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A holistic approach to access the viability of cultured meat: A review



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ABSTRACT

Background: Cultured meat has shown a great potential to address food sustainability and nutritional security in near future. Unlike conventional meat, the cultured meat is humane and doesn't offend the sentiments of animal lovers, hence may satisfy the needs of a larger segment of the society. The technology promises the designer, pathogen-free, ethical and eco-friendly meat product. But there are many techno-social, economic and other challenges that has not resolved yet and play a decisive role in survivability and viability of *in-vitro* technology. *Scope and approach:* The review covers wide range of challenges that cultured meat technology is facing right from Petri dish of lab to the plate of consumer. The factors behind survivability and viability of in-vitro technology have been reviewed. Further, the effects of technology on the economy of agriculture based developing countries have also been revisited.

Key findings and conclusions: Public acceptance, structural incompetency, and economy of the products are main areas which need due consideration for the successful acceptance of the cultured meat in food market. In a current scenario of Covid-19 pandemics, cultured meat may emerge as a basic need of muscle food industry. However, complete replacement of conventional meat with cultured meat may le to adverse long-term impact on agriculture-based economies of developing countries.

1. Introduction

Cultured/synthetic/in-vitro/lab/clean or animal free meat production, though an advanced technology, is now no longer new in this 21st century where basic methodology involves harvesting of differentiated mature muscle cells after culturing of loose myo-satellite cells on a substrate in a liquid medium under mechanical stimulation (Bhat and Bhat, 2011a; Stephens et al., 2018). In simpler words, the in vitro meat is closely analogous to animal-derived meat that we eat, but it circumvents slaughtering of animals to obtain the flesh (Post, 2014). Initially, lab grown meat was called as in-vitro meat and later in around 2011, the term 'cultured meat' was used more, owing to culturing techniques involved. Then the term 'clean meat' advocated since 2015 appears to be more appealing and attracts a broader attention of the consumers (Datar, 2016; Bryant & Barnett, 2019; Friedrich, 2016; Kramer, 2016; Stephens & Lewis, 2017). However, Hocquette (2016), named the lab produced meat as 'artificial muscle proteins' arguing that word 'meat' implies maturation inside an animal and slaughtering the animal to harvest the tissues and organs. Though there are many names of lab grown meat as mentioned above, basic methodology in all the processes are more or less similar.

The process of conventional as well as precision livestock farming and slaughtering of animals for meat has religious, ethical (Heidemann, Molento, & Reid, 2020) and environmental (Tullo, Finzi, & Guarino, 2019) concerns. These problems can be overcome by *in vitro* produced meat which involves culturing animal adipose cells and the muscle fibers from muscle stem cells and satellite cells (Singh et al., 2020). Here, the cells are taken from a donor animal through biopsy and are cultured using matrices containing nutrients, energy sources and growth factors within a bioreactor. The cells proliferate and finally differentiate into muscle cells which then assemble into muscle fibers (Woll & Bohm, 2018). However, the acceptability of technology ultimately depends upon the end users, proportion of potential benefits and drawbacks and long run viability of that technology.

Cultured meat may appeal to increasing number of consumers who are concerned with the morality of killing animals for food. For instance, in March 2012, when the New York Times organized an ethicist contest among readers and invited essays, to express their views on "ethics of eating meat". The winning essay expressed that we have no right to kill and must choose the ethically raised food (Bost, 2012). In 2013, in a contest with theme 'Put Your Ethics Where Your Mouth Is' voting was in favour of the author who was about to eat meat for the very first time in

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40 years because "the very first laboratory-grown hamburger is to make its debut", real meat "without the mess and the misery" (Newkirk, 2012).

Apart from ethical concerns, shooting global meat demand and consumption have raised the concerns for sustainable meat supply; thus, hoping on cultured meat. The meat consumption has raised by 15.4%, between 1995 and 2005 (FAO, 2009). It has been speculated that global meat demand is going to be doubled by 2050 (FAO, 2009). The continuously growing demand cannot be satisfied by conventional meat as large ecological footprint of livestock production makes it unsustainable (FAO, 2006; Fiala, 2008; Steinfeld, Mooney, & Schneider, 2010). Adverse ecological concerns such as consumption of fossil fuels in animal farm operation, greenhouse gas (GHG) emissions, land, water and energy requirements and rapid evolution of multidrug-resistant superbugs has necessitated the significance of in vitro meat technology (Singh et al., 2020). Notably, energy use can be reduced by 45%, GHG emissions by 96%, land use by 99% and water use by 96% if we shift from conventional system to cultured meat production (Tuomisto & de Mattos, 2011).

Furthermore, since the technology is at its initial phase of development and its adoption will depend upon many factors. This article provides insights into salient prospective of the emerging technology from origin to its viability, survivability and the associated regulations. The factors responsible for realisation of cultured meat amongst stakeholders have been discussed. Impact of the cultured meat on economy of agriculture-based countries have been assessed, and the potential of cultured meat to substitute conventional livestock meat have been reviewed.

2. Origin of cultured meat: journey from mind to market (1927–2018)

The process of producing the cultured meat involves basic and applied cell culturing, and tissue engineering which were originally applied in regenerative medicine (Langer & Vacanti, 1993). The idea of developing cultured meat flashed long back in mind of Conservative politician Frederick Edwin Smith, 1st Earl of Birkenhead which was expressed through essay 'Fifty Years Hence' by Winston Churchill. Later

in 1932, same was published in book entitled 'Thoughts and adventures' (Ford, 2011). Consequently, a French science fiction author Rene Barjavel also described the cultured meat in his novel 'Ravage' in 1943 and later translated the same as 'Ashes, Ashes' in 1967. In early 1950s, Willem van Eelen of Netherlands came up with idea using tissue culture as a substrate for *in-vitro* meat, but it took long time (till 1999) to get patented as the concept of stem cells (Bhat, Kumar, & Fayaz, 2015). Indeed, the technology was first acknowledged and highlighted when NASA funded group of researchers and a team of bio-artists, called as Tissue Culture and Art Project endeavoured to produce in vitro cultured protein system or cultured meat for space travellers (Benjaminson, Gilchriest, & Lorenz, 2002; Catts & Zurr, 2002). Benjaminson et al. (2002) successfully cultured common goldfish's muscle tissue in Petri dishes followed by cooking and tasting of muscle explant. Catts and Zurr (2002) grew semi-living frog steaks i.e. the frog skeletal muscle cells over biopolymer for human consumption. The chronology of salient events in full journey of cultured meat (Dolgin, 2019; Just, 2017; Stephens, Kramer, Denfeld, & Strand, 2015) has been summarized in Fig. 1.

3. Technological aspect: methodology

Improvisations as well as focused research is still needed to establish and motivate the industry to produce highly-structured unprocessed cultured meat (Bhat & Bhat, 2011b). Broadly, there are two types of classifications based on the techniques involved: scaffold-based technique and self-organizing technique (Shishira, 2018).

3.1. Scaffold-based technique

The basic scaffold-based technique of producing cultured meat has been illustrated in Fig. 2. The basic idea is to make embryonic myoblasts or adult skeletal muscle cells taken from farm animals proliferated and subsequently attached to a scaffold or carrier such as a collagen meshwork or microcarrier beads immersed in plant origin growth medium inside stationary or rotating bioreactor. The stem cells are allowed to differentiate into myofibers (Kosnik, Dennis, & Vandenburgh, 2003), harvested and processed to develop the desired products. Highly structured meat such as steaks cannot be produced through scaffold-based



Fig. 1. Timeline of important events/research held in field of in-vitro meat technology.



Fig. 2. Basic schematic view of scaffold-based technique (A continuous flow of oxygen as well as nutrients is required in bioreactor for the successful culturing and to avoid spoilage).

techniques but ground and soft textured boneless meat is the end product. With advancements in biomaterials engineering, it is possible to grow animal cells *in vitro* and allow the development of "self-organizing constructs" to produce more rigid structures (Bhat et al., 2015).

3.2. Self-organizing technique

In self-organizing technique, biopsy or explant taken from the donor animal is cultured in a nutrient medium under ambient conditions. The tissue formed through this technique may closely mimics the conventional meat in terms of its composition i.e. the similar proportion of muscle, adipose and other cells (Sharma, Thind, & Kaur, 2015). Therefore, the meat produced by this technique will not only have the well-defined 3-D structure but similar or enhanced organoleptic attributes (Edelman, McFarland, Mironov, & Matheny, 2005). However, the technique faces some challenges like proliferation of cells in the culture media and the requirement to collect multiple biopsies from donor animals (Sharma et al., 2015). Though the technique holds the promise to produce the highly structured and well-proportioned meat, substantial growth is impeded. As unlike in vivo conditions there is no blood supply, the cultured cells undergo necrosis if separated for long periods by more than 0.5 mm from the source of nutrients (Dennis & Kosnik, 2000). However, a design using the artificial capillaries for the purpose of tissue-engineering has already been proposed (Zandonella, 2003) and still need more research.

4. Components of cultured meat

Post and Hocquette (2017) have suggested three basic components to grow *de novo* the muscle tissue and other components of meat, such as fat and connective tissue:

- 1. Tissue specific cells
- 2. Biomaterials
- 3. A bioreactor

4.1. Tissue specific cells

Tissue specific cells are the elementary component of cultured meat assembly (CMA). Adult stem cells, satellite cells, adipose tissue-derived adult stem cells (ADC) etc. are few types of stem cells proposed for CMA as per Shishira (2018) and Burkholder (2007) owing to their ability to retain in the undifferentiated form (Roelen & Chuva de Sousa Lopes, 2008). Many types of potentially suitable mammalian stem cells have been reviewed and summarized by Arshad et al. (2017). Though, the regeneration ability of adult tissue-derived stem cell in living system make them a suitable candidates for cultured meat, stem cells fail to grow and proliferate in vitro and ultimately undergo senescence (Mann et al., 2013). Cell multiplication is better in satellite cells which easily differentiate into myotubes and more mature myofibrils, and therefore are the preferred cells (Post, 2012). However, recent data claimed the better regeneration capacity of satellite cell subsets (Collins, Zammit, Ruiz, Morgan, & Partridge, 2007). ADC (s), the multipotent unique cells derived from subcutaneous fat of adipose tissue have ability to get transdifferentiated into variety of cell lineages like myogenic, osteogenic, chondrogenic or adipogenic (Kim et al., 2006). Further, the mature adipocytes could dedifferentiate in-vitro into a multipotent pre-adipocyte cell line known as dedifferentiated fat (DFAT) cells, which have the ability to transdifferentiate into skeletal myocytes (Kazama, Fuije, Endo, & Kano, 2008), thus could be used in CMA (Burkholder, 2007). The associated tissue engineering with adipocytes have been well described by Frerich, Winter, Scheller, & Braumann, 2011: Verseijden et al., 2012. In addition, genetically modified cells are also regarded as alternatives to normal stem cells (Kazama et al., 2008; Shishira, 2018). In a cell culture, cells controlled by teleomerase gene determine the number of doublings and some species may undergo multiple doublings to produce daughter cells in cultured media. Thus genetic modification by transfecting telomerase gene in other species may ensure higher Hayflick limit (Edelman et al., 2005). Further, induced pluripotent porcine stem cells (iPSC), the differentiated cells have been generated which may also be an alternative cell source for CMA (Ezashi et al., 2009). Fibroblasts exemplify the iPSCs which have been rendered pluripotent by driving embryonic gene expression programs in the cell through stable transfection with a set of four specific transcription factors (Oct4, Sox2, KLF4 and c-Myc) (Takahashi & Yamanaka, 2006). Despite their remarkable capacity to de-differentiate into myogenic cells

and ability to repair muscle injury, reports are scarce on use of iPSCs for producing cultured meat (Mizuno et al., 2010).

4.2. Biomaterials

4.2.1. Culture media

Continuous nutrient supply is needed to culture the cells in-vitro in CMA. Animal sera derived from adult, newborn or fetal bovine source are commonly used as a standard nutrient media (Coecke et al., 2005). However, large scaly use of such medium is expensive and unaffordable. Further, due to its in-vivo source, it has inconsistent, variable composition and act as potential carrier of pathogens (Shah, 1999). Moreover, the process of obtaining fetal bovine serum (FBS) has stern ethical concerns and its acceptance is questionable among vegan consumers. Furthermore, use of animal-derived supplements for cell growth undermines many of the envisaged benefits of cultured meat due to ethical and environmental consequences. Thus, now focus is more towards culture media devoid of animal-origin components owing to its potential to take care of all above mentioned issues right from cost to pathogen contamination (Froud, 1999). On the same lines, serum free media was developed by McFarland, Pesall, Norberg, and Dvoracek (1991) to sustain myosatellite cells obtained from turkey under in-vitro conditions. Thereafter in 2002, in continuation of previous, plant based growth medium from maitake mushroom was developed and found comparable to animal serum. This mushroom extract was used for fish explants and found potent to promote its surface area expansion (Benjaminson et al., 2002). Though, amino-acid rich mushroom extract fits ideal in animal-derived free model, but it also raises public health concerns due to presence of potential plant based allergic proteins (Datar & Betti, 2010).

However, the composition of growth medium for different satellite cells derived from different species may not be similar owing to species specific responses to certain additives. (Dodson, McFarland, Grant, Doumit, & Velleman, 1996). This notion is supported by the fact that, avian species were cultured using high glucose Dulbecco's Modified Eagle Media (DMEM-Glutamax I) with 10% horse serum and 4% chick embryo extract, but equine and bovine cells were grown and differentiated in DMEM-Glutamax I supplemented with 20% fetal calf serum (Baquero-Perez, Kuchipudi, Nelli, & Chang, 2012). Similarly, different serum-free growth mediums were developed for myosatellite cells derived from different species like sheep (Dodson & Mathison, 1988) and pig (Doumit, Cook, & Merkel, 1993).

Till now, commercially available serum free growth medium is Ultroser G, a replacer of fetal bovine serum, containing all nutrients necessary for eukaryotic cell growth (growth factors, binding proteins, adhesin factors, vitamins, hormones and mineral trace elements (Duque et al., 2003). The product is more viable than the animal based one, but cost is the limiting factor like former (Benders, van Kuppevelt, Oosterhof, & Veerkamp, 1991). Furthermore, exact formulations are copyright protected and assessment of their suitability at large scale evaluation is cost dependant. Some alternatives like Cyanobacteria, a fast-growing photosynthetic bacteria have been suggested as a potential source for cell growth supplements for cultured meat. Cyanobacteria protein content is up to 70% of their dry matter, and can be easily cultured for biomass (Ford, 2011). Nevertheless, a deep knowledge of metabolic modelling and flux balance analysis to determine the metabolic and functional state of the cell is essential to understand the optimum nutritional requirements of the cells to grow in vitro (Post et al., 2020).

4.2.2. Scaffold

Mammalian cells need solid surface to attach and utilize food materials. Myoblasts in particular require substratum or scaffold for proliferation and differentiation in CMA (Stoker, O'Neil, Berryman, & Waxman, 1968; Haagsman, Hellingwerf, & Roelen, 2009). An ideal scaffold must have following characteristics (Datar & Betti, 2010).

- a) Large surface area to enable attachment and growth of cells
- b) It must be flexible to allow for contraction
- c) It must allow maximize medium diffusion
- d) It must get easily disassociate from the final produced (cultured meat)

Besides these characteristics, a best scaffold must not only mimic the in vivo situation as myotubes differentiate optimally on scaffold with a tissue like stiffness (Engler et al., 2004) but obtained by-products must also be edible, natural and must be derived from non-animal sources. Thus, collagen based scaffolds must be replaced with suitable alternatives as collagen is derived from meat (Post et al., 2020). The major drawback with scaffold-based techniques as mentioned in 3.1 section is that steak-like highly structured meat cannot be produced. and the consumers have to be satisfy with only boneless meat with a soft consistency. On contrary, to develop an ideal scaffold, different types of edible and inedible polymers like cellulose, collagen and biodegradable synthetic polymers such as poly(L)-lactic acid have been suggested as the base materials (Williams, 2012). Use of edible collagen as a substrate was proposed by Edelman et al. (2005) and concluded that use of edible, stimuli-sensitive porous microspheres made from cellulose, alginate, chitosan, or collagen that undergo, at minimum, a 10% change in surface area following small changes in temperature or pH would prove as an excellent approach to obtain mechanically stretch myoblasts. Further, Jun, Jeong, and Shin (2009) documented that use of electrically conductive fibers to grow myoblasts required no additional electrical stimulation and induced differentiation, came up with more myotubes of greater length. However, the technique required simple and non-destructive way to remove culture from the scaffold. A new scaffold composed of textured soy protein (TSP), a readily available byproduct of soy (Glycine max) could be a cost-effective produce cultured meat (Abbasi, 2020).

Conventionally, two methods viz. enzymatic or mechanical were used to remove confluent cultured cell sheets, but both are destructive one (Canavan, Cheng, Graham, Ratner, & Castner, 2005). A non-destructive, thermoresponsive coating have been described which become hydrophilic from hydrophobic at lowered temperatures and can release cultured cells and extracellular matrix as an intact sheet upon cooling (Da Silva, Mano, & Reis, 2007). Other methods to detach culture as a confluent sheet from a non-adhesive micropatterned surface involves biodegradation of selective attachment protein laminin (Lam, Huang, Birla, & Takayama, 2009).

4.2.3. Oxygen carriers

Oxygen carriers in CMA do the same job that blood does *in-vivo*. The oxygen requirement in CMA is directly proportional to cell density as viability of cell is oxygen dependant (Radisic, Marsano, Maidhof, Wang, & Vunjak-Novakovic, 2008). Modified versions of haemoglobin or artificially-produced perfluorochemicals (PFCs) are two types of oxygen carriers (Lowe, 2006). Though PFCs dissolve large volumes of oxygen, but it is a potent GHG compound and therefore has urged the researchers to develop alternatives that are non-toxic and environment friendly (Shine et al., 2005).

4.3. Bioreactor

To carry out *in-vitro* reactions smoothly at large scale with proper and adequate culture medium perfusions, bioreactor is one of the essential components (Datar & Betti, 2010). Since, a closed and large surface area is the prime requirement for culturing, proliferation and differentiation in sufficient numbers at large scale, bioreactor is crucial component of CMA (Bhat & Bhat, 2011; Martin, Wendt, & Heberer, 2004). The important contribution to CMA is that tissue assemblies can be easily suspended, fluid shear is low and cells are in near-continuous suspension (Shishira, 2018).

5. Viability of cultured meat: basket of benefits

Future sustainability relies on both food and environmental sustainability which are the major global challenges in current scenario. With regard to sustainable meat production, growing social implications like animal welfare and environmental concerns in livestock slaughter seeks a great attention. A survey has shown that Western meat-eaters are interested to change their meat preferences owing to its environmental implications (Sanchez-Sabate & Sabaté, 2019). Moreover, animal welfare and ecological concerns were found to be the strongest positive driver among consumers for the acceptance of cultured meat (Weinrich, Strack, & Neugebauer, 2020). In addition, growing concerns of food safety, health issues, antibiotic resistances, nutrition-related diseases also contribute towards seeking alternative protein source (Fig. 3). These challenges are driving forces which make the cultured meat, a viable option as it will ensure sustainable production of safe and functional alternative protein source as the conditions can be controlled and culturing media can be manipulated. Furthermore, being less reliant on climate, land quality and area (FAO, 2013), it is proposed that cultured meat could enable more of the global population to have consistent protein access. The role of driving forces to make cultured meat a viable option has been briefed below.

5.1. Sustainable production of meat

Rapidly growing world population heading towards starving conditions. The human population is projected to reach 9.9 billion by 2050, an increase of more than 25% from the current 2020 population of 7.8 billion (Kaneda, Greenbaum, & Kline, 2020). The parallel increase in demand for sustenance will increase the demand for animal-origin meat and dairy foods (Singh, Mal, Gautam, & Mukesh, 2019, pp. 515–520). This demand for livestock products and the subsequent and associated increase in production and production methods is commonly referred to as the "livestock revolution". Thus, satisfying the demand for meat will be a challenge as total meat consumption worldwide in 2050, is expected to hike by over 60 per cent to 464 million tonnes (Revell, 2015).

Further, FAO (2012) has predicted that the capacity of conventional meat production system will soon be stagnant and is close to its maximum. Though the predictions are always associated with some errors, but the situation of rising population and subsequent demand of meat is definitely an alarming one. Furthermore, urbanisation is expected to increase and speculated to be 5 billion in 2028 and 6 billion in 2041, where nearly 90 per cent of the increase would be in developing owing to higher average household incomes and changing lifestyles with more food-consumption propensity outside homes (United Nations, Department of Economic and Social Affairs, Population Division, 2019). This helps fuel the demand for food including livestock products. Current consumption data show that the share of livestock products in household diets has increased steadily in developing countries over the past two decades. Higher demand and lower production in near future may raise the marketing price of the commodity and may pose meat as a luxury item.

5.2. Environment sustainability

Conventional meat production system puts a great environmental load in terms GHG emission, land, water and energy usage. The contribution of livestock in production of three main GHG viz. CO₂, CH₄ and N2O, are 9%, 39% and 65%, respectively (FAO, 2006). At present, 15-24% of total greenhouse gas emissions is because of world meat production system. Though, contributions of livestock in percentages may vary in different nations or continents, but deforestation to create grazing land shares a great proportion of this percentage (Steinfeld et al., 2006; Peters et al., 2010; Steinfeld et al., 2010). Notably, beef production system requires 15,500 m^3 /ton of water, while chicken requires 3918m³/ton (Hoekstra & Chapagain, 2007) putting extra load to water resources and environment as well. Compared to conventionally produced beef, mutton, pork and chicken, cultured meat production involves less GHG emissions and less land, water and energy usage as approximately 78-96% less emission and 99%, 82-96% and 7-45% less use, respectively (Tuomisto & de Mattos, 2011). Though energy use in poultry meat production was less than that in cultured meat. Tuomisto,



Fig. 3. Challenges that make cultured meat a viable option.

Ellis, and Haastrup (2014) compared the results of cultured meat with other livestock products and found that energy requirements were at the same level with beef production, whereas GHG emissions and land use were lower than any of the livestock products. However, water footprint was at the same level with poultry. Similarly, anticipatory life cycle assessment of cultured meat carried out by Mattick, Landis, Allenby, and Genovese (2015) have suggested that scores of global warming potential, land use and eutrophication potential were in favour for cultured meat. Moreover, energy returns on investment or energy conversion efficiency was depicted to be more for cultured meat.

5.3. Animal welfare and social implications

The rising concern of public and animal welfare societies have raised ethical issues in meat lovers which have ultimately decreased consumption of meat. Tonsor and Olynk (2011) reported that public debates or awareness campaigns of animal welfare through public media have decreased the proportion of non-vegetarians. Furthermore, quantum of publications on animal welfare issues in conventional meat production system has increased gradually during 1982-2008 which consequently affecting the consumer liking towards meat. Further, the religious beliefs interfere a lot in slaughtering of animals. For example, in India, in view of status of sacred animal, the cattle slaughter is an offence though cattle are important sources of milk, beef and skin in other countries (Sathyamala, 2018; Singh et al., 2020). As cultured meat aims to use theoretically one farm animal as donar; from an animal protection perspective, this would not be only appealing to meat-lovers but could also appeal to vegans, vegetarians and to those conscientious omnivores interested in reducing their meat intake on ethical grounds (Bryant, Szejda, Parekh, Deshpande, & Tse, 2019; Hopkins & Dacey, 2008). Thus, cultured meat will be welcomed not only on moral grounds by animal welfare societies alike meat produced after slaughtering of animals, but also on social grounds. The concept of growing meat in lab would entirely replace the animal death (Alexander, 2011; Hopkins & Dacey, 2008). It will decrease the loss of animal genetic resources as livestock owners sell the unproductive females irrespective of their genetic merit and the most males to butchers, or abandon them.

5.4. Food safety

Red meat bears many health issues including cardiovascular disease (CVD), diabetes and colorectal cancer (CRC) (Larsson & Wolk, 2006; Song, Manson, Buring, & Liu, 2004; Aykan, 2015). Key, Davey, and Appleby (1999) have summed up that over-consumption of meat may be the reason for the 1/4th cases all ischemic heart disease, or 1.8 million deaths, annually. More specific meta-analysis documented that 120 g red meat/day or 30 g processed meat/day would significantly raise the relative risk of colorectal cancer (Aykan, 2015). Besides this, food safety is other issue associated with meat consumption. The foodborne pathogens like Salmonella, Campylobacter and E. coli are variably found in meat and responsible for quantum of illness each year (CDC, 2011). Further, human affecting pathogens and diseases like avian and swine influenza aggravate with increase in intensity of livestock farming and other anthropogenic developments in the bio-industry (Greger, 2007; Slingenbergh, Gilbert, de Balogh, & Wint, 2004). The process of cultured meat would not only reduce the bacterial contamination and intensity of meat borne diseases (Siegelbaum, 2008), but also reduce the prevalence of pesticides and fungicides residues owing to restricted and controlled cell culturing environment (Bhat et al., 2015). Current worldwide emergence of severe acute respiratory syndrome Coronavirus 2 (SAR-S-CoV-2) pandemic (COVID-19) has further raised questions on the use of meat from livestock and the unconventional or bush meat (Daly, 2020; Volpato, Fontefrancesco, Gruppuso, Zocchi, & Pieroni, 2020). COVID-19 pandemic has resurrected debate on permanent ban on use of wild animals for food, cosmetics and medicine to prevent humans from infectious diseases.

5.5. Designer, functional and oxidative stable products

Cultured meat technology provides the provision to change the composition of meat according to desires. For example, desirable fatty acid profile enriched meat can be cultured by manipulating the composition of the culture medium. Here, ω -3 fatty acids may replace the saturated ones resulting in designer products. Similarly, low fat meat products can be designed by restricted supplementation of fats. The *invitro* meat obtained by manual culturing may also be designed to be antioxidant- and vitamins-enriched and oxidative-stable (VanEelen, vanKooten, & Westerhof, 1999). Further, Amy Rowat, a biophysicist at the University of California, Los Angeles is working on designing of such scaffolds that can grow combinations of cells to achieve fat marbling in lab-grown steaks (Dolgin, 2019). This kind of research may open the doors to address structural incompetency.

Thus, while considering the future demand and many issues related with conventional meat production system, cultured meat production system may seem to be less prone to biological hazards and disease through standardised production methods, and through tailored production could contribute to improved nutrition, health and wellbeing (Post, 2012). The other potential benefits have been reviewed in Table 1.

6. Survivability of cultured meat: full of challenges

The survivability of a new product or emerging technology in the market depend upon the no. and type of challenges it is facing. The consumers are the ultimate stakeholders in the market and the product acceptability among consumers is multifactorial ranging from perception to economics of the product. Further, in initial stages, many challenges ranging from technical to social and political impediments will affect the future survival of the technology.

6.1. Market response

Market response towards new food or technology depends upon the perception and habits of consumers as well as sensory attributes and economics of the product to be launched. A survey conducted by Bryant, Anderson, Asher, Green, and Gasteratos (2019) in United States among 1185 adults, regarding the consumption of lab grown meat revealed that 66.4% adults showed interest in trying the cultured meat once; 48.9% would eat regularly; 55.2% would eat instead of conventional meat. The survey by Bryant, Szejda, et al. (2019) revealed the consumers'

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Potential	benefits	of	cultured	meat.
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S. N.	Benefits of cultured meat	References
1.	 The risks of exposure to pesticides, arsenic, dioxins, and hormones associated with conventional meat could also be significantly reduced. Production of exotic cultured meat could be possible Comparable less requirement of amount of feed and labour per kilogram of <i>in-vitro</i> cultured meat 	Bhat and Bhat (2011)
2.	 Efficient nutrient and energy conversion in bioreactor Reduced land usage would provide free land to restore many endangered species Vegan meat for vegetarians Would provide fresh meat to astronauts 	Bhat et al. (2015)
3.	 Possibility of considerably higher returns per animal than traditional agriculture as large number of cells may be harvested from a small number of donor animals Potentially contribution towards retention of the genetics of traditional breeds and subsequently safeguard of biodiversity Probable solution to food wastage as prime cut alone is produced for consumption or processing rather than the whole carcass 	Stephens et al., (2018)

"extremely like or very likely response" towards purchase of cultured meat in different countries like US, India and China and was found to be 29.8%, 48.7% and 59.3%, respectively. Though, the acceptance of lab grown meat among consumers seemed to be better than genetically modified foods and other proteins substitutes like insects, but not as appealing as plant-based proteins. However, acceptance may be speculated more among those meat eaters, who are resistant to other alternative proteins, and it is more appealing to certain demographic groups (Bryant & Barnett, 2020). The factors which are more or less equally responsible for the success of new product/technology in market have been reviewed below:

6.1.1. Perception

The perception of consumers is decided by both implicit and explicit attitudes about the new technology. Implicit attitude refers to automatically retrieved evaluations without reasoning and depending upon the stored evaluation, the attitude may be positive or negative towards acceptability (Fazio, 2007; Gawronski & Bodenhausen, 2006). On the other hand, explicit attitude is a reflection of both cognitive elaborations of available information and implicit attitude (Gawronski & Bodenhausen, 2006). The methods to measure these attitudes are different. Time based measurement determines the implicit attitude (Gawronski, 2007) which is more predictive for spontaneous behavior (Perugini, 2005), however, cognitive elaboration dependent explicit attitude is typically measured by self-report scales (Hendrick, Fischer, Tobi, & Frewer, 2013) and more predictive for deliberate behavior. These attitudes were measured by Bekker, Fischer, Tobi, and van Trijp (2016) in case of cultured meat and have been elaborated in article entitled 'Explicit and implicit attitude toward an emerging food technology: The case of cultured meat'. It is concluded that commercial success of cultured meat could be driven by influencing the explicit attitude with the provision of content-based information about cultured meat in a relevant context. Therefore, the positioning of cultured meat as a substitute or as a complement to natural meat would be the major determinant of consumers' acceptance as consumers are likely to refer to products with a similar positioning in the market. Therefore, cultured meat producers and advocates should seek to highlight the benefits of cultured meat.

6.1.2. Habits

The eating habits of consumers also predict the acceptability of emerging product/technology. The consumers' habits towards meat consumption specially in Western countries have changed during past decade and still seems continue owing to growing meat safety concerns (Verbeke, Pérez-Cueto, de Barcellos, Krystallis, & Grunert, 2010; Vanhonacker, Van Loo, Gellynck, & Verbeke, 2013). In addition, sustainable production of meat and variable meat quality are the elements which further play a vital role in variability of consumption habits (Aston, Smith, & Powles, 2012; Austgulen, 2014). To address these consumption habits, cultured meat may be a solution. In view of which, cultured meat burger was tasted at London in August 2013. However, consumer perceptiveness decides the acceptance of this novel product in the future. Surveys were conducted to examine the knowledge, acceptability and notion of consumers about the cultured meat (Hopkins & Dacey's, 2008; Flycatcher, 2013; Marcu et al., 2015). Verbeke et al. (2015) have noted insight reactions and attitude of meat consumers towards cultured meat in three countries, namely Belgium, Portugal and the United Kingdom. The acceptance of cultured meat or products was found to largely depend upon their expectations and their experienced performance. Mancini and Antonioli (2019) carried out survey on 525 adults in Italy and found that 54% people were ready to try, 44% were ready to buy and 23% were even ready to pay a premium price for cultured meat. On similar lines, Weinrich et al. (2020) conducted a survey on 713 adults in Germany and found that 57% showed interest in tasting the cultured meat and 30% were willing to buy it.

6.1.3. Economics

In addition, economics of the product presents a major bottleneck for the acceptability of the product and market penetration. The Maastricht team appear to be successful to lower production costs for one burger patty to \$11.36, compared to the costs of the first cultured meat burger, which had amounted to roughly \$325,000 (Schwartz, 2015). However, according to the survey conducted by EKOS company over the consumers' preferences to purchase beef, plant-based protein, or cultured meat available at nearly same price, the Slade (2018) concluded that even though the consumers were briefed about the similar tastes and price, 65% showed a marked preference for the beef burger, only 21% for plant-based burger, and 11% would choose the cultured meat burger.

6.1.4. Sensory attributes

Colour and appearance is the foremost sensory attribute which influence the consumer acceptability. The meat which was tasted in 2013 at Riverside Studios, London, though possessed the same taste as that conventional one, but, was colourless for which a bit of red beet juice and saffron was incorporated (Zaraska, 2013). Thus, consumers' acceptability would definitely be a challenge for cultured meat industry. Therefore, many determinants play decisive role while consumer acceptability and which are needed to be addressed.

6.2. Structural incompetency

As suggested by Hocquette (2016), the cultured meat is just an artificial muscle protein solely containing muscle fibers, but the conventionally available meat is a skeletal muscle with naturally included or adherent fat and connective tissue (European Parliament, 2003). In other words, meat obtained from animals may be defined as an exsanguinated and aged product of musculoskeletal system containing skeletal muscle, bone, connective tissues, blood vessels and nerves and each lay a determinant role to meat taste and consistency (Gillies & Lieber, 2011). Thus, a real imitation requires all at a same time, which may not be the cost effective and require further technological developments in this regard. Moreover, to grow true steaks and to have a real imitation of meat, highly sophisticated facilities with 3-Dimensional technologies are required which have not been set up yet (Verbruggen, Luining, van Essen, & Post, 2018). The structural incompetency has been thoroughly reviewed by Stephens et al. (2018) under technical challenges of producing cultured meat where the basic definition of conventional meat, brief description of muscle biology, challenges faced while mimicking in-vivo environment during culturing and other technical troubleshoots have been reviewed to address current issues in cellular agriculture.

6.3. Sustainable cultured meat production

Many technical challenges are still to be addressed to establish production plant of cultured meat on large scale (Bhat et al., 2015). To date, the only successful muscle tissue constructs are a few hundred microns in thickness, which is acceptable for minced but not whole muscle cuts (Lovett, Lee, Edwards, & Kaplan, 2009). Cultured meat technology is more inclined towards culturing of myocytes alone via regenerative pathway owing to major component of conventional meat. Mostly 2D experiments (cell lines) are used for skeletal muscle analysis (Burattini et al., 2004). Though 3D structures ('bioartificial muscle') are available, but, limited up to regenerative medicine and alternative in-vitro model to represent native skeletal muscle tissue (Snyman, Goetsch, Myburgh, & Niesler, 2013). To mimic the later completely, culturing of different cell types altogether at the same time in common bioreactor is a pre-requisite and a very important factor in its market acceptance. Thin 3-D cultures can be utilised to form cultured processed meat (burgers, sausages). But for complete replica of conventional meat, optimisation of thicker 3D structures with a nutrient and oxygen supply and waste removal to sustain the inner core of cells which are immobile and

embedded within the tissue are the basic requirements. Cell sheets are being explored for thicker tissue construction (Hinds, Tyhovych, Sistrunk, & Terracio, 2013), however, for highly structured and organised tissues the engineering of highly perfused scaffolds would be required. A scaffold is required with appropriate characteristics to allow cell adhesion and subsequent proliferation and tissue development. Investigations have turned to forming channels within the tissue, and there has been specific research into 3D structured tissue formation using channelled networks made from sacrificial scaffolds (Mohanty et al., 2015), removable structures and lithography (Muehleder, Ovsianikov, Zipperle, Redl, & Holnthoner, 2014), whereby flow could be perfused throughout the tissue.

3D-printing seems a promising concept in creating these channelled networks, with examples including cultured leather purveyors. Modern Meadow patenting a method and device for 'scalable extrusion of cultured cells for use in forming three-dimensional tissue structures', and Harvard researchers' 3D-printing a perfusion network that was able to sustain a culture for six weeks (Kolesky, Homan, Skylar-Scott, & Lewis, 2016). However, an alternative to scaffold is to develop a cell line that is non-adherent, and which would greatly reduce cost and the carbon footprint of the cultured meat production process. The additional consideration is whether the scaffold should be part of the product and therefore edible and degrade during the culture process to leave 'just' the cultured meat; or, whether the cells are removed from the scaffold so it can be reused to save material. Cost is also important and it is expected that new scaffolds will continue to evolve as long as cultured meat products are developed. These systems all present their own arrays of challenges for tissue engineering, based cellular agriculture, which are needed to be addressed to make the cultured meat a sustainable supplement to conventional one.

Further, the development and commercialization of cell lines derived from the muscles of cows, pigs, fish and other food animals are futuristic demands, otherwise, researchers must either obtain tissues from slaughterhouses or run their experiments with desired cells. The Norwegian Center for Stem Cell Research in Oslo is planning on same lines to build Frozen Farmyard, a repository of agriculturally relevant cell lines with aid of GFI grant (Dolgin, 2019).

7. Economic impacts on developing countries

In low-income agrarian economies, like South Asia and sub-Saharan Africa, livestock sector plays a major role to sustain livelihood, after larger-scale staple crops. Though, output is not that much high as that of staple crops, but livestock sector has impact on reducing poverty impact. The livestock contributes about 40 percent to the agricultural gross domestic product (GDP) globally and constitutes about 30 percent of the agricultural GDP in the developing world (World Bank, 2009). The majority of the world's estimated 1.3 billion poor people live in developing countries where they depend directly or indirectly on livestock for their livelihoods (World Bank, 2008; FAO, 2009). In other terms, livestock sector serves as an economic backbone of developing countries as animals provide food, income, employment, soil fertility, livelihoods and transport. Furthermore, estimates show that globally, livestock provide animal traction to almost a quarter of the total area under crop production (Devendra, 2010). Livestock also provide a safety net in times of need in the form of liquid assets and a strategy of diversification for food production (Freeman, Kaitibie, Moyo, & Perry, 2007, p. 8). Livestock serve as a buffer to mitigate the impact of fluctuations in crop production on the availability of food for human consumption, and thereby stabilize food supply (FAO, 2012). In short, livestock, especially, sheep and goat serve as ATM (Any Time Money) for farmers as they can sell their animals anytime in need of money. Livestock function as insurance policies and bank accounts in many parts of the developing world (Pell, Stroebel, & Kristjanson, 2010).

Further, due to their ability to transform vegetation from non-arable land, crop residues, by-products from food processing, and organic waste into human food of high nutrient density and nutritional quality, livestock contribute to nutrition security directly. Therefore, livestock enhance total household labour productivity through smoothing the demand on family labour over seasons, genders and generations. To have a thorough view of livestock's role in developing countries, the documentation of Swanepoel, Stroebel, and Moyo (2010) can be consulted.

Settlement of cultured meat industries may adversely affect livestock agriculture-oriented developing countries, where sheep and goats are reared mainly for meat production. It will not only ruin the export potential of countries, but also affect the employment in the agricultural sector. Though, cultured meat would certainly not presage the elimination of livestock production, but may affect the sustainability of farmers rearing animals for meat production. Cultured meat entrepreneur may hamper the export of conventional meat to developed nations which can lead to economy inflation of such nations.

8. Regulatory framework of cultured meat

It is imperative to accesses the public safety aspects of a new technology or a product before being launched in food chain. There are many regulatory issues related to cultured meat industry which are needed to be addresses through appropriate legislation and regulations. Food fraud is the main regulatory issue for cultured meat where it can occur as marketing of cultured meat as conventional one or vice-versa. Further, mislabelling may be issue if in case, combined cultured and conventional meat products are packed in proportions. Cultured meat being of animal origin is itself a regulatory issue requiring surveillance and regulations at several points right from animal tissue biopsies to the serving in plate. Though, it is still debateable that cultured meat should be considered as meat or not (Bryant, 2020); quality assurance and appropriate hazard monitoring system are pivotal to the products preparation which are required to be addressed. In addition, eco-friendly green disposal of metabolic waste would be the matter of concern. Livestock, Animal Welfare & Slaughter Regulation, including the Department for Environment, Food & Rural Affairs, The Animal and Plant Health Agency, the FSA, and Local Authorities are the regulatory bodies which may play a vital role to address these issues. Further, processing of cultured meat into different products requires HACCP-based system to identify possible hazards, (Stephens et al., 2018).

Currently, frame work of regulations is unclear and in progress. Many debates, meetings at administrative and public level are going on for the construction of suitable regulatory framework. In this context, recently in 2019, the FDA and the USDA concluded a formal agreement ("7 March Agreement") on their cooperation to oversee the production of cell-based meat from livestock and poultry. Accordingly, cell culturing and their harvesting will be taken care by FDA and USDA will be responsible for the actual production of clean meat products (Verzijden, 2019).

In European Union (EU), under the Novel Foods Regulation (EU) No (2015/2283), European Food Safety Authority (EFSA) is the competitive authority to draft the regulatory framework for cultured meat and member states for its implementation (Verzijden, 2019). Although, in both EU and US, cultured meat does not comply to the category of meat as per existing norms and meat industry is also reluctant to include cultured meat as meat, but allergy and health concerns associated with the same, suggest revision in the existing norms (Flynn, 2019; Simon, 2018).

9. Cultured meat: conventional meat replacer or not

Intense debates are going on worldwide to position the cultured meat at its best. The accompanying logics are like two sides of the same coin. One side put forward the potential pros of technology as mentioned above and deems cultured meat as potential alternative to address

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ecological footprint and food security. On the other side, cons of technology make it unacceptable to a great extent.

One side or segment says though cultured meat might be acceptable on ethical ground, but it will widen the livestock and human relation developed for the centuries. As per Fairlie (2010), cultured meat won't be an apt solution for the unsustainability of muscle foods and the researcher proposed suitable alternatives like decreased meat production and traditional farming. Futuristic technologies viz., stem cell engineering, synthetic biology, nanotechnology and cultured meat would undoubtedly satisfy the vegans, but may estrange humans from nature and the animals. The other side emphasizes the fact that global meat production is very unsustainable due to the bioconversion inefficiency of plant biomass to animal proteins (with conversion losses of 60%-90%). Nevertheless, around 70% of all arable land is already used for livestock production and to sustain the inflating demand of meat, we need to explore alternative means of nutritional requirements for future security. Otherwise, meat production cost will be high and availability will be confined to richer section of the society (Sample, 2012).

In our view, cultured meat would only be able to replace the conventional meat thoroughly, if technology evolves as economical and completely of non-animal origin. Food security and sustainability are the ultimate goals of cultured meat without hurting the sentiments of animal lovers, holding an upper hand over animal ethics and welfare concerns and minimizing the ecological foot prints. However, shifting of practices is complex as various societal factors are involved. There is trend amongst consumers to be more ethically minded without change in the composition of their diet (Hocquette, Chriki, & Tourre, 2019; Post, 2012; Bodiou; Moutsatsou, & Post, 2019).

10. Conclusions

Advancements in tissue culture techniques and the culture-media devoid of animal-origin supplements may make large scale cultured meat production successful provided physical properties *viz.*, colour, aroma, texture, muscle cell and adipose cell proportional and palatability are comparable to animal-derived meat. Development of more sustainable cell lines, balanced flora based nutrient media, quality scaffolding materials and large scaled bioreactors for sustainable production are some of the technical hurdles that need to be addressed to make the cultured meat a viable option for future. Though the basic principles behind *in-vitro* meat technology are the same as that of tissueengineering, more focus research is required to overcome the technical glitches related to scaffold and bioreactor designs. Since the lab grown meat yet produced is of first generation, lot of scopes are there for improvement. The improved technology may definitely boost up the food sustainability without breaching animal welfare.

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