Use of Agri-Food Waste in Aquaculture

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The agri-food industry generates a large amount of waste every year, which is both an environmental and economic problem, especially for the countries in charge of its disposal. It has been highlighted that plant waste may have not only positive effects on growth performance, but also beneficial effects on modulation of the innate immune system and antioxidant defenses.

Keywords: agri-food ; waste ; Aquaculture ; Antioxidants

1. Introduction

During the past century, the world population has increased three times more than the growth that occurred during the entire history of mankind [1][2]. In particular, it grew from 1.5 billion in 1900 to about 7.1 billion in 2003. According to current growth stages, it is expected that the world population will be about 9.4–10 billion in 2050 [3]. Since the population boost is linked to a greater demand for food, during the 20th century, it would not have been possible without a reliable rise in food production [4][5][6].

Land and water are two of the most important factors affecting food production, and they are in turn influenced not only by environmental changes but also by population growth [5][6][7][8][9]. For example, it has been estimated that from 2005 the lands devoted to agriculture or farming needs have been reduced by about 38%, resulting in an endowment of 0.76 ha per capita [6][7]. For this reason, modern strategies to support the large demand for food have focused mainly on finding innovative solutions to intensify the production process, rather than reclaim new areas. As a result, although areas committed to agriculture or livestock farming have decreased over time, total food production has sharply increased in the past 20 years, thanks in part to economic developments and technological advances [6][10]. On the other hand, the increase in food production is almost always followed by an increase in food waste. In particular, a recent study has shown that every year the processing of food for human consumption can generate up to 24% of waste during the different stages of the production chain, starting from cultivation, breeding, processing, storage, sale, up to the same domestic consumption [11][12]. While in under developing countries, food waste is mainly concentrated during the distribution phases, in developed countries, such as in Europe, food waste mainly occurs during the earlier steps, especially during the processing one [11][12]. A high level of food waste has negative consequences not only on the environment, but also on the society and economy of the countries charged with disposing of it according to current regulations [13]. Considering that the fruit and vegetable processing industry is one of the largest waste producers after domestic wastewater, finding new strategies for its reuse is one of the main goals of the modern circular economy. Recently, agricultural waste has been successfully used for the formulation of various products not only for agronomic purposes [3][14][15], but also for human or animal consumption [16][17][18][19]. Interest in this type of waste stems from the presence of bioactive compounds that can demonstrate great variability in biological actions. In particular, in the plant field, it has been shown that phytochemical compounds can increase the resilience of plants to different types of abiotic and biotic stresses, reducing the use of pesticides and fertilizers [8], while the same compounds can play important roles for the maintenance of redox balance, promotion of immune defenses, or prevention of some diseases in animals [19][20][21][22]. The use of plant waste as a potential ingredient in animal diets should not be underestimated. Indeed, because these molecules exert interesting properties, sometimes comparable to drugs, they can be a viable alternative to the administration of chemicals, hormones, or other exogenous substances that could compromise not only food quality but also the safety of food [19][20]. Moreover, analogous to human dietary supplements, it is reasonable to think that an animal diet supported by a constant and safe integration of plant-based bioactive molecules can be effective not only in preventing chronic diseases, but also in reducing stress factors, including those related to farming conditions [23].

2. Use of Agri-Food Waste in Aquaculture

In the past, it was always assumed that seas and oceans were an endless source of food. However, with the industrialization of fishing, wild fish stocks have become increasingly depleted [24]. Accordingly, to meet the demand of a growing global population, the aquaculture, particularly fish production, has rapidly intensified. For example, while aquaculture produced about 3 million tons of fish in the 1970s, today it is estimated that farmed fish exceeds 60 million tons. In particular, the Asian and Pacific regions dominate this scenario, accounting for 88.5% of the global production [25]. Moreover, global demand for aquaculture feed is expected to reach 70 million tons per year by 2025, doubling 2008 production and increasing almost 10 times that of 1995 [26][27].

The nutritional value of fish food is very high. Proteins derived from the consumption of fish products are more assimilable than meat ones, and the lack of connective tissues greatly facilitates digestive processes, making fish food more edible. Fish contains a considerable amount of calcium, which combined with its high vitamin D level and low cholesterol content makes it an extremely beneficial food for human health. Finally, fish is also a food rich in unsaturated fatty acids, especially ω3, essential fatty acids of limited distribution in both plant and animal kingdoms, which play an important role in the prevention of cardiovascular disease [28]. However, fish is a very expensive food. Its high cost depends on several factors, including (i) its easy perishability, which not only makes it difficult and very expansive to trade in inland regions, but also drastically reduces its shelf life after thawing; (ii) the obligation not to catch, or release after catching, fish that according to European directives are undersized; (iii) and the presence of local directives that prevent fishing to promote the restocking of the sea. The latter problems are obviously minimized by aquaculture techniques, to which however is added the additional cost of feeding fish. Currently, although the cost of farmed fish is much lower than that of wild fish, it has been calculated that more than 50% of the total cost of farmed fish is influenced by feed ingredients [29]. In this scenario, the use of food waste for fish farming would be a sustainable strategy not only to avoid the cost of organic waste disposal, but also a way to decrease the cost of feeding fish in aquaculture, and thus the final price to the consumer.

Nowadays, although the price of fish food is increasingly expensive, the demand for this product is rising worldwide due to the appreciation of its nutritional value. Feeding fish by using feed that is completely or partially composed of agri-food waste may be one of the strategies to reduce the cost of fish products, also from a circular economy perspective. On the other hand, using as little feed as possible to achieve maximum fish growth performance is another important goal that should not be underestimated.

Inflammatory insults cause the activation of a cytokine cascade, the balance of which provokes the subsequent release of Tumor Necrosis Factor α (TNF-α). TNF-α is a member of the TNF superfamily, which consists of a series of transmembrane proteins with a homologous TNF domain. It is considered a key cytokine that regulates the complex network of pro- and anti-inflammatory cytokines. Indeed, TNF-α can trigger its own production and that of other pro- and anti-inflammatory cytokines, including IL-1β, IL-6, and IL-8. This indicates its active role not only in inflammatory processes but also in the proliferation, apoptosis, and differentiation of different cell types, such as macrophages, fibroblasts, and endothelial cells. [30]. Once released, the production of other compounds acting as chemoattractant (chemokines) is also positively modulated, whose function is inducing the migration of neutrophils and macrophages to the site of infection, thus to stimulate the inflammatory process [30][31]. TNF signaling occurs through TNF receptors (TNFRs), which are transmembrane proteins with jelly-roll structure and spatially arranged in β-sandwich conformation. This family includes some lymphotoxins, the CD40 ligand, the CD30 ligand, and the CD29 ligand [32]. While this process had long been known in mammals, little was known about the immune response to inflammatory stimuli in fish. In recent years, evidence has been collected on the existence of TNF-α in fish, but, only recently, TNF-α and TNFR genes have been cloned and identified in different fish species, including rainbow trout, common carp, catfish, zebrafish, and grass carp. Although the homology with typical mammalian TNF-α is very low (<30%), the multiplicity of TNF-α gene isoforms isolated and cloned in different fish species is very high (>85%). [33][34]. The fish TNF-α cDNA consists of 1217 bp containing (i) an untranslated region of 188 bp; (ii) an open reading frame of 675 encoding the amino acid peptide; and (iii) another untranslated region of 354 bp. The untranslated regions are composed of several "TAAAT" supply motifs that, when translated into mRNA, are characterized by high instability. This characteristic is common to almost all inflammatory genes [35]. Regarding the cDNA of fish TNFR, it is 2729 bps and encodes for a protein composed of 395 amino acids. In the structure of the protein, there is a so-called "death domain", which is also characteristic of Fas proteins. Activation of this domain follows in the initiation of all those biochemical processes that lead to apoptosis [35].

Phylogenetic analysis carried out by sequencing the genes encoding for TNF in different fish species suggests that there could be at least two different isoforms of the protein, namely TNF-α type I (TNF-α1) and TNF-α type II (TNF-α2). TNF-α2 differs substantially from the first one in the presence of a linear amino acid structure linked to the protein scaffold, whose function should be the anchoring of the TNF-α protein to the membrane. Consequently, it is believed that type I, lacking this portion, is probably the soluble version in the cellular environment. In any case, the expression of all isoforms of TNF-α is positively modulated by pro-inflammatory agents, such as LPS, peptidoglycan, polyinosinic:polycytic acid, IL-1β and IFN-γ, as well as by bacterial and viral infections [33].

With regard to IL-1β, it is a cytokine included in the β-trephile family. Genes for IL-1β have been cloned and sequenced for various fish species, which again show a large phylogenetic distance from the respective mammalian proteins (<25%). However, as shown by the circular phylogenetic tree, a greater variability within fish species was also observed in comparison to TNF-α. In this case, the protein amino acid sequences share less than 45% amino acid identity [35]. Finally, analogous to TNF-α, IL-1β expression also appears to be upregulated by the exposure of the same pro-inflammatory agents [36][37][38]. In order to exert its biological function, IL-1β may bind two different receptors, IL-1R Type I (IL-1R1) and IL-1R Type II (IL-1R2). However, for the promotion of the inflammation process, the binding of IL-1β to IL-1R1 is exclusively required. In this process, similarly to mammals, the simple IL-1β/IL-1R1 protein complex is not sufficient for the activation of the inflammatory process, and the transmembrane accessory protein (IL-1RAP) must also be involved [39].

3. Agri-Food Waste and Antioxidant Defense System

Since fish are aerobic organisms, molecular oxygen (O_2) is essential to ensure their normal and physiological functions, including metabolic processes and energy production [40]. However, equally to mammals, it has been observed that, under various metabolic conditions, aquatic organisms also fail to completely reduce O_2 into water (H_2O). Specifically, it was estimated that, in a mitochondrial environment, about 3–5% of O_2 is inevitably converted into superoxide ion ($O_2^{\bullet-}$) [41][42][43]. Although it has been frequently pointed out that low concentrations of $O_2^{\bullet-}$ play important roles in modulating a variety of biochemical and molecular processes, the excessive production of $O_2^{\bullet-}$ and other reactive oxygen species (ROS) is toxic. Indeed, in order to achieve its own stabilization, $O_2^{\bullet-}$ oxidizes biological macromolecules causing extensive damage, including DNA hydroxylation, protein denaturation, lipid peroxidation, apoptosis, and eventually cell death [44][45].

However, excessive $O_2^{\bullet-}$ production cannot be resolved by the simple action of soluble antioxidants. Therefore, the participation of the non-soluble fraction is essential in this process. A specific adapted enzymatic system represented by superoxidase dismutase (SOD) and catalase (CAT) has been detected in most of the fish species investigated so far [20][46][47]. SOD is the primary enzyme involved in the enzymatic detoxification of ROS. In particular, it catalyzes the reduction of $O_2^{\bullet-}$ into hydrogen peroxide (H_2O_2). Without SOD function, this free radical leads to the formation of hydroxyl radicals ($^{\bullet}OH$), which are considered the most dangerous ROS because no antioxidants are available to prevent the action of $^{\bullet}OH$ [20][47]. However, although H_2O_2 is not a free radical, it can extend oxidative damage in cell cytoplasm because it can easily cross biological membranes [3][43]. Here, in the presence of transition metals such as copper and iron, H_2O_2 may originate further $^{\bullet}OH$. In this context, CAT mediates the reduction of H_2O_2 in H_2O before it becomes a potential menace for the cellular environment [43].

Living organisms, both plant and animal, have therefore learned to preserve themselves from potential oxidative insults by developing soluble as well as insoluble defense systems. For example, plants have gradually refined their secondary metabolism by producing phytochemical compounds that can not only increase their resilience to abiotic and biotic threats [3][48][49][50] but that can also act as protectants against oxidative menaces [15][16][51][52][53]. On the other hand, animals can produce soluble and endogenous compounds that, among other functions, are strong antioxidants [45][54][55]. However, unlike plants, animals are unable to produce a large amount of endogenous antioxidant molecules, both in terms of quantity and quality [54][55]. For this reason, scientific research has recently become interested in the evaluation of the antioxidant properties of plant raw materials that can be used as a potential ingredient in the supplementation of animal diet [56][57]. Indeed, as demonstrated by in vitro and clinical studies, dietary supplementation with phytochemicals can induce beneficial effects on the oxidative state of animal cells [58][59]. The main mechanisms hypothesized and described are related to (i) a direct reduction of oxidants into inoffensive species, through the radical scavenging or metal chelating properties of phytochemicals; (ii) an indirect stimulation of the transcription of genes coding for antioxidant enzymes, resulting in an increase in the amount of insoluble defenses; (iii) a direct modulation of the enzymatic activity of insoluble defenses, which are much more efficient in enzymatic detoxification even if not increased in amount [19].

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