

Adjuvants

Introduction

The term adjuvant has been derived from a Latin word *adjuvare*, which means to help, thus any material that enhances the immunity is referred as adjuvant. An adjuvant by definition is a diverse range of substances those modulate/enhance the immune response when used in combination with antigen. Addition of adjuvants helps in lowering the dosage of vaccine given, efficient absorption and slower processing of antigen, application of vaccine at low temperature and reduction of side-effects of antigenic preparations. The use of adjuvant is quite common in human and veterinary medicine and goes together with the concept of immunization/ vaccination and has gradually been shifted to aquaculture.

Adjuvants can act as immunostimulators, immunomodulators and immunopotentiators. They can either be administered in combination with or before or after the immunization while some of them can also be given alone. Those are given along with the antigen are FCA, FIA, MDP, polynucleotides, aluminium salts, endotoxins etc. Some of them are immunostimulants and given after the antigen administration, they include glucan and others, however, if given before, they cause immune tolerance. Some are given as immunopotentiators to restore the depressed immunity and others are either given alone or prior to antigenic stimulation. These include levamisole, BCG, dextran sulphate, etc.

Classification of adjuvants

1. Microbial/biological substances

These include *Mycobacterium sp.*, *M. tuberculosis* incorporated in Freund's complete adjuvant (FCA), BCG, *M. marinum*, mixed bacterial toxins, cholera toxin beta unit, saponin including quil-A and immunostimulating complexes (ISCOMs), hemin and haemoglobin, crustaceans, insects and cell wall of certain fungi) etc .

2. Chemically defined yeast/bacterial/fungal products

Most important of these include lipopolysaccharides (LPS) such as β (1, 3)-D- glucan (laminaran), lentinan, muramyl dipeptide (MDP) and cord factor trehalose dimycolate (TDM) of *Mycobacteria*, polar glycopeptidolipids (PGPL) of *M. chelonae* and peptidoglycan.

3. Biological products of immune system

They include lymphokines, cytokines, lactoferrin, growth hormones and prolactin.

4. Synthetic biological analogues

Double stranded complementary RNA homopolymers, synthetic MDP, synthetic TDM, lauroyl tetrapeptide, stearyl tyrosine hydrochloride, dimerized lysozyme, inosine pranobe, formyl peptide (FMLP), short chain peptide, and FK-565 (a peptide related to lactoyl tetrapeptide isolated from cultures of *Streptomyces olivaceogriseus*) are common adjuvants of synthetic biological analogues.

5. Chemical preparations

These include aluminium compounds like aluminium hydroxide, aluminium sulphate and aluminium phosphate, calcium phosphate, dextran sulphate, oil emulsions including mineral and vegetable oils in Freund's complete (FCA) and incomplete (FIA) adjuvants, wax D, levamisole, liposomes, polyacrylic adjuvants, serum albumen beads. CP-20, CP-960, synthetic polymers, squalene, rnicrosilica, quaternary ammonium compounds hydrocarbon adjuvants like aliphatic amines of chain length around C 16- like dimethyldioctade cyclamine and N,N-dioctadecyl-N-N-bis (2 hydroxyethyl) propanediamine.

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 defence 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 defence system and keeps the defence system in alert to combat any invading pathogen.

Immunostimulant can be defines 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.

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 most commonly used adjuvant is Freund's complete adjuvant (FCA) because it serves as a storehouse for immunogen over a prolonged period thus helps in prolonged release of antigens. It is a combination of paraffin oil, lanonin-like substances and killed *Mycobacterium* sp. Its bacterial component stimulates T-cell response. Freund's incomplete adjuvant is used after FCA to enhance vaccine effect, this adjuvant doesn't contain bacterial component as in FCA. Other commonly used adjuvants are light oils and lipopolysaccharides.

Application in aquaculture

The success of aquaculture industry directly depends on the health aquatic animals. Since these animals are in surrounded by potential pathogens in aquatic media, these animals often get clinical syndromes caused by many infectious organisms, where some of them may leads to serious disease and vaccination can be given to fish against that pathogen in order to protect the fish form disease. This vaccine is given along with adjuvant. In fish vaccination alum and oil are used as adjuvant. Some new adjuvants like hemin and haemoglobin, ECP of *Mycobacterium*, microsilica, and polar glycopeptidolipids of *Mycobacterium chelonae* are introduced newly in fish vaccine. Also the immunostimulants like B-D-glucan, levamisole, vitamine E, vitamin C etc. have been used to enhance the immunity in immunocompromised aquatic animals. Light oil adjuvants are successfully used with injectable vaccine of *A. salmonicida*, a multivalent vaccine containing *A. salmonicida*, *Yersinia* sp. and/or *Vibrio* sp. Some of these adjuvants can be used alone as well.