

Immunostimulants

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- **Immunostimulants**

- Due to the absence of specific vaccines to many diseases, other methods of prophylaxis are tried which includes use of immunostimulants, bioremediators and probiotics.
- Fish depends on non-specific defence mechanisms more heavily for health maintenance, so immunostimulants play a significant role in the management of fish health and disease control.
- Immunostimulant is a chemical, drug, stressor or action that elevates the non-specific defence mechanisms by increasing phagocytosis, leucocytic activity, macrophage and neutrophil migration or specific immune response.

- In addition, they also reduce the immune suppressive effects of stress.
- Different compounds like select proteins, lipids, carbohydrate based cell wall extracts and synthetic compounds have been used as immunostimulants in farm reared fish and shellfish.
- The immunostimulants used in aquaculture include glucans, lipopolysaccharides, chitin, chitosan, peptidoglycans, muramyldipeptides, polypeptides, levamisole, Vitamin C, Vitamin E etc.

- An immunostimulant is defined as a substance which enhances the innate or non-specific immune response by interacting directly with cells of the immune system and activating them.
- Immunostimulants can be grouped under different agents based on the source, such as bacterial preparations, polysaccharides, animal or plant extracts, nutritional factors and cytokines .
- The pathogens that were controlled successfully by using immunostimulants in fish/shrimp, include bacteria *Aeromonas salmonicida*, *A. hydrophila*, *Vibrio anguillarum*, *V. vulnificus*, *V. salmonicida*, *Yersinia ruckeri*, *Streptococcus spp.*; viruses causing infectious such as hematopoietic necrosis, yellow head virus, viral hemorrhagic septicemia and the parasite like *Ichthyophthirius multifiliis* [

- Immunostimulants are dietary additives that enhance the innate (non-specific) defense mechanisms and increase resistance to specific pathogens .
- There is no memory component developed and duration of the immune response is over a short period.
- Immunostimulants are chemical substances which activate leukocytes .
- Adjuvant (FCA) is one of the first immunostimulants used in animals to enhance the specific immune response, and it has also been successfully used in conjunction with injection of fish bacterins

- So far glucans, which are polymers of glucose, found in the cell walls of plants, fungi and bacteria appear to be most promising of all the immunostimulants investigated, in fish and shrimp culture ponds through oral application, which was found to be the route of choice

Types of Immunostimulants used in Aquaculture

- **2.1 Muramyl dipeptide**
- Muramyl dipeptide is a simple glycoprotein, also a purified form of mycobacteria.
- It can enhance the antibody activity, stimulation of polyclonal activation of lymphocytes and activation of macrophages.

2.2 Chitin and Chitosan:

- Both chitin and chitosan have a major role in aquaculture. They are non-specific immunostimulators which are effective on a short term basis.
- Chitin is a polysaccharide which constitutes the principal component of exoskeletons of crustaceans and insects and cell walls of few fungi.
- It can stimulate macrophage activity and give resistance from certain bacteria
- Chitosan is a deacetylation product of chitin.

2.3 Lentinan, Schizophyllan and Oligosaccharide

- Lentinan, Schizophyllan and Oligosaccharide can increase cellular and non-cellular defence mechanisms like lysozyme activity, phagocyte activity and complement activity in fish.

• 2.4 Levamisole

- It is an anthelmintics chemical that has been shown to have
- some stimulating effect on the immunological reactivity of
- animals and humans.
- Activities of this agent are: enhancement of cell mediated cytotoxicity, lymphokine production and suppressor cell function, and stimulation of phagocytic activity of macrophages and neutrophils.

2.5 Yeast derivatives

- Glucans- long chain polysaccharide extracted from yeast are good stimulators of non-specific defence mechanism in animals, including fish and shellfish like phagocytic activity and protection against bacterial pathogens.
- Several types of glucans have been investigated in fish such as yeast glucan,
- peptideglucan,
- β -1, 3 glucan (VST).
- Yeast glucan (β 1-3- and β 1-6-linked glucan) and β -1,3glucan (VST) is derived from cell walls of baker's yeast such as *Saccharomyces cerevisiae* and *Schizophyllum commune*, respectively
- β -glucans comprise diverse group of polysaccharides of D-glucose monomers linked with β -glycosidic bonds.

- **Vitamin C & E**

Vitamin C play an important role in several physiological functions including growth, resistant to infections, wound healing, response to stressors and possibly lipid metabolism through its action on carnitine synthesis while administering with feed.

- Vitamin C (Ascorbic acid) is a co-factor in many biological processes including collagen synthesis and cellular functions related to neuromodulation, hormone and immune systems.
- **Vitamin E** can enhance specific and cell-mediated immunity against infection in fish.

Mechanism of action of immunostimulants

- Levamisole, Freund's Complete Adjuvant (FCA), Glucans, Muramyl dipeptide, FK-565 (Lactoyl tetrapeptide from *Streptomyces olivaceogriseus*)- stimulators of T lymphocytes
- Bacterial endotoxins, Lipopolysaccharides, Macrophage activator- Glucans, Chitin and Chitosan- stimulates of B cells.
- Inflammatory agents including chemotoxins
- Detergents and Sodium dodecyl sulphate, Quaternary ammonium compounds (QAC), saponins- Cell membrane modifiers
- Vitamin C and E, n-3 fatty acids- Nutritional factors
- Cytokines- Leukotriene, Interferon
- Animal and fish extracts- Mitogens

- Mechanism depends on the type of immunostimulants, dose, and route of administration, time and period of exposure.