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Review Article

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Red Tide: Why a Biologic, HDFx, and Magnesium Could be used to allay Inflammatory and Lung Problems Caused by Algal Blooms: Hypothesis

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Introduction

Over the past decade, there has been a growing concern over invasion of Florida Gulf Coastal Waters and beaches by several algal blooms created by "red tides". These algal blooms create various toxins that pose high risks for marine life, livestock, birds, and humans [1, 2]. The algae become so numerous that they discolor gulf waters and beaches. Since the 1980's, red tides have been seen in many countries throughout the globe (i.e., South America, Central America, Japan, caribbean, South Pacific regions, etc.).

The organisms primarily responsible for the red tides are microscopic algae called dinoflagellates [1]. When these blooms occur, it is not uncommon for beaches to be littered with thousands of dead fish, birds, and molluscs. These dinoflagellates produce several different neurotoxins that not only kill marine life (e.g., turtles, manatees, dolphins, etc.) and livestock, but can cause multiple inflammatory effects in humans from discomfort in the skin, rashes, burning in the eyes, throat infections, and coughing to serious lungs problems People with serious asthmatic conditions, emphysema, or chronic lung disease could get in serious life-threatening situations. As of the moment, there are no proven countermeasures ether to treat against these neurotoxins or to prevent red tides and their effects, especially in humans.

Discovery and Development of a New Biologic Host-Defense Factor, HDFx

Our laboratories, for more than 50 years have been working on a new approach to develop host-defense factors that stimulate various arms of the innate and adaptive immune systems [3-43]. To this end, we have discovered a new host-defense factor our group termed "HDFx" that is a conserved protein found primarily in macrophages and natural killer (NK) cells [44-48]. So far, we have found its presence in rodents, rabbits, guinea-pigs, dogs, cats, and subhuman primates.

Approximately 135 years ago, Elie Metchnikoff, the father of immunology, and Nobel laureate, hypothesized that the body, under stressful circumstances and adverse conditions, would produce powerful immunostimulants which could act on different arms of the innate immune system and serve to protect against major insults, inflammatory conditions, and diseases [49]. Metchnikoff's early studies pointed to the important contributions of macrophages and phagocytic leukocytes to natural (innate)resistance against pathogenic bacterial and viral microorganisms. Over the past 40 years, considerable evidence has accumulated to support a strong relationship between the functional (physiological) state of the microcirculation, circulating macrophages, alveolar macrophages, NK cells, the reticuloendothelial system (RES), and "pit cells" in the liver to host-defense and resistance to pathogens, trauma, sepsis, wounding, circulatory shock and combined injuries [7, 10, 20, 21, 24, 26, 27, 30, 38, 40, 43, 50-54].

Ongoing studies from our laboratories have shown that HDFx is protective (to varying degrees) against a variety of insults ranging from hemorrhage, trauma, endotoxins, a variety of bacteria (*i.e., E. coli, S. enteriditis, C. welchii), combined injuries, fungal toxins, sepsis, experimental NASH, and inflammatory conditions [45, 46, 48, 55]. HDFX also protects against cytokine storms as is often the cause of death in many infectious diseases* [56-59]. A unique attribute of HDFx is its ability to accelerate wound healing [46].

Most importantly, HDFx has been demonstrated to inhibit release of multiple cytokines and chemokines, including TNF-alpha, IL-6, IL-8, IL1-beta, IFN-gamma, and numerous macrophage factors [44, 56-59]. Thus, HDFx can either

prevent or ameliorate "cytokine storms" induced by gram-negative and gram-positive microorganisms, trauma, and systemic inflammatory conditions, among other dangerous bodily insults [44, 56-59].

Magnesium as a Pulmonary Vasodilator and Ant-inflammatory Agent

Approximately 50 years ago, we reported that magnesium (Mg) can be a powerful vasodilator of arteries, veins and microscopic blood vessels as well as an inhibitor of vasoconstrictor agents and pulmonary hypertension in animal models, neonates and adults [60-73]. Mg has been found, both experimentally and clinically, to be useful as an anti-inflammatory agent [74].

Suggested Use of Combined HDFx with Mg for Treatment and Amelioration of Rashes, Skin Lesions, Inflammations, and Coughing Induced by Red Tides in Humans

It Is now clear, in the case of vasculitis, and red tide inflammations in humans that these insults are associated with increased levels of cytokines and chemokines (e.g., INF-alpha, IL-1-beta, IL-2, IL-4, IL-8, IL-10, TNF-alpha, MCP-1, among others) which are pro-inflammatory in nature [1, 2, 75]. We have found that rats placed on Mg deficient diets for 21 days generate all of these pro-inflammatory cytokines and chemokines, in bloods, cutaneous tissues, myocardium and blood vessel vascular and endothelial cells, and demonstrate inflammations [76, 77]. Other investigators have also reported finding many of these cytokines and chemokines in Mg deficient animals and humans [78]. Many of these cytokines and chemokines, in Mg deficient animals, were found to be associated with microvascular remodeling and pathological alterations in the postcapillary venules, the major sites of inflammatory lesions [79-81]. Under high in-vivo microscopic observation, the venules were associated with reduced lumen sizes and adherence of leukocytes and macrophages, similar to that observed in various forms of vasculitis, and most likely in cases of red tide. In view of our extensive findings, it is difficult to dismiss the probable role of a deficiency produced by red tides. Thus, we believe it is worth trying to administer Mg salts and Epson salt baths to victims of red tides-induced inflammatory conditions.

Since our work on "HDFX" demonstrates, it poses remarkable anti-inflammatory actions and accelerates wound healing, we believe the Mg treatment should be combined with HDFx.

Conclusions and Future Thoughts

Although no "tried and true "countermeasures exist for treating the harmful effects of red tides in humans, animals and sea creatures the discovery of a new biologic, HDFx, presents cogent reasons for trying this conserved protein for its potential therapeutic actions along with Mg salts, due to their anti-inflammatory actions. HDFx has an added benefit since it accelerates wound healing. Mg has powerful vasodilator actions in the microcirculation allowing tissue perfusion and oxygenation of ischemic-inflamed tissues, as is found in the effects of red tides on the skin and lungs. We believe a cream containing HDFx and Mg would be powerful anti-inflammatory agents in the treatment of red tide poisoning.

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