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Current applications, selection, and possible mechanisms of actions of synbiotics in improving the growth and health status in aquaculture: A review

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ABSTRACT

Synbiotics, a conjunction between prebiotics and probiotics, have been used in aquaculture for over 10 years. However, the mechanisms of how synbiotics work as growth and immunity promoters are far from being unraveled. Here, we show that a prebiotic as part of a synbiotic is hydrolyzed to mono- or disaccharides as the sole carbon source with diverse mechanisms, thereby increasing biomass and colonization that is established by specific crosstalk between probiotic bacteria and the surface of intestinal epithelial cells of the host. Synbiotics may indirectly and directly promote the growth of aquatic animals through releasing extracellular bacterial enzymes and bioactive products from synbiotic metabolic processes. These compounds may activate precursors of digestive enzymes of the host and augment the nutritional absorptive ability that contributes to the efficacy of food utilization. In fish immune systems, synbiotics cause intestinal epithelial cells to secrete cytokines which modulate immune functional cells as of dendritic cells, T cells, and B cells, and induce the ability of lipopolysaccharides to trigger tumor necrosis factor-α and Toll-like receptor 2 gene transcription leading to increased respiratory burst activity, phagocytosis, and nitric oxide production. In shellfish, synbiotics stimulate the proliferation and degranulation of hemocytes of shrimp due to the presence of bacterial cell walls. Pathogen-associated molecular patterns are subsequently recognized and bound by specific pattern-recognition proteins, triggering melanization and phagocytosis processes.

Contents

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1. Introduction

Annual aquaculture production reached 73.8 million metric tons (MT) in 2014, of which inland and marine aquaculture production respectively accounted for 63.8% and 36.2% of the total and were equivalent to 47.1 and 26.7 million MT, respectively [1]. During farming operations, most recent investigations indicated that feed costs accounted for 84% of total production costs for freshwater fish [2], whereas in penaeid shrimp, they accounted for 66%–68% [3]. In order to ensure profitability, reducing feed costs through improving feed formulations, feed ingredients, and feed efficacy practices is of greatest concern. Hence, developing feed additives incorporated in feed formulations to improve the feed efficiency in aquaculture has become a major trend in the last decade. It appears that numerous researchers have been interested in incorporating prebiotics and probiotics into aquafeed to improve the food value, digestive enzymes, and growth and immune responses in aquaculture. There is no doubt that applications of probiotics and prebiotics have obtained remarkable achievements in enhancing growth and health benefits of aquaculture species. For example, previous studies reported that fish and shellfish fed diets supplemented with either prebiotics or probiotics could improve intestinal microbiota, microvilli and absorptive ability [4–9]; digestive enzyme activity [10,11]; growth performance [7–10,12]; expression levels of immune-related genes [13,14]; and disease resistance against viral and bacterial infections [12,15,16]. The advantages of prebiotics and probiotics in aquaculture have been reviewed by several researchers in recent years [17,18]. Synbiotics, a combination of probiotics and prebiotics, have been introduced and first used to enhance the immune responses of fish since 2005 [19]. Over the past 10 years, numerous studies on uses of synbiotics to improve aquatic animals' health were published. However, it is surprising that those studies still left unanswered questions regarding the underlying mechanisms of action of synbiotics in benefiting hosts. Therefore, the aims of this work were to address the current status of applications of synbiotics in aquaculture and the selection of prebiotic and probiotic for establishing relevant synbiotic formulations. In particular, this document also provides a better understanding of the mechanisms of how synbiotics work as growth and immunity promoters in aquatic animals.

2. Synbiotic concept

Gibson and Roberfroid [20] defined a synbiotic as "a mixture of probiotics and prebiotics that beneficially affects the host by improving the survival and implantation of live microbial dietary supplements in the gastrointestinal tract, by selectively stimulating the growth and/or by activating the metabolism of one or a limited number of health-promoting bacteria, and thus improving host welfare". Since this first definition, synbiotics have not been redefined. However, Kolida and Gibson [21] stated that both synergistic and complementary synbiotic approaches should be considered when applying synbiotics in animal science. From this, the synergistic effect of a probiotic is chosen based on effects on the host, while the prebiotic is chosen to specifically stimulate growth and activity of the probiotic. The complementary effect is when a probiotic is chosen based on specific effects on the host, and the prebiotic is independently chosen to selectively increase concentrations of microbiota components. The prebiotic may promote growth and activity of the probiotic, but only indirectly as part of its target range (Fig. 1) [21]. However, the situation may be more complicated that the recent studies revealed that prebiotics such as β-glucans in parts of synbiotics can act directly the immune system with disregarding the possible effect on intestinal microbiota of the aquatic animals [22,23] while others reported β-glucans provided substrates for growth, viability and colonization of probiotic bacteria [24–26].

3. Current applications of synbiotics in aquaculture

Over the past decade, most studies focused on the roles of probiotics and prebiotics in improving growth performance and immune responses of aquatic animals. To date, probiotics and prebiotics in aquaculture have mostly been reviewed separately [17,18,27,28]. Although synbiotic concepts appeared early [20], the first introduction of synbiotics were reported in rainbow trout *Oncorhynchus mykiss* [19] and white shrimp *Litopenaeus vannamei* [29]. Shortly afterward, some investigators reported the health benefits of synbiotics in various commercial fish species, such as the large yellow croaker *Larimichthys crocea* [30], cobia *Rachycentron canadum* [31], Japanese flounder *Paralichthys olivaceus* [32], and rainbow trout *O. mykiss* [33]; and in shellfish, such as the European lobster *Homarus gammarus* and Kuruma shrimp *Penaeus japonicus* [34,35]. Then, Cerezuela et al. [36] produced an overview on the uses of synbiotics in fish aquaculture. Applications of synbiotics in aquaculture have actually been blossoming since 2012. In fact, most studies investigated the effects of synbiotics on growth performance, enzymatic digestion, and immune response improvements in fish, while several studies reported on shellfish (Table 1), and then a review of the uses of a synbiotic on sturgeon culture appeared [37]. Most recently, Ringo and Song [38] reviewed applications of synbiotics and probiotics in combination with plant products and β-glucans in aquaculture. However, those reviews did not propose selection or pathways of synbiotics involved in growth and immunity enhancement when incorporated into aquafeed.

4. Selection of prebiotics and probiotics for synbiotic formulations in aquaculture

Since their first introduction to aquaculture, some previous studies reported that either single applications or combinations of prebiotics and probiotics had positive effects on aquatic animal health [15,32,39–42]. However, most studies clearly showed synergistic effects [43–47]. This indicates that the effects of synbiotics are now the most relevant in terms of the synergistic effects, while the primary role of prebiotics is to improve the survivability and implantation of the probiotic. To establish a relevant synbiotic, the *in vitro* efficacy of the specificity of the prebiotic for selective stimulation of the selected probiotic needs to be examined. The implication is that probiotic bacteria can utilize a prebiotic as a source of carbon to achieve high growth rates and cell yields during fermentation. However, this method is limited due to a lack of