Phycotoxins in sea spray aerosols: friend or foe?

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Throughout our history, coastal environments have been linked to the promotion of human health. While the first written references date back to ancient Romans, there is evidence that ocean-therapy was already used to treat health conditions in Ancient Egypt. Today, epidemiological studies continue to observe that coastal populations are healthier and have longer life-expectancies than urban populations. The food and air quality (physiological hypothesis), as well as the recreational possibilities oceans and coastal areas offer (blue gym hypothesis), are suggested as main contributing factors. At the same time, these aquatic systems are under pressure by global change, the introduction of invasive species, overfishing and eutrophication. The relative recent increase of harmful algal blooms (HABs), previously referred to as red tides, is believed to be a consequence of these anthropogenic disturbances.

About 100 HAB-species are classified as toxin producing algae, able to cause human intoxications via several exposure pathways. The **consumption of poisoned fish and shellfish** is the main documented pathway for human exposure to these phycotoxins. Much less is, however, known about the exposure via the **inhalation of sea spray aerosols** (SSAs). Phycotoxins that are actively excreted or released after cell rupture may aerosolize by bursting air bubbles at the sea surface. So far, exposure to brevetoxins and ovatoxins via SSAs has caused severe respiratory irritation in vulnerable groups living around the Gulf of Mexico and the Mediterranean. These events show that the inhalation of phycotoxins, via SSAs, is an important and underappreciated exposure pathway. However, such an exposure does not have to be strictly negative, i.e. causing adverse health effects. It was recently hypothesized that the improved health in coastal areas could be related to the regular exposure to low levels of airborne biogenic compounds (**biogenics hypothesis**). Products from bacteria, algae, fungi and plants are thought to inhibit specific kinase pathways (PI3K/Akt/mTORC1) whose activity has been linked to pathological conditions such as tissue inflammation, cancer, diabetes, immunosuppression, and neurodegenerative diseases.

To test this biogenics hypothesis we conducted a series of proof of principle experiments. We examined the effects of this respiratory exposure by exposing human lung cell lines for two days to several major phycotoxins (brevetoxin, okadaic acid, domoic acid & yessotoxin). Using MTT assays on alveolar (A549) and bronchial (BEAS-2B) epithelial cells, the cell metabolic activity was measured as a proxy of cell viability. In these experiments, compared to the other tested phycotoxins, yessotoxin (YTX) exhibited the highest toxicity. This is somewhat surprising since YTX is generally accepted to be one of the least potent marine toxins. Extrapolating these effect concentrations of YTX to environmental concentrations in the air, based on the surface area of the exposed cell tissue, the levels causing an effect were of the same magnitude as the measured brevetoxin concentrations during a bloom of *Karenia brevis*. This illustrates the possible human health importance and environmental relevance of the tested concentrations range. Analysing the effect of YTX on the activity of the PI3K/Akt/mTORC1 pathway, using SDS-page and western blotting, a possible hormesis effect (i.e. a positive effect at (very) low exposure concentrations) was found at concentrations approximately ten thousand lower than the discussed viability effect concentrations. Algae producing YTX, however, do not have the same blooming capabilities as *K. brevis*. It can thus be suggested that in ambient coastal air (cf. sea spray) only YTX concentrations producing a hormesis effect – i.e. a health promoting effect - can be reached in natural circumstances. If confirmed by subsequent testing, these experimental results are the first supporting the biogenics hypothesis.

Keywords: harmful algal blooms; biogenics hypothesis; phycotoxins; sea spray aerosols