A new option for health management: marine algal polysaccharides

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Nowadays, poultry producers are looking to have the best livestock health, while limiting the use of antibiotics.

Alternatives maximising the efficiency and profitability of prophylactic vaccination strategies and protecting the animal against pathogens are therefore of major importance.

To achieve this goal, new avenues are constantly being explored. One of them concerns the use of new molecules extracted from seaweeds for the stimulation of the body's natural defences and its response to vaccination strategies.

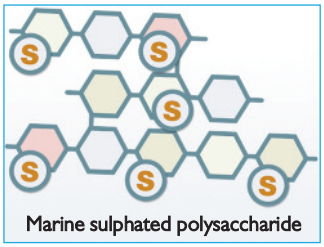
Seaweeds

In recent years more and more publications have highlighted the relevance of seaweeds in numerous biological applications, particularly to immune mechanisms, taking special interest in some of their components, namely the sulphated polysaccharides. These are complex carbohydrates which do not occur in terrestrial plants.

With their great potential of structural variability, they offer a high capacity to transport biological information. Indeed their flexibility is required for exact regulatory mechanisms in different cell-cell interactions in higher organism. In addition, one of the particularities that numerous marine polysaccharides possess is their polyanionic and sulphated character, which confers them a high chemical reactivity (for example agar, ulvans, carrageenan and fucans).

MSPs and immunity

Marine sulphated polysaccharides (MSPs), which are widespread in macroalgae, have been shown to possess anti-infectious (anti-viral, anti-bacterial, anti-tumoral), anti-oxidant and anti-thrombotic activities, as well as immune-modulating activities that might find relevance in stimulating the immune response or in controlling the activity of immune cells in order to mitigate negative effects such as inflammation.



One of the MSP action's pathways is via the activation of cell-associated pattern recognition receptors, such as TLR (Toll-Like Receptor).

TLR are transmembrane proteins of immune and epithelial cells which detect invading pathogens by binding to ancestral molecules of microbial origin called Pathogen-Associated Molecular Patterns (PAMPs).

It therefore appears that TLR play a key role in the adaptive immune response, but the signals produced by their activation lead to the activation of numerous other cells and functions of the immune system, which makes them essential elements of both the innate immune mechanisms and of adaptive immunity.

Indeed, the activity of some MSP as TLR activating agents might be the result of a certain structural similarity between these marine polysaccharides and molecular structures that are characteristic of microbial pathogens such as bacterial lipopolysaccharides (LPSs).

Bacterial LPSs are a type of structure occurring at the surface of the bacterial external membrane and recognised as bacteria-specific recognition elements (Figs. 1 and 2)

Microbes have a high multiplication capacity. So the immune response is often surpassed because of the time required for immune activation. In this case the infection leads to the disease.

The interest of MSP would be to stimulate the innate immune system to increase its reaction capacity in maintaining the pathogen population at a non-invasive level and/or to contribute to the destruction of the microbes before multiplication.

MSPs and viral infection

Several publications demonstrate the antiviral activities of MSP. This is explained by three mechanisms:

- Formation of complexes that block the virus-cell interaction. The virus-cell complex is formed by ionic interactions between the anionic (mainly sulphate) groups of the cell surface polysaccharide (Heparan sulfate) and basic amino acids of the viral glycoprotein, and non-ionic ones depending on hydrophobic amino acids interspersed between the basic ones in the glycoprotein-binding zone.

The antiviral activity of the MSP is based on the formation of structurally similar complexes:

- Interaction between the anionic groups of the MSP and basic amino acids of viral glycoprotein.
- Ionic Interaction between the MSP and the cell receptor: leading to a masking of the positive charge of the host cell by the negative charge on the MSP.

These interactions block the virus-cell binding and prevent the viral entry in the cell (Figs. 3 and 4).

The viruses are kept in the extracellular environment and are available for elimination by leukocytes and other immune stimulated cells. Moreover, the cellular integrity is preserved because when a cell is infected it is inevitably destroyed by the virus release or by the immune system action.

- Inhibition of virus transcription and replication processes after entry into host cell. This inhibition may be due to the direct interference of viral replication enzymes by MSP (reverse transcriptase)
- Induction of leukocyte release due to the immunomodulation by MSP. Leucocytes are able to fight

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Fig. 1. Modulation of immune activity by microbial LPS recognition.

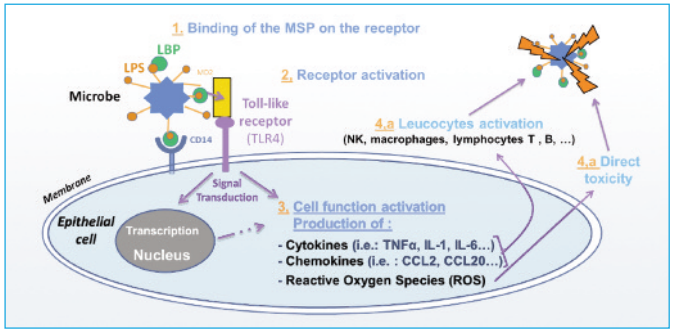
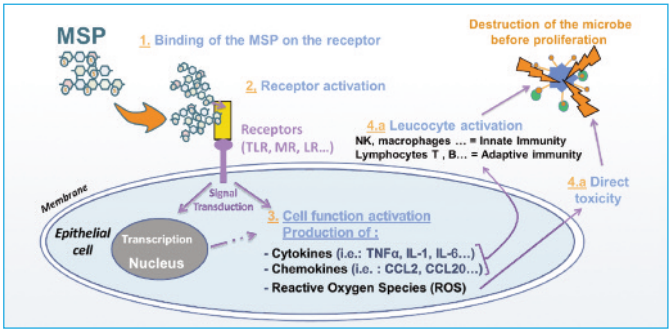


Fig. 2. Modulation of immune activity by MSP recognition.



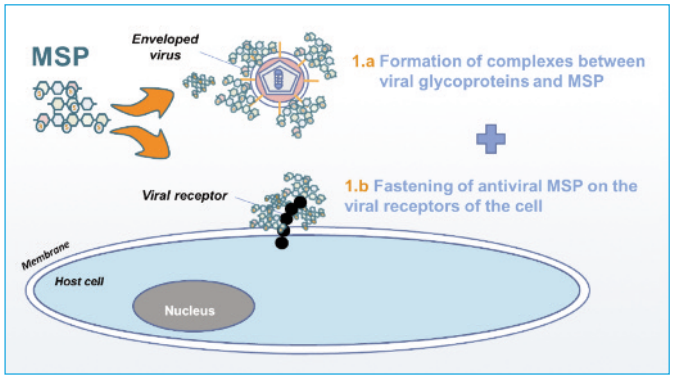


Fig. 3. Binding of the marine sulphated polysaccharide (MSP) on the virus surface and cell receptor.

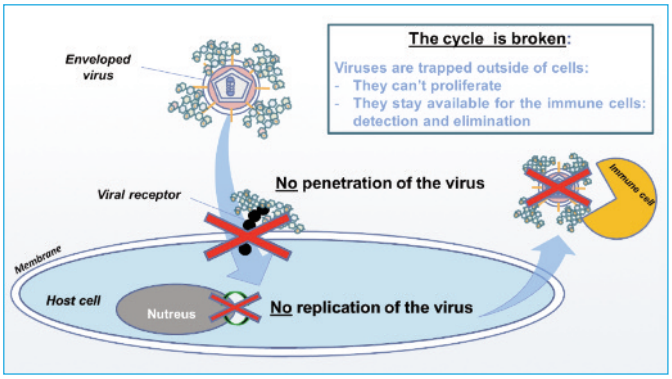


Fig. 4. Blocking of the viral entry into the cell thanks to the marine sulphated polysaccharide (MSP).

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not only bacteria but also viruses ('virus clearance').

Possible applications

In conclusion, seaweeds appear to contain sugars in the form of polysaccharides, some of which – the sulphated polysaccharides – are complex polyanionic structures which possess various biological properties.

A vast number of studies have already shown the effects of some of these sulphated polysaccharides, particularly the fucoidans, the carraghenans and the ulvans, on certain mechanisms of inflammatory response and on immunity.

The identification and selection of these polysaccharides extracted from suitable macroalgae makes it possible to envisage the use of these molecules as agents for the stimulation of the various mechanisms associated with the body defence and, in particular, of the innate immunity mechanisms. Within the framework of the potential applications in the fields of poultry breeding and poultry health two non-exclusive strategies can be proposed:

- **Regular sequential intakes for general stimulation of the body's defence:**

By a regular intake unrelated to vaccination, they allow the strengthening of the body's defence via a stimulation of innate and adaptive immunity.

The use of MSP upstream or downstream of a prophylactic program may be an asset in enhancing the level of immune protection of an individual or group of individuals within a flock and in contributing to a better control of the infectious pressure on the flock, preventing the appearance of recurrent infectious pathologies. In broiler production it is recommended to apply MSP on the third or fifth day of life and then to make a regular immunostimulation one day per week.

- **Targeted intakes within the framework of a vaccination program:**

As part of a vaccination program, they would enhance the vaccine protection. As potential 'adjuvants' in future vaccination strategies for poultry, this would definitely provide the possibility to improve the immunological impact and persistence of a high protective level of the vaccine and thereby to improve the technical and economic performance of vaccine prophylactic programs.

In poultry production it is recommended to apply MSP one day before the vaccine administration and the two days after. ■