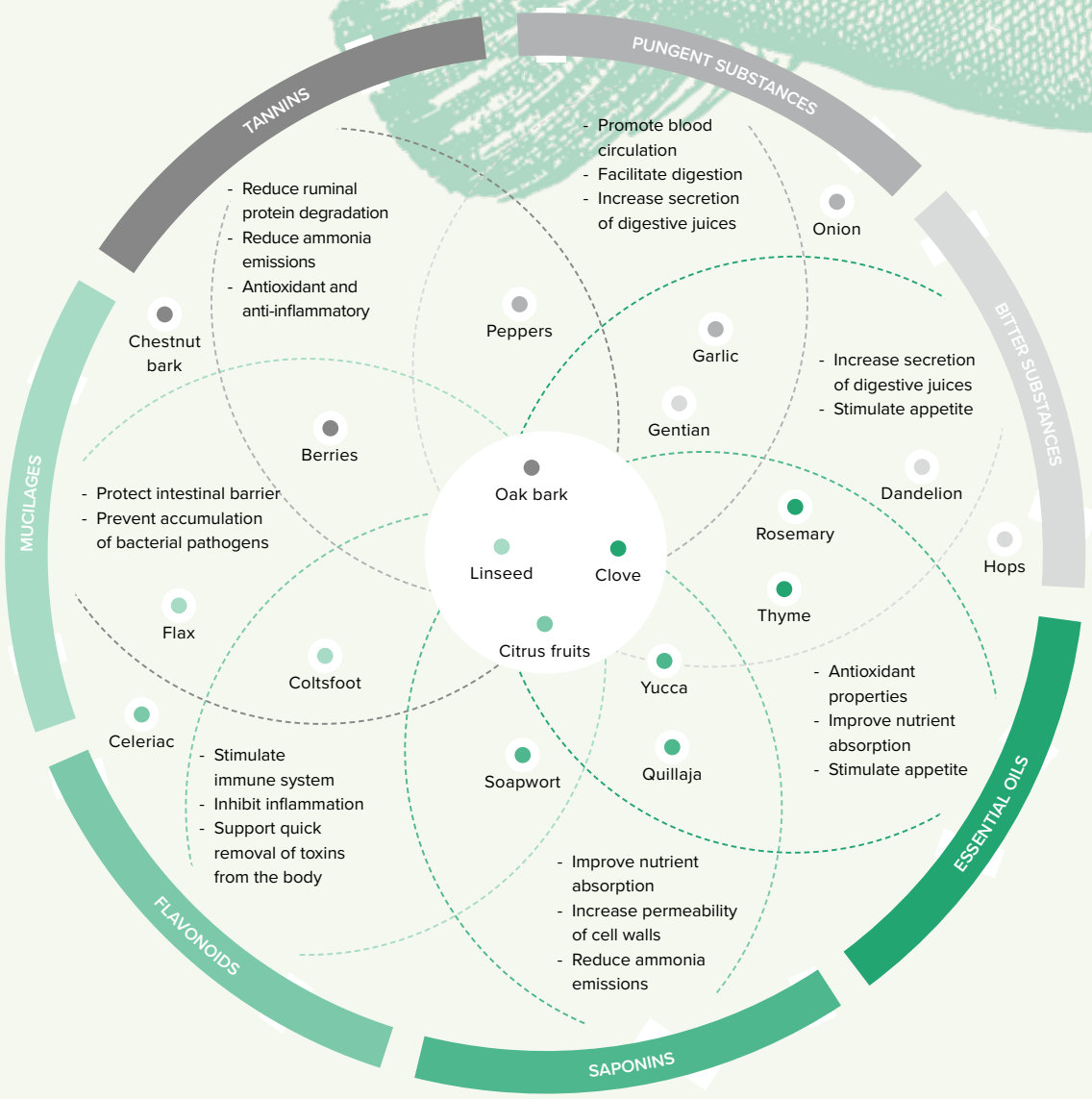
Phytogenics in aqua: Looking for the 'big fish'?



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As a direct consequence of the stagnation of capture fisheries and globally increasing fish consumption, aquaculture represents one of the fastest-growing sectors in food production.

However, the limitation of marine raw materials in aquaculture diets and their replacement by more sustainable protein and lipid sources of terrestrial origin, in some cases, is associated with negative consequences on the metabolism and immune system of aquaculture species and may slow down the development of the sector.

The global trend to ban antibiotic growth promoters, for fear of the development of resistant bacterial strains, and to protect consumers' health, has driven the sector to invest into research in natural alternatives instead.

Plant substances on the rise

Phytogenic feed additives (PFAs), commonly defined as plant-based feed additives or botanicals, represent a group of natural substances used in animal nutrition. These substances are derived from herbs, spices, other plants and their extracts consisting of highly active plant substances and encompass much more than essential oils: they include spicy or bitter substances, saponins, flavonoids, mucilages or tannins.

During the last two decades, research on phytogenics as potential functional ingredients has increased, and with it, their commercial use in the animal production sector. However, a deeper understanding of the mode of action of the bioactive

compounds of phytogenics in fish and shellfish is key to improve their use in aquaculture.

Some of the bioactive phytogenic compounds have been proven to stimulate digestive enzymes production, support liver function, modulate gut microbiota imbalances, and have potent antioxidant and anti-inflammatory properties.

Fortunately, during the last years, scientists and companies have done a lot of research to elucidate, how specific phytogenics may improve nutrient uptake and/or disease and stress resistance in fish and shellfish as an important basis for optimal sector expansion.

The understanding of the mode of action of newly formulated complex phytogenic mixtures (blends) will help the aquaculture sector to use available phytogenics properly, to explore synergies and antagonisms among bioactive compounds and to clarify interactions with other feed ingredients. These facts will additionally help the aquaculture sector to improve its production performance.

Growth performance effects

Growth performance is the most frequently used parameter to determine adequate production management, and it may be affected by different factors, like nutrition, environment, pathogens or handling. Maintaining an optimum growth rate during stressful situations or even promoting it under normal conditions is one of the main demands in the sector.

Specific phytogenics have been demonstrated to promote growth performance and feed efficiency in several fish and shellfish species. For example, Aloe vera (*Aloe barbadensis Miller*) extract improved growth performance in common carp (*Cyprinus carpio*) when fed for eight weeks.

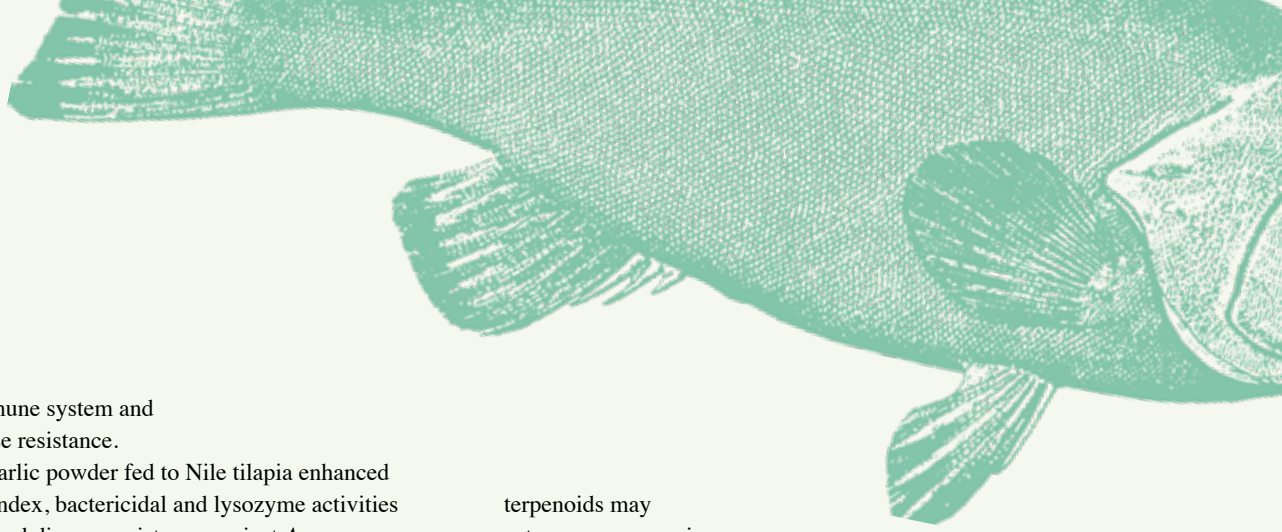
Extracts of garlic (*Allium sativum*), oregano (*Origanum heracleoticum*), ginseng, quillaja (*Quillaja saponaria*), mentha (*Mentha piperita*) and sweet basil (*Ocimum basilicum*) promoted growth performance of Nile tilapia (*Oreochromis niloticus*) in several trials.

Similarly, for channel catfish (*Ictalurus punctatus*), growth performance and feed efficiency were enhanced, when fish were fed with oregano oil. These benefits could be associated with a positive effect on the fish microbiota composition, derived from the well-described antimicrobial properties of oregano. Garlic and onion (*Allium cepa*) extracts supported growth in European sea bass (*Dicentrarchus labrax*) and in the case of Whiteleg shrimp (*Litopenaeus vannamei*), several phytogenic substances, like yucca (*Yucca schidigera*), quillaja, ginger (*Zingiber officinale*), curcuma (*Curcuma longa*) and astralagus (*Astralagus membranaceus*) promoted growth performance.

The potential mode of action of the above mentioned individual phytogenics, in general, has been associated with improved feed palatability, promoted digestive enzyme secretion, enhanced nutrient uptake and balancing effects on the intestinal microbiota. It is interesting to remark that the effect of phytogenics is directly related to the fish species, the extraction process and to their bioavailability of actives rather than to the inclusion rate.

Supporting resilience

An optimal immune function of cultured fish and shellfish is a main determinant to protect them against infections with pathogens. Several studies have been addressed to determine how phytogenics may boost the innate and/or adaptive immune system when supplemented to cultured fish and shellfish. In this context, garlic is the most studied phytogenic in terms of



boosting the immune system and increasing disease resistance.

For example, garlic powder fed to Nile tilapia enhanced phagocytic fish index, bactericidal and lysozyme activities as well as increased disease resistance against *Aeromona hydrophila*.

Similarly, rainbow trout (*Oncorhynchus mykiss*) fed with garlic extract showed enhanced phagocytic activity, respiratory burst, lysozyme activity and, consequently, reduced fish mortality when challenged with *Aeromona hydrophila*.

Recently has been proven that a mixture of garlic oil and labiatae plant extracts supplemented for nine weeks enhanced disease resistance and immune system response, promoted a healthier microbiome and reduced cortisol levels in European sea bass fed low fish meal and fish oil diets.

Indeed, oregano, ginger and rosemary (*Rosmarinus officinalis*) have shown to immunomodulate Mozambique tilapia (*O. mossambicus*) and European sea bass response. Turmeric oil and *Gynura bicolor* reduced mortality of whiteleg shrimp infected with *V. harveyi*, *V. alginolyticus* and white spot syndrome virus (WSSV), partially due to their enhancing effects on lysozyme, prophenoloxidase (proPO) and superoxide dismutase (SOD) activity.

Further, it seems that nutritional and environmental factors considerably influence the gut microbiome. The composition of the diet, including plant-derived actives, thus represents a crucial factor, hence being responsible for the modification of bacterial populations.

In this context, phytogenics may modulate gut microbiota by enhancing the proliferation of lactic acid bacteria (LAB) like Lactobacillus and decrease the presence of potentially pathogenic bacteria. By the way, phytogenics have been shown to unroll a higher activity against pathogenic bacteria than against commensal microbiota.

There are probably different mechanisms underlying this modulation, including direct and specific antimicrobial effect against specific bacterial species, or a quorum sensing inhibiting effect. Direct antimicrobial effects of different phytogenics against specific pathogens have been demonstrated in different *in vitro* assays based on the Minimum Inhibitory Concentration (MIC) capacity of the phytogenic.

However, it is important to remark that results obtained in MIC assays differ between bacterial strains. Depending on the extraction method for the phytogenics, differences in MIC may occur due to potential synergies among main actives and trace compounds contained in specific extracts.

For example, different extracts derived from eucalyptus (*Eucalyptus globulus*), oregano, and cinnamon (*Cinnamomum verum*) have been very effective against several fish pathogens like *S. iniae*, *A. hydrophila*, *Photobacterium damselae subsp. damselae* and *V. parahaemolyticus*. Phytogenics also affect bacterial quorum sensing by reducing biofilm formation and by suppressing bacterial toxin production, which in the end, will inhibit or reduce the incidence of the disease outbreak.

Several plant extracts, like phenolics, flavonoids, alkaloids, and terpenoids may act as quorum sensing inhibitors via different mechanisms, as the inhibition of N-acyl-homoserine lactones (AHL) synthesis, altering transport or secretion mechanisms, the binding and storage of AHLs, or the antagonistic actions or inhibition of targets downstream of AHL receptor binding.

Stress-reducing effects

Stress during aquaculture production is implicated by the production procedure (transport, stocking, grading or sampling) and can be reduced to a minimum by proper production management.

Stress directly results in reduced feed intake, a lower performance rate and higher susceptibility to disease outbreaks due to a down-regulation of the immune system and alterations in fish physiology, affecting the metabolism as well. Some- even when controlled - production practices (e.g., handling) mean stress for the cultured fish and require the use of anesthetics.

However, sometimes, the application of the anesthetic itself may act as a stressor. Recently, specific phytogenics per se have attracted attention, acting as anesthetics. Concomitantly to anesthetic effects, phytogenics come along with numerous of the above-mentioned beneficial aspects like antioxidant function, anti-microbial effects and stress-reducing properties. The most studied phytogenic anesthetic is clove oil which effective anesthetic concentration depends on the target fish species.

Interestingly, other phytogenics, like Lemon verbena (*Aloysia triphylla*), Eucalyptus (*Eucalyptus sp*), *Lippia alba*, close basil (*Ocinum gratissimum*) and garlic have been shown to act as stress relievers by reducing cortisol levels in Nile tilapia, European sea bass and South-American catfish (R. quelen). Though the route of application is important for the desired effects. Whereas phytogenics for sedation during transport and handling are applied in bath, general stress-reducing effects can be achieved by supplementing phytogenics into the diets.

Conclusions

Phytogenics can modulate physiological functions and intestinal microbiota, showing a clear potential for enhancing growth performance, and for improving disease and stress resistance in different cultured fish and shellfish species. However, there is still little knowledge about the mode of action of several of their bioactive compounds, possible interactions and synergies among them, as well as the most appropriate form of administration.

Consequently, further research is necessary to properly identify the most suitable phytogenics and blends that are tailored to the current challenges in the aquaculture production sector. Understanding the phytogenics' mode of action in detail represents a crucial tool in the development of new, well formulated, effective products.

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