable, ethical, and scalable substitutes for traditional animal/agriculture, these start-ups are significantly influencing the direction of food in the future.

Table 1 Summary of cellular agriculture-based start-ups in the world

S. No.	Name of company	Location	Type of food	Reference
1	UPSIDE Foods	California, USA	Cultivated beef meatball	https://upsidefoods.com/
2	Mosa Meat	Maastricht, Netherlands	Cultured burger	https://mosameat.com/
3	Aleph Farms	Rehovot, Israel	Cultivated Steak	https://aleph-farms.com/
4	Meatable	Delft, Netherlands	Cultivated pork	https://www.meatable.com/
5	Wildtype	San Francisco, California, USA	Cultivated salmon	https://www.wildtypefoods.com/
6	BlueNalu	California, USA	Cultured tuna toro	https://www.bluenalu.com/
7	Finless Foods	California, USA	Cultured tuna	https://finlessfoods.com/
8	TheEVERY Company	California, USA	Cultured egg white protein	https://every.com/
9	Perfect Day	California, USA	Microflora-based whey proteins	https://perfectday.com/
10	TurtleTree	Singapore/USA	Sustainable Lactoferrin	https://www.turtletree.com/
11	Remilk	Rehovot, Israel	Cultured milk and dairy products	https://www.remilk.com/
12	Imagindairy	Haifa, Israel	Animal free milk proteins	https://imagindairy.com/

Safety, regulatory and ethical considerations

For the successful commercialization of cultivated meat, there is a need to strongly address several crucial issues like guaranteeing nutritional, chemical, and biological safety and navigating the global regulatory environment. It is also essential to identify and eliminate any possible risks throughout the cultivation process to guarantee the biological safety of lab-grown meat. The use of cultivating material originating from animals, microbial contamination, and the possibility of viral or prion infection are among the other issues. Likewise, growth media residues, scaffolding materials, and other bioprocessing agents are examples of chemical risks. The nutritional properties of cultivated meat should be like traditional meat for consumers acceptance. This corresponds tosufficient protein, essential amino acids, vitamins, and minerals. Furthermore, a thorough evaluation of the safety of cultured meat regarding allergenicity and the presence of anti-nutritional components is also necessary.

With respect to regulatory aspects, there are notable geographical differences in growing regulatory environment for cultured meat. Several established laws, including the “Livestock Industry Act,” the “Food Safety and Standards Act, 2006,” and the “Livestock Products Sanitary Control Act,” control traditional meat products. However, because cultured meat is made without the use of traditional animal breeding, it does not fall into these categories. Therefore, there is no clear legislative framework to cultured or cultivated food. Although the USA has established a regulatory framework, incorporating US Department of Agriculture

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(USDA) and Food and Drug Administration (FDA), butSingapore is presently the only nation with approval for the market placement of cultured meat.Additionally, Singapore authorized the term for use on commercial cell-based meat. Singapore's policy specifies specific phrases, such as "mock" and "cultured," that can be used on labels. The cultivated meat presents unique opportunities in India to utilize its vast resources and manufacturing capabilities to employ strategically towards this emerging category and become a production powerhouse. India hasn't yet drafted any laws pertaining to cultivated meat, but Food Safety and Standards Authority of India (FSSAI) is working to frame guidelines.

Effective communication techniques are essential to aware customers about the benefits and security of the cultivated product. Numerous factors mayinfluence the public's perception about lab-grown foods like product familiarity, nutritional value, and ethical concerns. By addressing concerns about the naturalness, safety, and nutritional profile of cultured meat, the transparent and educational labelling can increase consumer trust and adoption. Labelling efforts for cultured meat should be supported by consumer education programs that explain the product's production method and sustainability and animal welfare advantages. Involving customers in conversations about scientific discoveries can alleviate worries and encourage wise choices. Manufacturers and regulators can better grasp consumer expectations by conducting surveys. Furthermore, labels that use brief, plain language and include visual aids can help consumers better comprehend the advantages of cultured meat for their health and towards environment.

Future Perspectives

No doubt,thecultured food is a promising substitute for conventional food or proteins offering potential for animal welfare and conservation of natural resources. However, nutritionalcomposition, biochemical safety and regulatory compliance are still severely hampered. Biological safety is mandatory in careful procurement of animal cells as well as performing aseptic biopsies to minimize contamination. The problem of microbiological contamination can be reduced by maintaining hygiene and sanitation at personnel, equipment, and environmental level.Also, the residues of antibiotics, herbicides, pesticides, etc. can be minimized to ensure chemical safety. Further, the hazardous residues can be thoroughly tested and avoided, if possible, by selecting eco-friendly and biodegradable materials.

Around the world, there are differences in the commercial approach of cultivated meat. Singapore is a model for commercialization because of its proactive approach. The cultured meat sector has recently reached significant milestones, including the opening of commercial restaurants, regulatory licenses, increased private and public investments, tasting events, and advanced product advancements from several entrepreneurs in a select few nations. However, the coherent regulatory frameworks to encourage the acceptability of cultured meat are still lacking in many nations. Strategies addressing nutritional integrity, regulatory compliance, and biological and chemical safety are essential to the mass acceptability of cultured meat. The stakeholders must continue their research and work together to overcome the obstacles and fulfil the potential of cultured meat as a sustainable and moral substitute for conventional meat production.

Conclusion

For cellular agriculture to be successful, numerous stakeholders must collaborate across disciplines and be highly innovative. It can significantly impact agricultural output and ownership, policymaking, eating habits, land use, and ethical issues. However, issues like global scalability and distribution persist because cellular agriculture is still in its infancy. Even though a lot of innovation and progress are still made in private companies behind closed doors, government support and expanding public research initiatives will help to improve openness, transparency, and trust as well as to identify barriers and investigate solutions.

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