Beyond the stench, bromine bodes well

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Bromine (symbol, Br) is a chemical element with atomic number 35. It was discovered in the ashes of fucus (a seaweed) in 1826 by the French chemist, Antoine Balard, and was initially named brôme (Balard 1826). Due to its unpleasant odor, the name bromine derived from the Greek word *bromos* meaning "stench" was coined. Bromine belongs to the halogen group, with properties that are in-between those of chlorine and iodine. At room temperature, bromine (chemical formula, Br_2) is a red-brown liquid that readily evaporates and is soluble in water. It is extremely reactive and so it is not found in free form in nature. It occurs in white crystalline bromide salts that are akin to table salt, sodium chloride.

As a medication, the bromide ion has inhibitory effects on the central nervous system. Thus, bromide salts, such as potassium bromide and sodium bromide, were mainly utilized as anticonvulsants and sedatives, until they were replaced by safer and faster-acting medicines. Excessive or long-term intake of bromide salts causes toxicity due to the action of soluble bromide ion resulting in bromism, a condition characterized by neurologic and psychiatric symptoms (e.g., psychosis), gastrointestinal symptoms (e.g., vomiting and anorexia), dermatologic symptoms (e.g., skin rashes) and other severe symptoms (Demsey 2012).

Bromine is quite rare in the Earth's crust, but bromide ion has accumulated in seawaters due to the great solubility of bromide salts. Bromine is an essential element found in rare amino acid residues of peptides isolated from marine animals, such as cone snails, ascidians, hagfish, annelids, sea urchins and sponges. These peptides are the subjects of a recently published review article (Jimenez 2019). The properties of these unusual peptides are summarized below.

A noncoded bromine-containing amino acid, bromotryptophan, is seldom found in peptides synthesized in the cell's ribosome (referred to as ribosomal peptides). Bromotryptophan is produced by post-translational modification; that is, the bromination process takes place after the peptide synthesis. Likewise, bromotryptophan and its analogs are rarely present in peptides that are not formed in the ribosome (referred to as non-ribosomal peptides). Among the peptides that have been characterized, the ribosomal peptides typically have 6-bromotryptophan, while the non-ribosomal peptides have different brominated tryptophan analogs and atypical peptide structures.

The peptides with brominated tryptophan analogs exhibit important bioactivities that the marine animals can employ for their chemical defenses and survival. Peptide molecules are normally prone to enzymatic degradation, but the presence of brominated tryptophan analogs may offer structural stability for the peptide due to the steric hindrance provided by the bromine atom.

Various peptides with brominated tryptophan analogs show pharmacological activities that can be further examined for their therapeutic uses. Some of the peptides elicit excitatory activities while others bind to certain receptors in the nervous system. The

other peptides reveal antibacterial, antifungal, insecticidal, antitumor, cytotoxic and hemolytic activities. The peptides that bind to specific receptors may be developed as medicines for nervous system disorders. Those with antimicrobial and insecticidal activities may be tapped as antibiotics and insecticides, respectively. The others with antitumor activity may be utilized as cancer medications.

To date, there has not been any brominated tryptophan-containing peptide derived from marine animal, that is approved as a medicine. The peptides with brominated tryptophan analogs have unique properties that make them stimulating subjects for future studies, including the biosynthesis and pharmacology.

REFERENCES

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The reference article published in *Protein & Peptide Letters*, an SCIE-indexed journal, was named the Editor's Choice. As such, it was featured in 2019 as a Public Release in EurekAlert! The Global Source for Science News of the American Association for the Advancement of Science (AAAS).

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