

## Immuno-stimulants

### Introduction

Immunostimulant can be defined as a chemical, drug, stressor, or action that enhances the innate or non-specific immune response by interacting directly with cells of the system activating them. During evolution the immune system has developed the mechanisms to detect foreign molecules that are part of the pathogen, so that once the pathogen enters the body of an organism these foreign molecules that are part of the pathogen are detected and activate the defense system against the pathogen. Simple presence of such foreign molecules is sufficient to trigger the immune system and can act as if pathogenic organism might have entered the body. So the administration of these foreign molecules which will act as immunostimulant can activate the defense system and keeps the defense system in alert to combat any invading pathogen. Most immune-stimulants are chemical compounds which exist as structural elements of bacteria, mycelial fungi and yeasts. However, there are also a couple of purely synthetic compounds that possess immune-stimulating properties.

The chemical nature of a number of different immune-stimulants are:

- Structural elements of bacteria [lipopolysaccharides (LPS), lipopeptides, capsular glycoproteins and muramylpeptides].
- Various  $\beta$ -1,3-glucan products from bacteria (Curdlan) and mycelial fungi (Krestin, Lentinan, Schizophyllan, Scleroglucan, SSG, VitaStim).
- $\beta$ -1,3/1,6-glucans from the cell wall of baker's yeast (MacroGard, Betafectin).
- Complex carbohydrate structures (glycans) from various biological sources including seaweed.
- Peptides present in extracts of certain animals or made by enzymatic hydrolysis of fish protein.
- Nucleotides, and
- Synthetic products (Bestatin, muramylpeptides, FK-156, FK-565, Levamisole).

Among all the immune-stimulants  $\beta$ -1,3/1,6-glucans more effective and widely used in veterinary medicine, human medicine, and also in traditional animal farming. Because this immune-stimulant acts at a very basic level of the immune system. i.e., the  $\beta$ -1,3/1,6-glucan molecule is recognized by the specific receptor present on white blood cells in all animal groups, from the simple invertebrates to humans, and switches trigger the most basic defence mechanisms.

### Mode of action of $\beta$ -1,3/1,6-glucans

$\beta$ -1,3/1,6-Glucans bind specifically to a "receptor molecule" on the surface of the immune cells that has been retained during evolution and is found in all animal groups from simple invertebrates to man. This is why  $\beta$ -1,3/1,6-glucans have the same basic biological effect within the whole animal kingdom. When the immune cells are stimulated by  $\beta$ -1,3/1,6-glucan, the cells become more active in engulfing, killing and digesting bacteria and at the same time they secrete signal molecules (cytokines) which stimulate the formation of new white blood cells. In vertebrates which have the specific immune system, the activated phagocytes produce cytokines which also activate antibody-producing lymphocytes. So  $\beta$ -1,3/1,6-glucan if used as vaccine it enhances the efficacy.  $\beta$ -1,3/1,6-glucans intern also contribute in growth, wound healing, repair of cells etc. Purified form of  $\beta$ -1,3/1,6-glucan do not induce any antibody production which is an added advantage because the immune system will not be stimulated to waste antibody against immune-stimulant itself.

Immune-stimulants are being used in the aqua-culture sector and in traditional animal husbandry to reduce mortality due to infections and to improve general performance of animals. Immune-stimulants when used may provide the benefits like:

- Reduce mortality due to opportunistic pathogens.
- Prevent virus disease.
- Enhance disease resistance of farmed shrimp.
- Reduce mortality of juvenile fish.
- Enhance the efficacy of anti-microbial substances.
- Enhance the resistance to parasites.
- Enhance the efficacy of vaccines.

### **Action in fish**

The most common immunostimulants used are non-virulent microorganisms or their by-products and in fish once the immunostimulant is injected, the first defense system are substance found in mucus secreted by endothelial cells, followed by macrophage activation that acts against pathogens. Then lytic factors, agglutinating factors, proteins and enzymes act directly on the molecules or on the microbe's surface to suppress bacterial growth or to assist in phagocytosis.