

1-7-2019

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Rajee, O., & Alicia, T. K. (2019). Biotechnological Application in Aquaculture and its Sustainability Constraints. *International Journal of Advanced Biotechnology and Research*, 10(3). Retrieved from <https://commons.erau.edu/publication/1289>

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Research Article

Biotechnological Application in Aquaculture and its Sustainability Constraints

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[Received: 10/06/2019;

Accepted: 29/06/19;

Published: 01/07/2019]

ABSTRACT:

The valuable nutritional and biochemical properties have made fisheries products one of the most vital high-quality protein sources for human consumption. Aquaculture has become the great alternative to substitute wild catches when the yield from fishing are no longer sufficient to sustain the massive food demand of the human population which is constantly burgeoning. However, aquaculture requires multidisciplinary approaches with holistic and environmental-friendly management measures to ensure its long term success and sustainability. Biotechnological applications have enhanced the effectiveness and cost-efficiencies of aquaculture by augmenting the productivity of aquaculture to meet global needs. Despite the benefits, the biotechnological application in aquaculture also brings several anthropogenic implications to human health, ecology, and environment. This paper discusses the major improvements in aquaculture industry upon advancement of biotechnology such as genetic hybrid stock, algae-infused commercial formulated feed, disease and health control via vaccinations, and water quality management. Meanwhile, this paper also addresses some sustainability constraints and controversial issues such as antibacterial resistance, gene modified (GM) escapees, and GM food that impede the success of biotechnology practices. Stringent environmental policies and awareness program are recommended in order to better control and also advocate biotechnology application in the industry.

Keywords: Biotechnological application, Aquaculture, Genetic hybrid stocks, Vaccination, Biosensors, Algae-infused feed

INTRODUCTION

The invaluable nutritional and biochemical properties of fisheries products have made it one of the most important sources of high-quality protein for human consumption. Among the animal protein consumed by humans, fisheries products contributed an average of sixteen percent, and it constitutes up to fifty percent in certain countries ^[1, 2]. In the past centuries, wild fisheries have been severely exploited to support billions of population around the world. Meanwhile, natural habitats of fisheries are also destructed as the

aftermath of urbanization and industrial development. With the pressure of depressing low catch of wild fisheries due to surpass of harvesting threshold, aquaculture has turned up as a good alternate solution for the dilemma. Being the sector with the highest growth across all food producing industry, inclusive of animal breeding, aquaculture has contributed more than 4.5 billion people with at least fifteen percent of their average per capita intake of animal protein ^[3]. This production rate has increased almost ten times as compared to

thirty years ago in 1970 when aquaculture only supplied 3.9% of the food source to the human population ^[1]. Aquaculture has been proving its ability to enhance human food security as it contains high quality of animal protein and essential nutrients, which are required essentially by nutritionally susceptible groups, such as lactating women and young children. The number of cases related to blindness and infant mortality has substantially reduced in protein deficiency areas after aquaculture was introduced ^[4]. Even with the current global issues like wild catch depletion and increasing demand for food supply for sustaining human population boom, the aquaculture industry is expected to continue growth at a significant rate. Food and Agricultural Organization (FAO) predicts that fifty percent of the fisheries products consumed by the global human population will be supplied through aquaculture by 2030 ^[1].

The aquaculture industry is given more and more attention at the global perspectives, not merely for the objectives of sustaining food supplies, but also due to its economic and socio-economic contributions. The small-scaled aquafarming creates employment opportunities and income for the locals, which eventually promotes their standard of living. Produce from aquaculture also assisted remote inlands residents from the Pacific Island Countries and Territories (PICT) to achieve self-sufficiency and food security ^[4]. Meanwhile, large-scaled aquafarming yields significant quantity for exportation and are a prominent part of the country's monetary income.

However, aquaculture is a highly instable and risk-prone industry which is also highly vulnerable to various environmental aspects. A slight change in aquafarming process could trigger an irreversible impact on the aquatic animals and bring consequential loss. Therefore, aquafarming requires multidisciplinary approaches with holistic management and environmental-friendly measures to ensure its success and sustainability in the long run. These include economic management, water quality control, customized feeding strategies,

environmental-friendly high quality feeds, genetically fit stocks, and integrated health and disease management.

As biotechnology emerged and matured, biotechnological knowledge is now more widely adopted in aquaculture in order to improve its success rate and sustainability. This paper discusses a few biotechnological applications in aquaculture: genetic information modification to customize for different habitat conditions or market demands; introduction of algae-infused commercial formulated feed in aquaculture due to its high unsaturated fatty acids, and adaptation of biosensors to provide extract real-time and accurate insights to cultured animals' welfare. In terms of disease management, this paper reviews on vaccinations that provide an option for cultured species to develop their own resistance towards pathogen inserted. These enhancements can never be fully achieved under natural conditions without human interference of biotechnology knowledge due to the nature of commercial aquafarming whereby species are mostly kept in high farming density in an enclosed environment. This is how biotechnology advancement came into the aquaculture sector and its application enhances the effectiveness and cost-efficiencies of aquaculture management. This paper also reviews the controversial issues and sustainability constraints which limit the wider adaptation of biotechnology in aquacultures, such as growing awareness of public concern on food safety hazard and ecological consequences.

Genetically Fit Stock

Genetic Hybrids

The first criteria for producing high-quality fisheries product is the quality of the stock. A good and healthy stock significantly eliminates the probability of hereditary disease or impairment, which will have a direct impact on the value of the produce. Before aquafarming was heavily influenced by technology, the most common method adopted for choosing stock was through selection programs, especially through

individuals' phenotype or pedigree information ^[5]. Resonance to Darwin's revolutionary theory, often the individuals portraying the most desirable characteristics will be chosen for breeding to reproduce offspring, hoping that the fittest traits can be inherited down to the offspring. This traditional practice has a long history in the aquaculture industry. The earliest record was dated back in the 1920s, where Embury and Hyford (1925) ^[6] chose individual brook trout (*Salvelinus fontinalis*) which survived from an endemic furunculosis outbreak for mating and the offspring of the third generation eventually illustrated to have an improved survival rate of up to sixty-seven percent. Traditional selective breeding was also practiced with rainbow trout by aquaculturist Donaldson in 1932 ^[7]. His research work has shown a huge success as there were a significant growth rate and fecundity of the directed selective breeding offspring. The strain of rainbow trout from his work was eventually noticed and widely distributed around the United States of America (USA) and other countries.

However, selective breeding within the same population of aquatic animals does not always reap the desirable or preferred outcomes in the long run. Due to the limited gene traits in the gene pool of the associated populations, offspring from the domesticated selective breeding program might fail to boost productivity. To widen the gene pool, aquaculturist started with intraspecific cross-breeding which involved mating of aquatic animals from the same species but different population, and also interspecific hybridization across different aquatic species. The main objectives of these gene hybridization activities are to achieve valuable quantitative traits such as feed conversion rate, growth rate, hardiness in a harsh environment, disease resistance and also meat quantity ^[8, 9]. Aquatic animals with these favorable characteristics are found with better adaptation to commercial aquafarming environment and fetch higher value in the selling market.

Siddiqui and Al-Harbi (1995) ^[10] has successfully

proven that hybrid tilapia between tilapia species *O. niloticus* and *O. aureus* progeny has outstanding overall performance in their harvest-ability, specific growth rate, survival, and yield across all growth stages of fry, fingerling, sub-adult, and adult stages, as per compared to the other native tilapia and red tilapia species. The quality of stock has been substantially improving due to the advancement of biotechnology and maturity of genetics knowledge. Genetics improvement approaches shifted beyond than just based on naked eye information, but relying upon genome-focused. New genetic improvement programs include genome-enabled selection, polyploidy, sex reversal breeding, Xenogenesis, gene transfer and genome editing ^[5]. Since then, the quality of stock has been improving tremendously as the genetic information in aquatic animals enabled to be modified to customize for different habitat conditions or market demands.

The effect of polyploidy is well illustrated in Scheerer and Thorgaard's ^[11] work, where they successfully proved that cross-breed triploid hybrids of the brook (*Salvelinus fontinalis*), brown (*Salmo trutta*), and rainbow (*Salmo gairdneri*) trout have higher survival ability than the conventional diploid hybrids, by approximately fifty percent. Fishes sex reversal program involves exogenous hormone induction or endocrine disrupting chemicals (EDCs) in the early juvenile stage of fishes when their reproductive systems are still immature ^[12]. The common steroid hormones used in fisheries are androgens and estrogens ^[13, 14]. Multiple studies had shown that mono-sex populations portrayed more outstanding growth rate and harvest-ability in terms of overall size and weight due to the diversion of reserved energy from reproductive development to growth ^[12, 15, 16-20]. In line with that, each aquatic species will then have their respective preferred single-sex to have the optimized growth characteristics, such as all-male stock for tilapia industry and all-female stock for the salmonid industry ^[21].

There is no doubt that genetics hybridization significantly increases the survival rates of aquatic

animals under farming condition, but it has also sparked fierce debate on this agenda at the same time. When a genetically-modified species is being released or accidentally escapes to the natural environment, escapees increase the competition of food, shelter, and outcross with the existing local species in the habitat ^[22]. These escapees born with better adaptation towards hardiness in the environment will gradually dominate over the native species and colonize the natural habitat. In the worst case if the escapees are not sterile; these species will interbreed with the native species and producing offspring with new sets of genetic composition, further exacerbating the damage to the ecosystem. These escapees or their hybrid second generation overwrite or alter the natural population and community dynamics, which might result in loss of invaluable domestic and exotic genomes from the wild. The population of native species might extinct from the ecosystem.

A good example of animals' escapees' problem would be the Atlantic salmon. The most commonly farmed fish species in sea cage aquaculture is *Salmo salar* ^[23]. In the Norwegian region, around 4.6 million salmon was accidentally released to the wild, between the year 2001 to 2012 [24]. As a result, introgression of farmed salmon was estimated to be 6 out of the 21 among the native populations spanning in the entire Norwegian coastline with a significant display of reduced survival rate and temporal genetic changes to wild salmon among the wild population compared [24- 26]. In many countries, genetics hybridization of animals is under stringent control with the aid of legislation to avoid misuse and mishandling, taking into consideration of its irreversible impact to the ecosystem. Therefore, genetic hybridization technologies in animals are currently facing a certain degree of constraints due to the backlash and can only be further advocated for a wider spectrum of application if there are better technologies or solutions to contain the adverse impact to the environment in the event of an

escapee.

Feed Management Microalgae

Algae cover a diverse group of aquatics, which can be differentiated into two subcategories: macroalgae or microalgae. Algae are mostly photoautotrophic but some species can also be found heterotrophic due to the nature of the living environment ^[27]. Their habitats are typically areas with sufficient oxygen and sunlight, liquid cultures, carbon dioxide and also other nutrients ^[28]. Due to the mushrooming of large scale commercial aquafarming, the food sources of cultured species from their original habitats are no longer sufficient to fulfill their food demand. Cultured species are now highly dependent on commercial feeds which make up forty percent of their food source ^[29]. Microalgae soon sparked huge interest among aquaculture scientists due to its incredible nutrient properties and ability to yield phytoplankton. In their natural aquatic habitat, algae are the base of the entire aquatic food chain, supporting the production of renewable resources by approximately 100×10^6 tons per year from fishing ^[2]. Hence, it is not difficult to find microalgae in commercial feeds for aquafarming. Statistics have shown that at least 7×10^6 tons of world aquaculture production in the year 1997, or in eighteen percent of the global aquafarming yield of that particular year, relied on microalgae as part of their food source. Two years later in 1999, microalgae production augmented to 1000 tons to support the huge demand from plants and animals of a total of 43×10^6 tons ^[2].

In fact, not only commercial feed of aquaculture but microalgae can also be integrated into feed for domestic pets and farmed animals. More than 30% of the global algae production has been sold to contribute feeding application, particularly *Arthrospira* ^[30]. The most commonly integrated microalgae species into commercial feed are *Chlorella*, *Tetraselmis*, *Isochrysis*, *Pavlova*, *Phaeodactylum*, *Chaeteceros*,

Nannochloropsis, *Skeletonema* and *Thalassiosira* [31, 32]. Microalgae containing high unsaturated fatty acids, such as eicosapentaenoic acid (EPA), arachidonic acid (AA) and docosahexaenoic acid (DHA) which are of high importance for the growth of most aquatic creatures.

On top of being incredibly nutritious for aquatic animals, microalgae are infused into commercial feeds of aquafarming species as food additives to enhance the appearance and market value of aquafarming final products. In France, there is a widely practiced French technique, named as *Greening of Oyster*, whereby oyster is placed in contact with microalgae. The diatom *Haslea ostrearia* from microalgae will produce blue-green color on the gills and labial palps of an oyster. The diatom *S. costatum* also has the capability to increase flesh size and glycogen content of oyster by two times under the optimal temperature range of 8 to 12°C [33]. Microalgae food colorant can be applied not only to the oyster, but other widely cultured species, for example, salmon, trout, and carp with different algae species [29].

The environmentally friendly features of microalgae also contributed to its rising popularity as feed in aquaculture. Microalgae are non-toxic and can be easily cultured in large scale or introduced to the aquafarming area as Integrated Aquaculture-Agriculture (IAA). The polyculture ideology of operating the two farming activities concurrently allows microalgae to improve and stabilize the culture medium through the photosynthesis process [30]. Any excreted algae compounds also induce a positive cycle of regulating bacterial contamination, probiotic effects and immune stimulation properties of cultured species in the culturing medium [28].

In spite of the aforementioned incredible facts of microalgae, algae application in the aquafarming commercial feed is still facing many restrictions today, deterring its sustainable adaptation in the field. Similar to other live feeds, the size, shape, and properties of the microalgae in the feed are crucial and critical to each aquatic species. Only microalgae with correct size, shape, and digestible

cell wall can be consumed by the specific cultured species without causing any issue of indigestion [29]. Any unconsumed algae left in the culture medium may induce proliferation of bacteria and affect the water quality as the sedimentation and turbidity in water rise [28]. More thorough and species-specific research needs to be conducted before administering any integrated feed with microalgae component to eliminate the chances of indigestion, and mortality cases from occurring. The government shall provide support to aquafarmers, either in terms of monetary via subsidies, and financial assistance (grant), or raising awareness of local field via joint research effort with reputable research bodies. Local aquafarmers will then explore new technologies available in the market to improve their products with encouragement from the government.

Water quality management

Biosensors

Water quality management is one of the utmost priorities in aquaculture which requires close monitoring around the clock. Water quality of culture medium is the crucial success-or-failure factor of the entire industry, determining factor for the survival of culture species.

In many countries, the issue of poor water quality is critical due to contaminated discharge from industrial waste, agriculture runoff, and domestic sewage. The contaminated water source may carry hazardous heavy metals, high level of poisonous chemicals from the pesticides and herbicides, toxic pathogens which eventually will be reflected on the water quality parameters such as extreme low dissolved oxygen (DO) level and extreme pH level. Under such severe condition, certain specific species may manage to adapt and fortunate enough to survive. However, adverse effects are inevitable. Some of the classic examples would be reproductive dysfunction with males displaying feminization and food infection on human due to biomagnification and bioaccumulation in the food chain [36].

The twenty-four hours monitoring of water quality

and health of the aquaculture species are never easy, due to the intensive manpower involved. There are different types of portable digital measuring devices available in the market which provides simple and accurate results of water quality parameters. However, the result of the sub-sample collected might be inaccurate due to different factors. Differing from terrestrially farmed animals in which the health condition of the animals can be easily observed with naked eyes, aquatic animals are reared underwater or encased with their hard shell, and hence the naked eye monitoring is nearly impossible and impractical. Meanwhile, when random samples are being selected and taken out from their culturing water for assessment, indirectly stress factor will be introduced and might affect the accuracy of results.

Therefore, to improve animal and environmental monitoring using conventional measuring digital device, biosensors are adopted in aquafarming to obtain real-time valuable and accurate insight to the well-being of cultured animals underwater and their living conditions ^[37]. Biosensors portrayed outstanding performance capabilities as compared to the conventional measuring techniques, as it only involves simple technology, yet high specificity and sensitivity. The response time is short and rapid, thus managed to provide 24/7 real-time analysis. Additionally, what adds to its merits is the low cost involved and relatively compacted size ^[38]. It can be integrated into a 4G cloud-based technology which can be monitor remotely ^[39]. All these advantages ultimately contribute to a better aquafarm management system with capabilities of increasing product yield and productivity.

As mentioned earlier, biosensors are capable of detecting chemical and biological components in the water. When applied in the aquaculture industry, biosensors managed to pinpoint a few water quality parameters which are critical to the operation of the industry. Potential areas in aquaculture where biosensors can be infused are antibiotics and other antimicrobials, Biochemical

Oxygen Demand (BOD), insecticides, health care of cultured species e.g. lactic dehydrogenase activity in body fluids; heavy metal, e.g. mercury, cadmium; herbicides, microbial toxins, nitrate, nitrite; pathogenic microorganism e.g. *Enterobacteria*; polyamines e.g. histamine, salinity and sulfides ^[40].

Venugopal (1990) ^[41] reported that the first biosensors for fish quality measurement were developed in the 1980s by Watanabe's group by using nucleotide concentration to assess the fish freshness. The biosensors were developed with an enzyme sensor specific for hypoxanthine (Hx) in fish using immobilized xanthine oxidase membrane and an oxygen probe. As technology improves, more biosensors system being developed, such as using xanthine oxidase electrode, amperometric electrode, and ammonia ion-selective electrode and are used to achieve different measurements ^[38].

Above that, biosensors are also capable of measuring the physiological and behavioral variables that are directly associated with the welfare and productivity of the cultured species ^[37]. From body temperature, animal orientation, depth, pathology to the stress level, biosensors measure the physiological variables of aquatic animals as well, which have high difficulty to track, such as heart rate increment during digestion. All this valuable information collected using biosensors can assist aquafarm operators to provide an optimum environmental condition for the cultured species and to make important management decisions.

As per research findings of Andrewartha et. al. (2015) ^[37], biosensors have been introduced to an oyster farm in Australia to collect variables associated to oyster health, namely dissolved oxygen, salinity, chlorophyll *a* concentration, heart rate, stress level for a monitoring period of six months. The results have illustrated that due to recent high-temperature exposure, the oyster cultured are still recovering from the stress. In line with the results, management decision such as delaying any further stressful farm activities or

mechanical grading could accelerate the recovery process of the oyster back to a normal health condition, in order to intensify their profit from the aquafarm.

Due to the fact that products from aquafarming are one of the main sources for human consumption, cultured species need to undergo stringent test and assessment, based on standards of the respective countries to which they are exported. Besides the use in aquafarms, biosensors can be further incorporated into the clinical food test stages due to its outstanding performance in detecting chemical and biological components^[38].

Biosensors have numerous advantages, such as wide linear range of detection limit, inexpensive and fast response, with proven statistics results [42, 43]. Nevertheless, the maintenance of biosensors requires a certain level of attention and care. Extreme thermal and chemical conditions may affect enzyme or mechanism inactivation of biosensors, which might result in the malfunctioning of biosensors [42]. In order to solve the uncertainties, businesses can consider infusing biological sensing elements into the conventional measuring device to ensure more sustainable application of biosensors in water sampling via a simple and user-friendly mechanism.

Disease Control and Health Management

Health management in aquaculture is a prime focus across all stages of the cultured species, regardless of types of intensive culture. The risk of being transmitted with disease increases as the cultured species are reared in higher densities. This is due to the gradually decreased unit space between individuals and hence shorter distance for the pathogenic bacteria or viruses to travel from one individual to another. On the other hand, cultured species that are reared in the open aquatic environment will definitely be more exposed and vulnerable towards the pathogen. In fact, it is almost impossible to prevent disease transmission in an open environment when water resources are not confined.

Health management in aquaculture has gained lots of attention upon a few drastic fish disease outbreak cases. A common example is the infectious salmon anemia (ISA) which severely affected the farming site of Atlantic salmon (*Salmo salar*). The first case was reported in Norway in 1984, followed by Atlantic Canada in 1996, Scotland in 1998, the Faroe Islands in 1999, and the USA in 2000. In Norway itself, there were a total of four hundred and thirty-seven reported outbreaks between 1984 and 2005. The outbreak cases reached its peak in 1990, and in that particular year alone eighty cases were identified^[46]. ISA caused mortality rates ranging from fifteen percent to a hundred percent and hence considered as one of the worst historical disease outbreak in the aquafarming industry which resulted in unprecedented economic losses^[47].

Infectious disease has been identified as the main course that impeding the development and expansion of aquaculture in many areas, due to its high fatality rate in a short period of time^[48]. Thus, disease control and health management of cultured species have become almost the top priority in the aquaculture industry around the world.

Vaccination

One of the biggest breakthroughs of biotechnological application is vaccination. Vaccinations are proven as the most cost-effective measures to limit the morbidity and mortality of the infectious disease, in other words, provide long term protection against infectious disease for almost all living organisms^[49, 50]. Vaccination is a multidisciplinary approach whereby each vaccine is formulated against a certain specific disease, with the specific delivery method, delivery timing, and re-vaccination means. Targeted disease morbidity and mortality have dropped almost ninety to hundred percent upon introduction of vaccination^[50, 51]. The knowledge of vaccination has been adopted and applied to aquafarming industry. The incorporation of vaccination has played a vital role in the health and disease management of aquafarming, augmenting its

global yield of production to satisfy the food demand of the burgeoning human population.

According to Sommerset *et al.* (2005) ^[52], vaccination has widely known as the prime contributor to the success of salmon cultivation. In the 1980s, salmon farming in Norway has suffered enormous losses and nearly came to total collapse due to the outspread of bacterial disease, mostly by *Vibrio* spp. The fall of the salmon farming was prevented by a massive use of antibiotics dosage to destroy the pathogen and inhibit it from further proliferating. The aquafarming of salmonid in Norway only managed to undergo re-development after the establishment of vaccination technology against *Vibriosis* disease ^[49].

Vaccination brought about the second evolution in disease management of aquaculture, after the development of antibodies which induces an immune response from an individual's body through antigens and adjuvants ^[52]. Nevertheless, the use of antibiotics and antibacterial resistance in crops and produce has soon arisen concern from the public due to its vicious and complicated environmental consequences. The usage of antibiotics in aquafarming drastically reduced and gradually being replaced with vaccines after vaccines illustrated outstanding consistent and effective results.

There are a few types of vaccination such as bacterial vaccines, live attenuated vaccines and DNA vaccines. Most commonly used bacterial vaccines are inactivated vaccines abstracted from specific strain and developed by broth fermentation and subsequent formalin inactivation ^[53, 54]. Whereas, live attenuated vaccines, the second generation of vaccination in aquaculture involved dissemination of antigen in the cultured populations, which later able to be inherited by their offspring ^[54]. DNA vaccination is also another popular option to affect the immune system of vaccinated. Genetic materials against pathogens are intentionally transferred to somatic cells of the vaccinated species/animals ^[55]. DNA vaccination has theoretical benefits over other vaccination types, as it is a combination of the

traditionally killed and attenuated vaccines with higher results assurance and low risk of catastrophic reversion to virulence ^[44]. Recent research has also explored the use of immune-stimulant in the vaccine for aquaculture, in replacing oil-based adjuvants to better mitigate adverse side effects and the potential hazard to consumers health ^[56-58]. One of the most widely applied commercial immune-stimulants is Ergosan, extracted from a seaweed-based meal rich in alginates and polysaccharides ^[59-62].

Vaccination of aquatic animals can be done through a few methods: oral vaccination through genetically modified feeds (GM food), intraperitoneal injection of vaccines into body cavity or immersion of cultured species into diluted vaccine suspension. Each delivery method has its respective advantages and drawbacks. The selection of vaccination delivery method depends on the type of vaccines, fish sizes, and available resources, such as manpower and financial investment.

The effectiveness of the vaccine is not granted upon delivery. The vaccination results may vary and are highly dependent on the condition of cultured species and criteria when vaccine being delivered. Vaccination needs to be conducted within a certain minimum period of time before the species are being exposed to a pathogen. Due to the fact that fishes and most aquatic animals are cold-blooded organisms, their body temperature will adapt to their surrounding temperature quickly by nature. Hence, to ensure a high efficacy of a vaccine, it has to be delivered under certain optimum temperature, which varies widely among different species. Above that, the cultured species should not be stressed during the vaccination period. The form of stress does not limit to photoperiod, seasonal changes, crowding, and stress from handling and transporting. For aquafarming in open environment, the properties of the water also have to be taken with extra care, including heavy metals content and basic parameters of water such as pH, salinity and dissolved oxygen concentration (DO) level.

As mentioned earlier, vaccination acts as a precautionary measure which provides protection to aquatic animals against a certain infectious disease that might cause fatality or a decrease in their market value. However, the benefits of vaccination are more diverse than the earlier mentioned. Due to the protection from vaccines, vaccinated species have higher tolerance with stress from over-crowding. Hence, vaccinated species can be reared in higher density without taking disease as the limiting factor. Additionally, vaccinated species do not require drug usage, or at least minimal drug usage because their infected risk is low, which in turn reduces their drug residue in final products. It also promotes food conversion rates, thus indirectly triggers appetite and growth rate of vaccinated species. With the comprehensive benefits, vaccinated species manage to reflect a better industry image for hygiene quality and eco-safety standards.

Similar to other biotechnology practices, vaccinations caused some controversies as they might pose vaccinated species into other dangers. Post-vaccination mortality might occur if the vaccination process was not conducted properly in a correct manner like improper handling or rearing practices^[54]. Other diseases such as myositis may be triggered depending on the consequence of improper handling techniques during vaccination. The decrease in growth rate is another common outcome if oral vaccination being prescribed due to the sudden change of feed that the cultured species might not able to adapt. DNA vaccination of pDNA integration into chromosomal DNA may also result in gene mutation, genomic instability and abnormalities^[63- 65]. The situation becomes worse when the vaccines or DNA vaccinated species accidentally escape to the natural environment. Escapees that carry these specific pDNAs might be consumed by other animals in the ecosystem or even by a human. When consumed, these specific pDNAs might react with intestinal bacterial or being secreted via feces and later further spread to other bacterial population in the consumer's intestine, soil or water, causing

pollution^[53].

Disease control of aquafarming thru vaccination is still one of the best comprehensive disease management measures due to the fact that it is cost-effective and suits to be adopted for the high-density farming environment. However, vaccination is not and would not be a 'one-for-all' solution for all infectious disease and virus. Rigid legislation and government bodies are required to draw boundaries and closely monitor the usage of vaccination on human consumption produce. Various countries have established agencies and regulations for better control of vaccination in food and aquafarming products. In the United States, the government has established the US Food and Drug Administration whereas the European Union has also a decentralized body of the European Agency for Evaluation of Medical Products (EMA) [66]. They are responsible for conducting an assessment and clinical testing of products with DNA vaccines before being launched in the market.

Due to the integration of artificial genetic content, DNA vaccinated produce together as genetics hybrid produce is under the category of Genetically Modified (GM) food. Based on the consensus agreement in UN [67], Genetically Modified Organism (GMO) is defined as 'an organism in which the genetic material has been modified through genetic technology in a way which does not occur naturally by reproduction or by natural recombination'. GM food is now a heated debate topic at global perspective due to the growth of food activist trend. Food activist trend focuses on the sources and content of human food, boycotting mass food production which is unnatural and bringing harm to the ecosystem. Schurman and Munro's work [68] have highlighted the cultural, and social challenges that arose due to the GM food trend and discussed the controversial issues between GM food safety, global food security, and sustainable agribusinesses. Several types of research have proven that biomedical and ecological risk of GM Food contradicting to the ideology of promoting

food security via GM food [69]. This topic is further being debated as there was a lack of concrete evidence and firm recognition from international groups and agreement supporting food safety of GM Food [70]. Under such unfavorable condition, the sustainable adaptation of vaccination, and genetic hybridization has faced limitation, and sustainability restrictions, from the government to food consumers.

These challenges need to be addressed through strong education and awareness program to improve public perception towards GM food. A research done by Cui [71] shown that there were a notable group of people in China has little or no knowledge on GM food with only a low of 11.7% of respondent claimed that they understand the basic principles of GM engineering in a survey conducted. Studies conducted in the UK and also concluded that the rejection of GM food was due to the public misperception of the absence of benefits and risk issue [72]. Therefore, the limitations could be lifted and more sustainable biotechnologies application can be expected through the strong communication with the public to eradicate any misunderstanding towards GM food and other biotechnologies application in food production.

CONCLUSION

In summary, biotechnology applications provide significant benefits and are the most significant contributor to the development of today's aquaculture industry. The increased application of biotechnological tools can certainly further revolutionize aquaculture to achieve absolute high-quality fisheries products. As technology develops, there might be more matured and different approaches being discovered to enhance aquaculture productions' efficiency, sustainability, product quality, the profitability of farm owner and also the food safety of consumers. Developing countries may adopt demand-driven approached instead of technology-driven when adopting biotechnology application in the aquaculture industry to maximize their economic effect and

achieve self-sufficiency. Nevertheless, multilateral environmental policies and legislation need to be implemented in order to scrutinize the use of transgenic aquatic organisms through a stringent protocol. Additionally, in the perspective of social responsibility, DNA-vaccinated or hybridized products sold in the market should be clearly identified to keep consumers well informed. Certification and eco-labels can be enforced to differentiate the different sources of food choices for easier identification and provide better food safety assurance for all food consumers.

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