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Bioactivity of Marine *Amphidinium Clap Et Zachm* Dinoflagellate

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ABSTRACT

*The marine *Amphidinium Clap et Zachm* dinoflagellate are contained within the rich structure of the novel, diverse bioactive macrocyclic vinegar and long-chain alkenes via quite compounds, their potential medicinal value has aroused widespread concern in this paper about the sulcus research progress chemistry and biological activity of dinoflagellate algae are reviewed, on this basis, the prospect of such medicinal marine microorganisms were discussed. Marine *Amphidinium Clap et Zachm* dinoflagellate genus belonging to the ring groove dinoflagellate algae Gang Branch of the dinoflagellate genus of about 33 kinds, mostly belonging to the temperate and tropical species, the waters of the South China Sea near San Ya, many have discovered. Our country has a very rich former ditch algae resource, and the vast majority of the distribution is very rich in marine biodiversity in tropical and subtropical waters. The marine *Amphidinium Clap et Zachm* dinoflagellate is the active sustainable use of resources in the library, which is worth further researching.*

Key words: *Amphidinium Clap et Zachm*; bioactivity

INTRODUCTION

Dinoflagellates are important phytoplankton taxa, including Dinophyceae and Syndinophyceae two categories. Syndinophyceae only a small number of parasitic species, about 40 kinds, and are usually referred to the students mainly dinoflagellates Dinophyceae flagellum position, number and shape of the shell plate is the main basis Dinophyceae classification, divided accordingly PERIDINIUM mesh, Prorocentrum mesh gonyautoxins head, fins and bare dinoflagellate algae and so on. Them as the main representative of extant dinoflagellates, is also common groups of marine dinoflagellate. Marine *Amphidinium Clap et Zachm* dinoflagellate genus as a special structure of marine microalgae, secondary metabolites special structure is active and diverse, especially its significant anti-fungal, anti-tumor activity, worthy of attention. International experts made a lot of research in this area of work, and achieved fruitful results, while domestic research in this area is still not mature enough [1].

Dinoflagellate has a very special reproductive and metabolic pathway, and it could produce chemical structure very special metabolites. Through the biosynthetic pathway structure is very complex dinoflagellate toxins naked short conducted a preliminary study, the results show that: glassy shoot acid, a light glutaric acid, propionic acid, acetic acid and α -ketoglutarate involved in the short gymnodinium microcystin biosynthesis, dinoflagellate can be able to use exogenous amino acids as a carbon source, and the remaining organic skeleton for anabolic secondary product. This feature is being between animals and plants. Thus, dinoflagellate has special significance in the history of biological evolution [2]. Figure 1 shows the evolution of dinoflagellate.

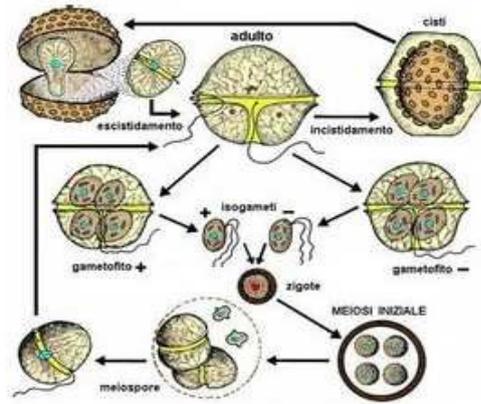


Fig. 1: Complex transportation system

CHEMICAL COMPOSITION ANALYSIS

Procentrum case studies of the chemical composition of algae and pharmacological activity areas are mostly concentrated in the composition of the original dinoflagellate toxins are produced by algae and its top anti-tumor activity. Procentrum genus of algae species can produce more than one person can cause diarrhea DSP, such P1lima, P1concavum, P1hoffmannianum, P1maculosum and P1faustiae so on. The DSP is the algae produce polyether or a class of macrolide compounds according to the structure of the carbon skeleton of these components are generally divided into three groups: natural okadaic acid and its derivatives (1) acid component Dinophysis toxins; polyether lactone (2) neutral component clam toxin; (3) scallops toxins and 4, 5 - hydroxy scallops toxins. Dinoflagellate is an important part of phytoplankton, diatoms and other phytoplankton together and started the food chain of marine ecosystems is an important primary producers in the ocean, play an important role in nutrient cycling and energy flow in marine ecosystems. Currently, there are more than 2000 kinds of dinoflagellates in half of the world is the type of camp life heterotrophic nutrition, natural sea heterotrophic dinoflagellate abundance and sometimes more than ciliates such as zooplankton, phytoplankton their feeding behavior would cluster structure produces a negligible impact, a phenomenon in many harmful red tide dinoflagellate found in both. Heterotrophic dinoflagellate dinoflagellate behavior makes the dual role of producer and consumer who is not only able to carry out photosynthesis, but also by other organisms feeding to meet their nutritional needs, so that a better convergence of dinoflagellates micro ring and food nutrient cycling and energy flow between metazoan, in the food web plays an important [3].

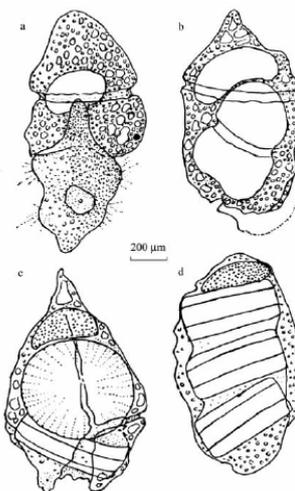


Fig. 2: Phagocytosis nutrition of naked dinoflagellate

Okadaic acid and fins algal toxin-1 is a protein phosphatase (PP1 and PP2A) and potent inhibitor, and therefore cause diarrhea degeneration diarrhea, intestinal epithelial cells and to promote the development of cancer. Many studies have confirmed the influence of diarrhetic shellfish poisoning and cell protein phosphatase regulation. Okadaic acid, fins and fin microcystin-LR -3 -1 or tumor-promoting factor, and both genetic toxicity can lead to the formation of DNA adducts. Okadaic acid but also by changing the concentration of intracellular second messenger role of calcium ions strongly increase the probability of myocardial cells in the L-type calcium influx and tracheal

smooth muscle cells calcium-dependent potassium channels in the open state [4]. Figure 2 shows the phagocytosis nutrition of naked dinoflagellate.

Although the original toxic dinoflagellate metabolites, but was developed as anticancer drugs or provide ideas for the design of new drugs. Studies have shown that okadaic acid is both one of the leading DSP toxins, but also has significant anti-tumor activity against P-388 and L-1210 cells with an IC₅₀ of $117 * 10^{-3} \text{Lg.mL}^{-1}$ and $117 * 10^{-2} \text{Lg.mL}^{-1}$, mice were injected intraperitoneally LC₅₀ is 0.192mg.kg^{-1} ; ionophore okadaic acid structural features are related to its tumor suppressor complex mechanism. Dinoflagellates can use organic matter to make growth and reproduction. There are several types heterotrophic. Nearly half of the dinoflagellate species have no pigment body, there are many dinoflagellates body will exist even with pigmented heterotrophic nutritional needs, and raise nutritional type is called. These support groups and do not necessarily get as mainly organic carbon sources, but merely necessary to add some organic growth such as vitamins, biotin. These groups to infiltrate and raised nutrition (DOM absorbed by osmosis the way) and rotten food nutrition (outside the cell through the mesh-like structure be digested, then absorbed into the cells) by way of nutrition and support, but can also parasitic and symbiotic manner way and nutritional support life. As a source of organic carbon, many non-pigmented dinoflagellates body mainly rely on heterotrophic way to survive, such as organic nutrition dinoflagellates, which are the subject of heterotrophic dinoflagellates nutrition, the main types of parasitic infiltration nutrition and swallowed nutrition [5].

BIOACTIVITY ANALYSIS

Algae are a large class of polyphenol compounds of different structures, mainly prorocentrum case studies of algae polyphenols anti-tumor activity, anti-bacterial, anti-viral activity, antioxidant activity, chemical defense activity, deodorant activity. Figure 3 shows the bioactivity analysis.

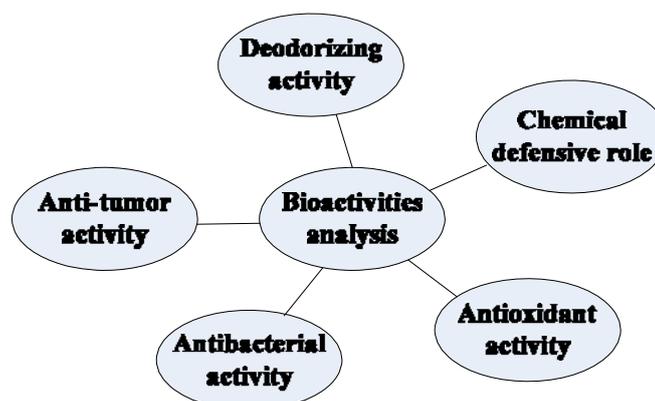


Fig. 3: Bioactivity analysis of Dinoflagellate

Dinoflagellates extract at a final concentration reaches a certain level, all the leukemia cell lines have strong cytotoxicity on human fibroblasts and HDF and mouse NIH-3T3 cells without toxicity possessed thermal stability, appropriate toxic side effects on natural resources as an anticancer agent. Dinoflagellates polyphenol compounds on the inhibition of tumor cell lines but also with the relative molecular mass of algae polyphenols on high relative molecular mass of dinoflagellate stronger anti-tumor effect of low molecular weight dinoflagellate. Secreted from dinoflagellates polyphenols has a broad spectrum of microorganisms resistant (including suppression of filamentous fungi, yeasts, bacteria, viruses, etc.), and does not affect the growth of animal cells in the corresponding inhibitory concentration. Dinoflagellate isolated from sulfur, nitrogen phenolic compound is a highly active antimicrobial agents having broad spectrum antimicrobial activity, antibacterial effect than some known antibiotics such as chlortetracycline, erythromycin, chloramphenicol [6].

Polyphenols as a strong antioxidant, free radical scavengers can make endogenous antioxidant enzyme activity increased by dietary supplementation or exogenous antioxidants play a role in the prevention of cancer and other diseases. But it's more complex antioxidant mechanisms generally believed: scavenge free radicals, the dissociation of the phenolic hydroxyl group, have catalytic metal ion complexation, UV absorption factors play a major role. In vitro experiments showed that plant polyphenols scavenge peroxide, hydroxyl radicals and inhibiting lipid peroxidation.

The dinoflagellate algae polyphenols are synthesized to withstand herbivore defense of a large class of chemical substances, substances in plants is the most common defense of secondary metabolites and only at the molecular level, there is food and poison resistance two effects. Its convergence astringent properties that can reduce herbivore

feeding; itself can also be combined with dietary protein to reduce its absorbability, and the herbivore gastrointestinal digestive enzymes combined with reducing its ability to digest. Plant extract from the current application of the results, the main structure of the deodorant active is a hydroxyl group of polyphenols, especially flavonoids, C6-C3-C6; tannins or the monomer structure, C6-C1, and with three or more hydroxyl groups, or C6-C3 phenylpropyl compounds. Dinoflagellates active substances are higher than their natural deodorant activity such as sodium copper chlorophyll and chlorophyll [7].

MACROLIDES

Marine Amphidinium Clap et Zachm dinoflagellate genus is Pyrrophyta organisms macrolide compounds in a class of rich dinoflagellate, which has been 37 of these compounds were isolated and identified. 26, 27-membered macrolide is a type from the most isolated dinoflagellate genus, a total of 15 as much. Although the same for 26 or 27-membered macrolide, but they are not the same type of skeletons. Amphidinolide B (2) the relative configuration was determined by X diffraction method. Determination of the absolute configuration by means of chemical reaction, the two first and then oxidized with NaIO_4 and then NaBH_4 reduction of acetylation. The reaction mixture obtained after C-22 to C-26 fragment (2a) of the separation and purification by HPLC, and then the (2S, 4S) - and (2R, 4R) - Pentanethiol synthetic C-22 to C-26 fragment (2a, 2b) compare and ultimately determine the absolute configuration of 8S, 9S, 11R, 16R, 18S, 21R, 22S, 23R and 25S. The team later assigned to compound 2 21 epimers Amphidinolide D (5). Shimizu team from the American University of Rhode Island also collected from a dinoflagellate American Brewer waters isolated the Amphidinolide B analogues B2 (3), B3 (4). Figure 4 shows the molecular structure of macrolide.

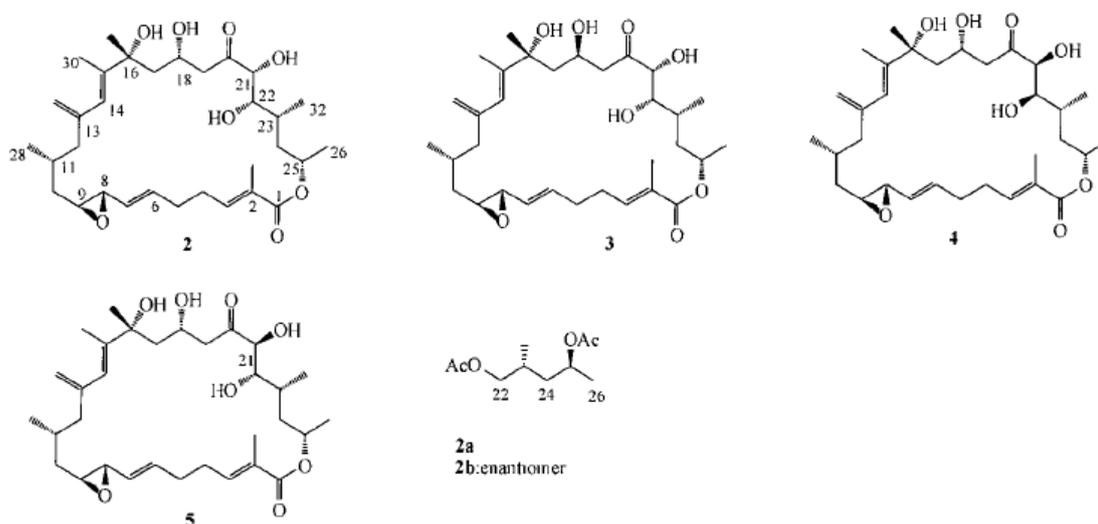


Fig. 4: Molecular structure of macrolide

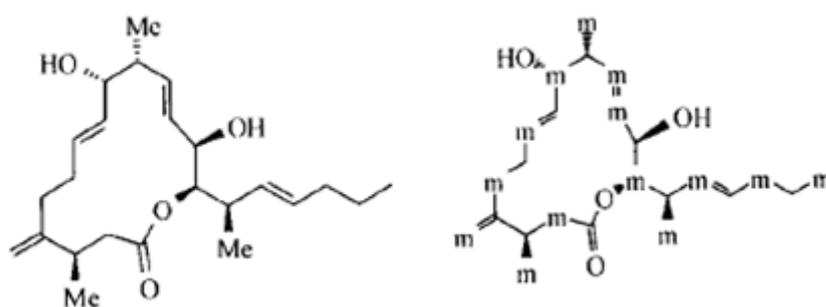


Fig. 5: Synthetic methods of macrolide

Macrolide natural product compounds are generally more than one way through the classical transformation comes, most of the even-membered ring. But in the past many macrolide compound ditch dinoflagellate algae isolated case but it is an odd-membered ring, such as: Amphidinolide J. Genus front groove macrolide compound isolated dinoflagellate has a strong biological activity, and the main anti-tumor activity has been reported in the current. Figure 5 shows the synthetic methods of macrolide. The labeling precursor feeding experiments show Amphihinolide J 24 carbon atoms in the molecule are derived from sodium acetate, its 15-membered carbocyclic ring formed may have originated in several molecular fragments a, b, c, d, e, f plus percent. Wherein b and d are derived from more than one classical pathway, and a and c are similar to the synthetic route via the BTX and DTX come, a precursor of 2 - carbonyl glutaric acid, and the precursor of succinate c acid [8]. Figure 5 shows the

Synthetic methods of macrolide.

LONG CHAIN POLYHYDROXY POLYENE COMPOUND

Long chain polyhydroxy polyene polyketide compounds belong, although they have the same or similar biosynthesis pathway, but the structure is often vastly different, the former ditch dinoflagellate algae are rich in these compounds are natural sources. Amphidinol type first representative component of long-chain polyhydroxy polyene compound Amphidinol 1 been reported in 1991, a number of analogs have been discovered, including Amphidinols 2 ~ 6 (39 ~ 43) and Luteophanols AC (44 to 46) and the like. Such chemical composition can be seen as a pre-ditch dinoflagellate algae are characteristic metabolic components in the field of marine microalgae chemistry, so far only the first ditch dinoflagellate algae are found [9]. Figure 6 shows the molecular structure of long chain polyhydroxy polyene compound.

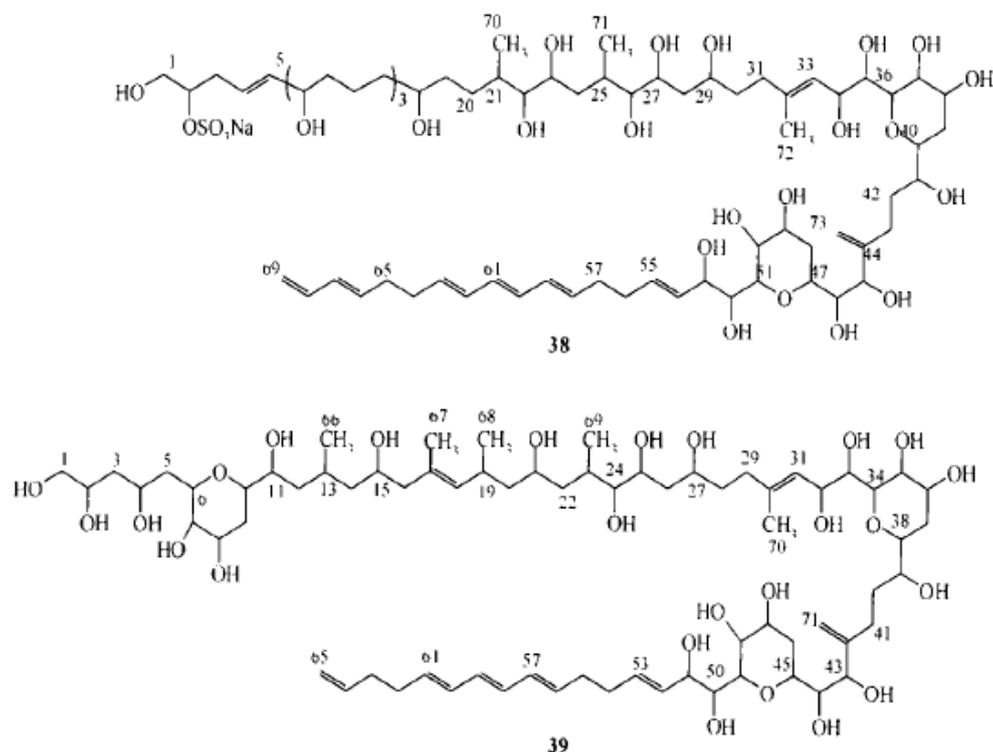


Fig. 6: Molecular structure of long chain polyhydroxy polyene compound

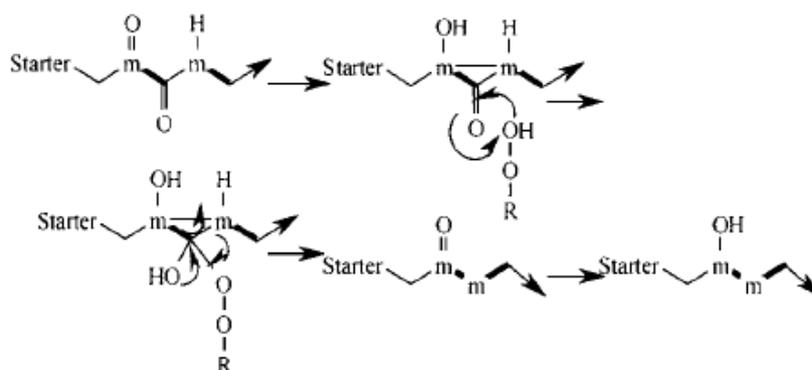


Fig. 7: Synthetic methods of long chain polyhydroxy polyene compound

The study of these compounds biosynthetic pathway is still in its infancy. Murata team member through the first feeding experiments confirmed that the isotope-labeled, Amphidinol 2 and all the four carbon atoms on the backbone molecules are derived from sodium acetate, the branched-chain methyl and methylene groups are also methyl sodium acetate as a carbon source. Their biosynthetic pathway similar to the classic multi-ketone way, but there are obvious differences, mainly in order to complete acetate C2 carbon chain extension unit, from time to time be interrupted by cleavage of the methyl acetate unit of carbon, Amphidinol 2 and 4 contain 4 mm pieces, such fragments may be formed Favorski rearrangement results. Dinoflagellate algae belong to the front groove of the isolated long chain polyene compound having a hydroxy strong biological activity, there has been reported mainly

hemolysis and anti-tumor, anti-bacterial and antifungal activity [10]. Figure 7 shows the synthetic methods of long chain polyhydroxy polyene compound.

CONCLUSION

Compared with other organisms, dinoflagellates algae are structural differences between the former ditch compounds isolated large, and each has a unique skeleton compounds, perhaps before the ditch dinoflagellate algae is the charm. Among the many new biologically active compounds, in particular its anti-tumor activity of chemists and pharmacologists should be highly valuable, and structure-activity relationship studies are based on this research and its pharmacological mechanism of action are very meaningful. As the marine natural product it shows great potential in anti-cancer, anti-viral, anti-inflammatory and anti-fungal and other parties, with the deepening and development of the study, more than the former ditch dinoflagellate algae metabolites will play a major in medicine and related fields effect. Our vast sea algae is rich in resources before the ditch, with the establishment of the development of new chemical separation technology and new models of biological activity screening, the former ditch microalgae algae are fully exploited the resources to develop new drugs bound for writing chapter. Chemical and pharmacological studies in recent years show that the structure type dinoflagellates contain abundant secondary metabolites, and multiple unique biological activity, in particular the mushroom compounds is of concern. As the marine natural product it shows great potential in anti-cancer, anti-viral, anti-inflammatory and anti-fungal and other parties, with the deepening and development studies, more seaweed metabolites will play a major role in medicine and related fields.

REFERENCES

- [1] Kobayashi J, Shimbo K, Sato M, et al. *J Org Chem*, 67:6585-6592, **2002**.
- [2] Tsuda M, Endo T, Kobayashi J. *J Org Chem*, 65:1349-1352, **2000**.
- [3] Kobayashi J, Shimbo K, Sato M, et al. *Org Lett*, 2000, 2 : 28051, **2002**.
- [4] Shimbo K, Tsuda M, Izui N, et al. *J Org Chem*, 67:1020-1023, **2002**.
- [5] Tsuda M, Izui N, Shimbo K, et al. *J Org Chem*, 68:5339-5345, **2003**.
- [6] Tsuda M, Izui N, Shimbo K, et al. *J Org Chem*, 68:91091., **2003**.
- [7] Huang XC, Zhao D, Guo YW, et al. *Tetrahedron Lett*, 45:5501-55041, **2004**.
- [8] Kobayashi J, Shimbo K, Kubota T, et al. *Pure Apple Chemistry*, 75(2-3):337-342, **2003**.
- [9] Kobayashi J, Shimbo K, Sato M, et al. *J Orq Chemistry*, 67(19):6585-6592, **2002**.
- [10] Tsuda M, Izui N, Shimbo K, et al. *J Orx Chem*, 68(23):9109-9112, **2003**.