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Novel aspects, environmental impacts and future prospects of cultured meat: A review

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Abstract
Cultured meat holds the promise to provide healthier, safer, and disease-free meat to consumers. It is tissue-engineering technique, with goal to produce meat without slaughtering of animals in controlled laboratory conditions. Cultured meat manufacturing at industrial scale is expected to be economical, safe to environment and possessing high nutritional attributes as compared to conventional meat. This review aims to discuss, the concept of cultured meat production system and success achieved till date in this innovative process. Some potential barriers like technological hurdles, consumer attitude and a little historical overview has also been discussed in brief.

Keywords: Cultured meat, *In-vitro* meat, lab-grown meat, slaughter free meat

Introduction

The use of livestock and food is an integral part of the human diet since the dawn of human civilization and customarily obtained from rearing and slaughtering farm animals. Over the period of time meat consumption has been provided with high regards in terms of nourishment, taste and heritage. At present, rearing of livestock for meat, wool, feather, leather and bones, contributes economically to GDP of agriculture sector. Global meat production and consumption has tripled over the past half century, mainly in newly industrializing countries (Smil 2002; Robinson *et al.*, 2011; Hoag 2013; Stoll-Kleemann and O'Riordan, 2015) [100, 88, 52, 104].

Animal meat represents 40% of total world meat consumption and demand is expected to be more than double for a projected population of 9 billion by 2050 (Sans and Combris, 2015 and FAO, 2009) [93, 37]. Being a valuable and inseparable part of diet, meat is a source of alternate energy supply to carbohydrates (proteins and fats), vitamins, and minerals. Further, inclusion of meat in diet is also linked with tradition for many cultures. Imprudent consumption of meat is considered to be reason for myriad health related issues (*like* overweight, obesity, atherosclerosis and cancer, Fergusson, 2010; Corpet, 2011; Buscemi *et al.*, 2013; Kim *et al.*, 2013) [38, 26, 17, 62].

About 70% of ice free-cultivable land is under livestock cultivation and merely 30% is used for plant based agricultural activities (Welin and van der Wende, 2012) [113]. Conversion efficiency of feed into meat is also not very productive, for instance, as reported by Rosegrant *et al.*, 1999 [90] that an estimate of that 2, 4, or 7 kg of grain is required to obtain 1 kg of poultry, pork, or beef, respectively. However, overall value of animal rearing could not be neglected, as apart from edible meat, other components of the carcasses is also utilized by industries in some form or another (*like* leather, casing, fertilizer, pet food, wool etc; Bhat, 2019 [10]. Consumption of insects and snails as protein supplement is a common practice in African and Asian cultures, but Westerners are reluctant to include this kind of nutrition in their menu cards. Moreover, many meat consumers who are aware of potential health hazards and environmental issues, are not willing to change their food habits or reducing their meat consumption levels, owing to cultural values, tradition, and extravagant lifestyles (de Bakker and Dagevos 2012; Sch¨ osler *et al.*, 2014) [28, 95].

Further, owing to popularity of meat products and perception of meat as healthy diet among meat connoisseurs, diverting meat consumption to other options *like* plant based proteins, is not a viable option (Verbeke *et al.*, 2010; Vanhonacker *et al.*, 2013; Alexander *et al.*, 2017; Macdiarmid *et al.*, 2016) [111, 110, 2, 69].

Though, Caldwell in 2015 [18] reported that there is a rise in UK consumers for embracing vegetarianism in their diets, this is contradictory to Hartmann & Siegrist, 2017 [50] findings that only a minority of meat eaters are inclined to substitute plant-based proteins for animal proteins. Animal meat industry also contributing adversely to environment *like* GHG emission (contributes to climate change), inefficient use of natural resources (arable land and fresh water), soil erosion, loss of biodiversity and soil/water pollution (Bhat *et al*., 2014, 2015, 2017; Asner *et al*., 2004; Savadogo *et al*., 2008) [11, 13, 12, 4, 94]. Degradation of environment has raised concerns among the policy makers, scientists and environmentalist, and stirred debates at global level for its protection in a long run (Hallstr¨om *et al*., 2014; Yadavalli and Jones, 2014) [48, 120]. Researchers have proposed to implement novel technology and biotechnology in meat industry to mitigate environmental impacts and shift toward sustainable mode of meat production such as cultured meat (Bhat *et al*., 2015, 2017; Lentz *et al*., 2018) [13, 12, 67]. Cultured meat is an emerging technology that has been proposed to be cruelty-free replacement for meat whereby eliminating the necessity of sacrificing the animal, with limitless supply of processed meat products such as sausages, burgers, nuggets and leaving very small ecological foot print (Bhat *et al*., 2015, 2017, Datar and Betti 2010; Hocquette, 2016, 2018; Haagsman *et al*., 2009) [13, 12, 27, 54, 55, 47]. This shift in production system is holds promise to alleviate some of the environmental impacts and ethical concerns associated with conventional meat production systems (Alexander *et al*., 2017; Cooney, 2014) [2, 25]. Though this new technology is in its infancy and production of cultured meat at commercial level has a long way to go. This review article seeks to address social, ethical and political challenges of this emerging cellular agriculture technology and also throws some light in relation to consumer acceptance, potential benefits and future concerns of slaughter free meat harvest.

Historical Overview

The impression of *in-vitro* meat production for human consumption was predicted by the writer and Conservative politician Frederick Edwin Smith in 1930, stating “It will no longer be necessary to go to the extravagant length of rearing a bullock in order to eat its steak. From one ‘parent’ steak of choice tenderness it will be possible to grow as large and as juicy a steak as can be desired” (Ford, 2010) [39]. Though in 1912, French biologist Alexis Carrel successfully demonstrated the possibility of keeping a chick’s heart muscle tissue alive, beating and dividing outside of the body in a Petri dish for 34 years (Carrel, 1912; Jiang, 2012) [19, 58]. Similar thoughts of future meat as cultured meat were also mentioned in essay of Winston Churchill “Fifty Years Hence” (published in “Thoughts and Adventures, 1932”) quoting “Fifty years hence we shall escape the absurdity of growing a whole chicken in order to eat the breast or wing by growing these parts separately under a suitable medium”. Similar idea could be read in a French science fiction novel “Ravage” by Rene Barjavel, 1943 (translated as ‘*Ashes, Ashes’* in 1967) affirming *in vitro* production of meat in restaurants (Eschner, 2017) [32]. In 1999, patent was secured by Willem Frederik van Eelen for industrial production and human consumption of cultured meat.

In 2002 NASA, for crew members of its space stations, intended to culture muscle tissue from *Carassius auratus* (Gold Fish) in Petri dishes containing fetal bovine serum substitutes as medium for growth, and performed sniff-tests to assess palatability, which was judged by a test-panel and agreed that the product was acceptable as food (Benjaminson *et al*., 2002) [7]. Similar project was performed by bio-artists in the Tissue Culture and Art Project in 2010 and concluded by taste-tests (Catts and Zurr, 2010) [21]. The most remarkable milestone was the launch of world’s first cultured meat-based beef burger in 2013 by a Dutch scientist, Professor Mark Post in a time frame of 3 months (Zaraska, 2013) [122]. The world’s first cultured beef burger was eaten by a panel of sensory judges in a London press conference, August 2013 and was concluded to be tasted similar to a conventional one (O'Riordan *et al*., 2017; Post, 2014) [79, 84]. The success of 2013 burger event prompted and influenced consumers, particularly those with animal welfare concerns, and company giants to persuade its production of cultured meat at commercial levels. To begin with, cultured meat might be a luxury item, providing exotic treats in form of snow leopard burgers or rhino sausages (Zaraska, 2013) [122]. Next brick in the wall was the launch of a fictional *In Vitro Cookbook* by the Dutch arts collective Next Nature, 2014, containing recipes 45 from cultured meat based products (Wurgaft, 2014) [118].

Emerging Company Giants

Among some leading players in the race are: Mark Post's Maastricht group, first cultured burger provider, Memphis Meats, demonstrated cultured meat products as meatball and beef fajita, JUST (Hampton Creek), released promotional video footage of cultured chicken nuggets on various online sites *like* https://vimeo.com/226196373 , Israel based set-ups-SuperMeat, Future Meat Technologies, and Meat the Future, Modern Meadow (United States) currently focusing on cultured leather and has demonstrated ‘steak chips’, Finless Foods Inc. promising to bring sustainable sea food and various TED talks on meat without killing, by the filed experts (Modern M and Marga, 2015; Just, 2017; Roberts, 2017; Chiorando, 2018; Stephens *et al*., 2018) [77, 61, 87, 22, 102].

Why cultured meat??

Animal rearing for meat consumption has always been a question of debate in food ethics. Slaughtering of animals is not considered moral by many cultural societies and animal welfare organizations. In 2015, 28.8 25.7 million cattle were slaughtered in US and EU, respectively and there are concerns regarding current slaughter practices (Welin, 2013; USDA, 2015; Eurostat 2018) [114, 107, 35]. Livestock resource conversion efficiency (in terms of feed to meet conversion) is extremely low, for instance, 5% of total feed and energy intake is converted in to beef and it takes 15K liters of water for production of 1 kg beef (Smil, 2002; Mekonnen and Hoekstra, 2010, 2011) [100, 74, 75]. As reported by Bhat *et al*., 2015 [13], from 75% to 95% animal feed is lost in regular growth metabolism and production of inedible parts.

Meat over-consumption has been reported to be directly associated with many diseases and health disorders *like* obesity, diabetes, colon cancer and cardio-metabolic diseases (Leroy *et al*., 2018; Micha *et al*., 2017; Zelber-Sagi *et al*., 2018) [68, 76, 123]. PhIP is most common aromatic amine which act as carcinogen, produced during meat cooking (Hoa *et al*., 2017) [51]. Livestock also poses risk for zoonotic disease like mad cow disease and influenza in particular (Leibler *et al*., 2009, WHO, 2015) [66, 116]. Intensive livestock cultivation also use antibiotics, pesticides, polychlorinated biphenyls, heavy metals, brominated flame retardants and heterocyclic aromatic amines which cause human health harm by contaminating consumable meat (Sanders, 1999; Yu *et al*., 2011; Xing *et al*., 2008; Gao and Wang, 2014; Kulp *et al*., 2003; Engel 2015) [91, 121, 119, 42, 63, 31]. Animal cultivation is major source of carbon footprint, and land and water utilization. Sustaining livestock industry annually requires about 4.7 billion tones of dry matter and ill impact on land and water resources is tremendously high (Mekonnen and Hoekstra, 2012; Bosire *et al*., 2016) [73, 15]. Few countries have lessen the environmental load by adopting new technologies and implementing scientific practices while other countries need intervention and backing in their policies to enhance their production efficiency and reduce environmental load associated with livestock sector (Bhat *et al*., 2019) [10].

These concerns of lower resource efficiency, insufficient nutritive value, food borne health issues, environmental pollution along with expected future meat demand lead the researchers to propose the idea of *in-vitro* production of meat from tissue culture biotechnology. Laboratory cultured meat is projected to be more sustainable and nutritious as compared to the conventional meat. Cultured meat aims to ensure food security and reduce the resource consumption load on environment. Most noticeable feature of this cellular agriculture is that it is a slaughter free meat production system. As cultured meat is an animal free harvest, therefore, expected to be healthier, safer, disease free and anticipated to alleviate negative environmental effects (*like* GHG emission and carbon footprint) associated with traditional meat production (Stephens *et al*., 2018) [102]. Moreover, livestock rearing contributes to biodiversity loss (52% of world's wildlife), grassland overgrazing, deforestation (80% in Amazon countries) and desertification throughout the world. (Garcia *et al*., 2017; Global Forest Atlas, 2019; WWF, 2018) [43, 45, 117].

Stephens *et al*., 2018 [102] proposed that *in-vitro*, lab grown meat will have wide innovation scope to reduce the present energy requirements and therefore, could cause positive environmental effects. In recent times, animal welfare is foremost deciding factor in assessing the ethical profile of brands (Schröder and McEachern, 2004; EC 2007) [98, 34] and thus, labeling meat and poultry products as being "cage free" and "free range, will also be beneficial to attract consumers on the grounds of animal welfare (Bhat, 2019) [10]. Benefits of cultured meat are numerous.

1. Alteration in composition of final manufactured product, in controlled factory environment, in respect of nutrition value, taste and texture, as per the demand of the consumers/ market (Post, 2012 and van Eelen, 1999) [85, 109].
2. Reduction in risk of antibiotic contamination and zoonotic diseases and therefore safe product (EC, 2010) [33] and therefore, safer consumable end products
3. Cultured meat indented not to involve animal suffering and slaughtering at any stage of production. In this regards, it would definitely attract vegans, vegetarians and animal welfare community (Hopkins and Dacey, 2008) [58]. Slaughter free method of meat production also welcomes the possibility of including variety of exotic meat in food menu (Zaraska, 2013) [122].
4. Retention of traditional genetic pool, more profit, less food waste and lower environmental impacts will contribute to industry and biodiversity (Stephens *et al*., 2018) [102].
5. Cultured meat production units could be established near or within the cities and thus in proximity to final consumers and therefore reduces land use and contributes to financial gains by reduction of transportation and long term storage. Free land in rural areas could be utilized for reforestation, restoration of endangered species and growing of biofuels, food crops and fruit crops.
6. As lab grown meat is expected to be slaughter free meat, this may lead to the possibility of availability of meat from exotic and rare wild animals in the form of variety of new products (*like* rhino sausages and snow leopard burgers, Zaraska, 2013 [122]).
7. A genetically altered cell line or tissue sample from a single livestock would be enough to meet numberless meat supply (at least theoretically) to meet the future demand (Rorheim *et al*., 2016) [89].

Processing at Industrial scale

Tissue engineering is a cellular agriculture system, which aims to culture meat and leather artificially *i.e* outside animal body. The technology entails differentiating stem cells into muscle cells, using mechanical, chemical and biological cues in the culture media (Langelaan *et al*., 2011) [65] and includes the cell expansion and differentiation; product manufacture; and waste valorisation as basic components. Further, Life Cycle Assessment (LCA) is essential to understand the carbon footprint (Schnitzler *et al*., 2016) [97]. Cell source/ starting material for tissue engineered cellular agriculture could be:

1. **Original tissue:** Harvesting tissue samples by biopsies, from small herd of animals and culturing them**.** Multipotent cells, *like* muscle stem cells and mesenchymal stem cells, possessing higher proliferation capacity are most researched source (Jung, 2012; Stern-Straeter, 2014; Oikonomopoulos *et al*., 2015) [60, 103, 78].
2. **Cell lines:** obtained *via* induction (genetic engineering or chemical) or spontaneous mutations. In both cases, cells are programmed to proliferate indefinitely (Eva *et al*., 2014; ThermoFisher, 2017) [2014, 105]. Culturing induced pluripotent stem cells (iPSC) is showing encouraging results but is also associated with hurdles *like* mis-identification, continuous evolution, passaging and sub-culturing (Genovese *et al*., 2017; Stephens *et al*., 2018) [44, 102].

Myogenesis (muscle development), is an important parameter determining meat quality and begins in embryonic development, continues in foetal development and post-birth could be observed during injury or trauma recovery and workload adaptation (Adams *et al*., 1999; Grefte *et al*., 2007) [1, 46]. The process of muscle growth and regulation is regulated by hormones, growth factors (cytokine) and neural activity. It is now possible to grow and differentiate muscle cells in controlled cultured environment (Orzechowski, 2015) [80], with required supply of nutrient and oxygen through diffusion gradient, and mechanical or electrical stimulation. External electrical stimuli are applied for development of mature muscle fibers and checking muscle function (Bach *et al*., 2004; Dennis *et al*., 2009) [6, 29]. Culturing a complex muscle tissue (*i.e* prime quality meat) with fully grown vascular system would require advanced biomaterial technologies and would require some time (Collins and Partridge, 2005; Bhat, 2019) [24, 10].

Growth medium is supplied with foetal calf or horse serum (0.5–2%), in some case chicken embryo extracts is also added. Antibiotics (to prevent infection), growth factors *like* vitamins, hormones, trace elements amino acids and fatty acids are also required for cellular growth and development, and maintaining cell viability (Arora, 2013; Brunner *et al*., 2010, Chiron *et al*., 2012; Aswad *et al*., 2016) [3, 16, 23, 5]. In some cases supplementary proteins or media like AIM-V, Sericin and Ultroser- G is used as a substitute for foetal serum (Fujita *et al*., 2010; Portiér *et al*., 1999) [41, 82], Cytokines also plays prominent role in muscle regeneration (particular to muscle damage).

For large scale multiplication of cells, bioreactors are used to. Use of bioreactors is common in industrial production of pharmaceuticals, vaccines and antibodies, and therefore, best choice for large scale cell multiplication. Bioreactors maintain controlled conditions of temperature, pH, oxygen gradient, ensures regular supply of nutrients, vitamins and other essential components in the culture chamber. For cultured meat production, customized bioreactors are assigned that maintain low shear force and provide uniform perfusion for large volumes, for instance, rotating bioreactors of NASA. Further, electro-magnetic, gravitational and fluid flow mechanics are maintained for proper differentiation and proliferation in *in-vitro* culture systems (Carrier *et al*., 2002; Radisic *et al*., 2008; Bhat and Bhat, 2011; van der Weele and Tramper, 2014) [20, 86, 2011, 108]. At present establishing a scaffold (necessary part of cultured meat research) and bioreactor conditions that allow differentiation in large bioreactor is the major confront for production culture meat at industrial level (Stephens *et al*., 2018) [102].

Hurdles and Obstacles

1. The aim is to provide natural environment (*in-vivo* niche) and a scaffold (3D structure) that allows cell adhesion, tissue replication, and fiber alignment as similar as native tissue. At present, 3D scaffolds are animal-derived (Bian and Bursac *et al*., 2009) [14]. However, "bio-artificial muscle" is under investigation (Snyman *et al*., 2013) [101]. An ideal scaffold should be biocompatible and nontoxic to the multiplying cells, and can form a matrix to which cell can bind compactly to form tissue. Naturally occurring materials (*like* Alginates, cellulose and chitins: Sandvig *et al*., 2015 [92]) and synthetic biomaterials (like Polyglycolic acid, polylactic acid, and polyurethanes: Bhat *et al*., 2019 [10]) are some considerations to produce attachment sites. Cell multiplication and differentiation to specific cell type must be optimised and scaled, adequate research is needed in relation to differentiation (Stephens *et al*., 2018) [102].
2. Foetal serum is expensive and is not available in volumes to meet the need for processing of cultured meat at industrial scale. Though possible, but difficult to culture animal cells under serum-free conditions, cause delay of culture development and therefore, the manufacture of a sustainable, animal-free, affordable media is a major challenge. Cynobacteria (having protein content upto 70% dw) can be a potential energy substitute for cell multiplication & growth in culture (Jochems *et al*., 2002; Ford, 2011) [59, 40]. Apart from energy, other growth factors are also required in the medium, which for instance, could be supplied by liver cells (Edelman *et al*., 2005) [30].

Future Prospects and Considerations

Meat culturing in bioreactors will be free from external stress factors (management and environment), lead to optimum production of consistent quality meat. This will open possibilities of meat production in areas where climate and land conditions are not favorable. Cultured meat will also attract consumers who prefer vegetarianism on ethical grounds. Moreover there will be less waste production in production of cultured meat (Bhat *et al*., 2019) [10].

Skilled technical workforce of agriculturalists, veterinarians, technicians, chemists, cell biologists, material scientists, food technologists etc would be required in production of cultured meat at industrial levels. Global food regulations, to meet the safety measures and quality assurance at every stage of production, and legal norms to ensure that the final product is not human, non-living living, and slaughter free, must be implemented. Need of regulatory bodies to confront potential food frauds *like* attempts to sell conventional meat at cultured meat *or vice versa*. Ethical and safety consideration are required to avoid mislabeling of meat type, selling of pet animals' meat or endangered/protected animal meat, human cellular agriculture (Stephens *et al*., 2018) [102].

Discussion

If slaughterhouse has glass walls, everyone would be vegetarian

- Sir James Paul McCartney

Cultured meat or *in-vitro* meat is an emerging biotechnology and engineering practice to produce meat/muscle for consumption as food. Cultured meat promises to offer numerous benefits in terms of human and environment health, and animal welfare. Conventional meat system, which involves breeding, feeding and killing of animals is perceived unethical compared to cultured meat, which involves obtaining desired cell sample to grown in controlled environment (Singer, 2013; Hopkins and Dacey, 2008; Tuomisto and de Mattos, 2011; Mattick, 2015) [81, 58, 106, 71, 72]. *In-vitro* meat production also provides effective control over quality, aroma, fat content, nutrient composition, texture and flavor (Bhat and Fayaz, 2011) [9]. Further, supplementary ingredients could be added to boost health and taste. The cultured meat production system is time and resource efficient, and also supported by the fact that it is relatively humane way to produce meat thus, invites attention from various communities of scientists, environmentalist and animal right activists (Schneider, 2013) [96].

In relation to public health and environmental benefits, there is positive perception among people. While, safety, quality and unnatural production of cultured meat has been perceived negatively. Generally, people voted for their willingness to try the cultured meat product, at least once (Hocquette *et al*., 2015) [53]. These qualitative analyses were made by examining people's perception to cultured meat from online news sources (Laestadius, 2015) [64] further, it was also observed from analysis online comment sections that the rural community is more reluctant towards acceptance of *in-vitro* meat (Mahar and Barnes, 2014) [70]. People are also not willing to pay more prices for cultured meat than for conventional meat (Post, 2014; Verbeke, 2015) [83, 112]. Apart from taste and personal choice, meat consumption also has deep cultural value across various communities, and acceptance of lab grown meat strongly depends on individuals' demography and cultural values, for instance, Muslims are ready to accept cultured meat it's Halal (Wilks

and Phillips 2017; Hamdan, 2018) [115, 49].
Cultured meat is in its infancy, though extensive research is going on considering key technical challenges *like* cell source, bovine serum free culture media, consumer acceptability and bio processing at industrial scale (Haagsman *et al*., 2009) [47]. Extensive research and testing is needed to optimize processing experimental condition. Detail studies are required to understand the psychological obstacles that may arise in future, and may lead to rejection of *in-vitro* meat by the consumers (Post, 2014) [83, 84]. The success of mass scale production and acceptance of cultured meat will depend upon social structure, religious background of the countries, food laws and policies, tax and subsidies regimes. The success of "project cultured meat" largely depends on two factors *viz* its closeness in mimicking conventional meat in terms of sensorial characteristics and flavor, and affordable price for the final consumer (Sharma *et al*., 2015) [99]. There is a need to make people aware of the potential benefits that cultured meat possess and make them understand the concept and procedure of its production. Another appealing expected outcome from the success of cultured meat is "home-grown meat" (Orzechowski, 2015) [80].

Conclusion
Conventional livestock rearing, meat production and consumption is reported to have numerous negative impacts on human health and animal welfare, and demands a sustainable solution to mitigate the high cost it places on environment. Opting for a vegetarian diet is an option, but not realistic. Moreover only a small group of meat eating population will be inclined to opt for this diet substitute. Cultured meat, *in-vitro* grown muscles, is an emerging solution but question is: *Are we willing to accept the lab grown meat in our plate?* Because as for now there is a high degree of disgust and sense of mistrust among the meat consumers regarding cultured meat and reasons are deep rooted owing to social and cultural reasons. Commercializing the idea that consuming cultured meat is by no means eating the animal is crucial. Moreover, it is important how media portray and represents cultured meat because naming could have strong impact in perceiving the reality. The "tug of war" between technology and tradition is ancient and there are still many technological obstacles regarding success of production of cultured meat at industrial scale and aiming to get a steak rather than a pile of cell mass of callus. Keeping in view the significant progress achieved in this area, the *in-vitro* cultivation of animal cells seems to be a practicable solution to meet growing meat demand. Further, if success achieved in producing high quantity and acceptable quality cultured meat in large bioreactors, then not only it will be cheaper and faster but also environmental friendly.

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