Study of Naturally Produced Organ Halogen Compounds in Algae

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Abstract

Organ halogen compounds identified and characterized in 2014 are summarized below. Algae, sponges, coral reefs, tunicates and bryozoans as well as fungus, bacteria and plants are all included in the list of chemicals. Chloromethane, hexachlorobenzene (PCBs), and organ halogens of mixed origin are all prevalent in the marine environment, which has a complicated pattern of organ halogens. These natural organ halogens are described in detail. The halogens Cl, Br, and I are the primary halogens of interest. Despite the fact that marine natural organ halogens are abundant as specified components, they are seldom synthesized in large quantities. Chloromethane is the most important in terms of worldwide output each year (methyl chloride). Global atmospheric mixing needs 3.5–5 million tones of yearly output. All the many types of peroxides in this family are described. Incubation tests show that haloperoxidases produce a broad range of unknown chemicals in side reactions that have not yet been explained.

Keywords: *Organ halogen; Haloperoxidase; Halo form reaction; Methyl chloride; Chloroform; Marine atmosphere; Bioproduction.*

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1. INTRODUCTION

Natural organ halogens discovered since 1968 have increased in number due to a number of factors, including a worldwide revival of natural products research, improved isolation and separation techniques and selective bioassays to identify biologically active extracts, and an increased awareness of folk medicine and ethno botany for guidance to potentially important compounds.

Six novel organ halogens and numerous previously known sesquiterpenes have been discovered in the red seaweed Laurencia okamurai collected off the shore of Nanji Island in the East China Sea. Seco-laurokamurone (1) has a novel carbon skeleton that may be formed by oxidative cleavage of the laurokamurane skeleton previously discovered. 1 was detected in fresh algal crude extracts and under circumstances where 6 was stable, indicating that it is not an isolation artifact. In Scheme 1, sesquiterpenes 2 and 3 have substantial antifungal action against Candida glabrata, whereas 3 or 4 have modest activity against Cryptococcus. Only three of the A - 549 cell lines are affected by the cytotoxicity of 3.

New brominated diterpenes glandulaurencianol A, B, and a unique non-brominated counterpart were discovered in a collection of Laurencia glandulifera from the Loutraki Bay in Crete, South Greece. The sea hare Aplysia punctata from the coast of Nea Makri in Central Greece also had the later compound (not shown) and Scheme 2, 7. Laurencianol has previously been linked to geranyl-linaloola as a source of laurencianol's biogenesis.

OHCs have become a symbol of environmental contamination in various ways. From polar bears in the Arctic to a few kilometers into space, man-made substances have been identified at locations far from their original source (Grimvall and Leer, 1995).

In the early part of the twentieth century, large-scale manufacture of OHCs began. Pesticides and insecticides were developed to protect crops from being damaged and illnesses from being transmitted. Among OHCs is DDT, which was used to combat the spread of malaria and typhus and whose inventor received t he Nobel Prize for his discovery. There were many who doubted the efficacy of DDT, though. Several articles and books, such as Rachel Carson's well-known "Silent Spring," helped increase public awareness of the dangers of DDT (Carson, 1963). White-tailed eagle populations in Sweden were under risk during the 1970s due to

environmental contamination with DDT and PCB (Brainstorm and Larsson, 2008). However, like with many other seabird species in the Baltic Sea region, the population has begun to rebound (Brainstorm and Larsson, 2008). It is now illegal or prohibited to use DDT, PCBs and many other OHCs because of their long -term toxicity.

2. LITERATURE REVIEW

Graeme F Wilkinson (2015) Recent years have seen a lot of discussion in the scientific literature about the repositioning or repurposing of drugs, which has led to the creation of both new intellectual property and submissions for investigational new drugs. The literature shows a clear trend toward the generation of early repositioning hypotheses using computational or informatics-based methods, followed by intensive evaluation of biological activity in phenotypic experiments. In vitro testing of well-known pharmaceuticals or drugs-like compounds, initially in disease-relevant phenotypic tests, to find and validate candidates for repositioning is another feasible approach. This strategy may make use of sizable compound libraries or may concentrate on subsets of well-known medications or compounds that are similar to drugs. In this succinct overview, we concentrate on methods to create and validate repositioning candidates in disease-related in vitro and phenotypic assays and present specific instances of this technique as applied to several disease domains. As a starting point for medication repositioning, we contend that in vitro screenings have significant advantages over biochemical or in vivo techniques.

Decha Kumla, (2018) Four previously unreported chromone derivatives, including pyanochromone (3b), spirofuranochromone (4), and 7-hydroxy-6-methoxy-4-oxo-3-[(1E)-3-oxobut-1-en-1-yl], as well as a previously unreported chromene derivative, 1-hydroxy-12-methoxycitromycin (1c), were also discovered. From cultures of the marine sponge-associated fungus Penicillium erubescens KUFA, -4H-chromene-5-carboxylic acid (5), a pyranochromone dimer (6), citromycin (1a), 12-methoxycitromycin (1b), myxotrichin D (1d), 12-methoxycitromycetin (1e), anhydrofulvic acid (2a), myxotrichin C (2b Tests were conducted on compounds 1a - e, 2a, 3a, 4, and 7-9 to determine how well they inhibited the growth of Gram-positive and Gram-negative reference strains as well as multidrug-resistant pathogens obtained from the environment. Nine indicated growth inhibition of methicillin-resistant Staphylococcus aureus, but only 8 showed an inhibition of the growth of all Gram-positive bacteria in vitro (MRSA). None of the investigated chemicals had any effect on Gram-negative bacteria.

PHILIPP ARENDT (2016) Terpenoids are the biggest class of naturally produced chemicals, with tens of thousands of described members. The primary purpose of certain terpenoids is to maintain cell membrane fluidity as pigments or phytohormones, but the majority serves as specialized metabolic processes involved in plant resistance to herbivores or plant–environment interactions. Human diet would be incomplete without terpenoids. Many of these compounds also have significant commercial value as medicines, aromatics, and next - generation biofuels. Biosynthesis of terpenoid compounds has become a key target for metabolic engineering and synthetic biology initiatives due to their limited abundance in their natural source, and because of the need for new or better bioactivities. These photosynthetic organisms' ability to synthesize plant-derived terpenoids that are either novel to nature or specifically tailored to their needs is the subject of this study. As we consider several photosynthetic hosts and recent breakthroughs in synthetic biology, we examine the possibility for (heterogonous) generation of (new) terpenoids from these sources.

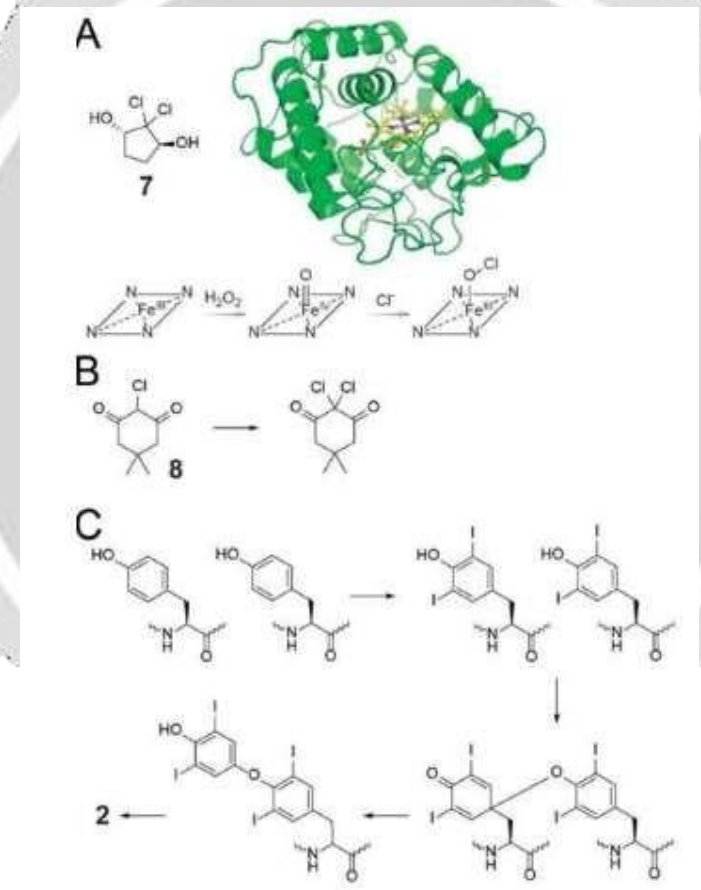
GRIBBLE, GORDON (2015) For the sake of brevity, we' the common belief that halogens - chlorine, bromine, iodine, and fluorine - are not found in nature is now shown to be incorrect. Halogen-containing compounds from a variety of marine and terrestrial plant and animal sources have been discovered using modern isolation and identification procedures. The anticancer, antiviral, and antibacterial properties of several of these substances have the potential to benefit humans. Organ halogen compounds identified and characterized in 2014 are presented in this brief overview. Algae, sponges, coral reefs, tunicates and bryozoans as well as fungus, bacteria and plants are all included in the list of chemicals. A number of new structural types have been discovered and described. It has grown from only 24 organ halogens in 1968 to more than 5000, and new ones are being identified in every location. In 2014, 114 new organ halogens from natural sources were found.

3. NATURAL PRODUCT HALOGENATION

First natural product halogenating biocatalyst was a hydrogen peroxide (H2O2) and heme-dependent chloroperoxide (CPO) released by the fungus Caldariomyces fumago, which was linked to the manufacture of

the halogenated cyclopentanediol fungal halometabolite caldariomycin, approximately fifty years ago. Electrophilic halogenating reagents with wide substrate specificity, as CPO, have subsequently been extensively investigated and even sold. The enzyme's structure has been figured out. The mechanism of action is similar to that of heme-dependent hydroxylases and oxygenases, as discussed ext ensively elsewhere. Hydrogen peroxide activates a cysteine thiolate-ligated heme Fe(III)-porphyrin to produce oxo-Fe(IV) species. Nucleophilic addition of a halide generates the catalytic Fe(III)-hypohalite species in a divergence from P450 hydroxylases. A halogenation strategy similar to that used by flavin-dependent halogenases may be used by CPOs to deliver the halenium ion to an electron-rich substrate, either by binding the substrate directly to the Fe(III)-hypohalite or by transferring the halenium ion to an active site residue side chain (vide infra).

The enzyme may also release hypohalite to non-selectively halogenate electron-rich substrate sites, which has been advocated in the literature. Vanadium-dependent haloperoxidases (V-HPOs) may also benefit from this proposed method, as explained in Section 3. Despite catalysing several processes outside halogenation, the CPO seems to have very permissive control over its catalytic cycle. Examples of these additional reactions include: oxidation, sulfuration, epioxidation, and hydrolysis. It's still unclear whether or not CPO's side activity of halogenation is related to its physiological job of producing 7 or whether this catalytically promiscuous enzyme performs both functions. The halide and substrate binding sites for heme-dependent haloperoxidases have not been discovered, according to a review by Drennan and associates.



Heme-dependent haloperoxidases in biological halogenations reactions

4. BIOGENIC FLUORINATED COMPOUNDS

Although the uncommon organ fluorine compounds are more extensively distributed in nature than first anticipated, the biogenic synthesis of fluoro-organic compounds is mostly of theoretical interest. For the time being, F-metabolites have been found in bacteria, fungus, and higher plants, but not yet in algae (Neidleman and

Geigert, 1986; O Hagan and Harper, 1999; O Hagan et al., 1999). Monofluoroacetate may be found in trace amounts in a wide range of higher plants. Monofluoroacetate concentrations in Ceylon tea may range from 50–160 ng/g, whereas China Green Tea may have a concentration of 230 ng/g. Vulcanoes have been shown to contain a geogenic formation of CF4.

The fluoride ion is initially accepted by an S-adenosylmethionine (SAM) in a biological fluorination mechanism recently proposed by O Hagan and his colleagues.

5. VOLATILE ORGAN HALOGENS IN THE MARINE ENVIRONMENT

There are two distinct types of natural organ halogen compounds: those found in marine environments and those found in terrestrial environments. It is possible to find the volatile organo-halogens such as CH3Cl and CH3Br in the marine environment across the globe, as well as halogenated methyl-phenyl ethers (anisoles, XzC6H5z–(OCH3), (X 14 Br, Cl) in the marine environment, as well as CH2Cl2, CH2Br2, CH2I2, CH2ClBr and CH2ClI. (Table 1) Some of the most recent studies are (Lovelock, 1975; Moore, 1977, 1979; Khalil et al; 1983; Kirschmer et al; 1983; Kirschmer et al; 1983; Moore and Tokarczyk, 1985; Moore et al., 1985; Kirschmer et al., 1985; Moore and Tokarczyk, 1985; Kirschmer et al., 1985) It is important to evaluate both biological and anthropogenic origins for the existence of certain of these chemicals. It is characterised by industrial production and point and non-point source applications that determine the emission pattern of anthropogenic organ halogens In the environment, the sources of biogenic organo-halogens are extensively distributed, geographically and temporally variable. Tropical places with high primary production rates, such as coral reefs, or cold water near shore or offshore may serve as generalizing descriptors in the marine environment (Class et al., 1986; Class and Ballschmiter, 1987a,b, 1988).

Many authors have shown that macro and microalgae, particularly brown algae (Phaeophytae), release dihalo- and trihalomethanes and further brominated and iodinated compounds. Fungi living in soils are the primary source of organohalogens in the terrestrial environment.

Global wind systems, the general circulation, and the intensity of all anthropogenic and natural sources and sinks influence troposphere organ halogen concentrations (Ballschmiter, 1992). In the troposphere, for example, OH radical degradation is the primary worldwide sink for CHCl3. To put it another way: The CHCl3 atmospheric lifespan is between 40 and 400 days, depending on the location. Knowledge of the long -term environmental destiny of natural volatile organ halogens may help us better understand the effect o f anthropogenic chemicals. Interest in the atmospheric chemistry of bromo-/chloro- and bromomethanes in the near surface atmosphere and stratosphere has been sparked by the naturally occurring compounds. Depletion periods of ozone at polar dawn in the lower Arctic atmosphere are connected to the photochemistry of CHBr3 in an inverse connection (Barrie et al., 1988). Further bromo/iodomethanes in the Arctic atmosphere may be analyzed using the photolytic destruction of CHBr3 as a source of Br atoms.

Table 1 Selection of volatile halogenated compounds found in the environment

C_1 compounds		
H_3CX,	X ¼ Cl, Br, J	(and mixed halogenation)
H_2CX_2;		
HCX_3,		
(CX_4)		
C_2 compounds		
$XCH_2–CH_2X$	(X ¼ Cl, Br, J)	(and mixed halogenations)
$X_2CH–CH_3$	(X ¼ Cl, Br)	(and mixed halogenations)
Haloacetonitriles	$XnCH_{ð3\ nÞ}CN$	

Haloacetoaldehydes	$XnCH_{ð3\ nÞ}CHO$	
Halo acetic acids	$ClCH_2$–COOH	
C_3 compounds		
CH_3–CH_2–CH_2J		
Haloacetons	(Cl, Br, J in Asparagopsis sp., a red algae)	
Aromatic derivatives		
Halophenols	Xn(Phe)OH	
	X ¼ Cl, Br;	(and mixed halogenation)
Halophenylmethyl	$Xn(Phe)OCH_3$	
ether	X ¼ Cl, Br;	(and mixed halogenation)
Bromodiphenyl ether	$Br_3(Phe)O(Phe)Br_3$	

6. CONCLUSION

Although additional compounds may be discovered in the future, the range of naturally volatile organ halogens seems to be well-established in terms of quality. Astonishingly, the exact chemical pathways for the generation of very simple and volatile organ halogens are frequently not understood. Incubation investigations with the haloperoxidase group indicate that a broad range of unknown chemicals are produced in side reactions in pathways that have yet to be fully elucidated. An exciting future task is to discover how simple organ halogens are generated in nature, as well as to uncover the entire chemistry of well-known enzyme systems, such as those found in the haloperoxidase family.

7. REFERENCE

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