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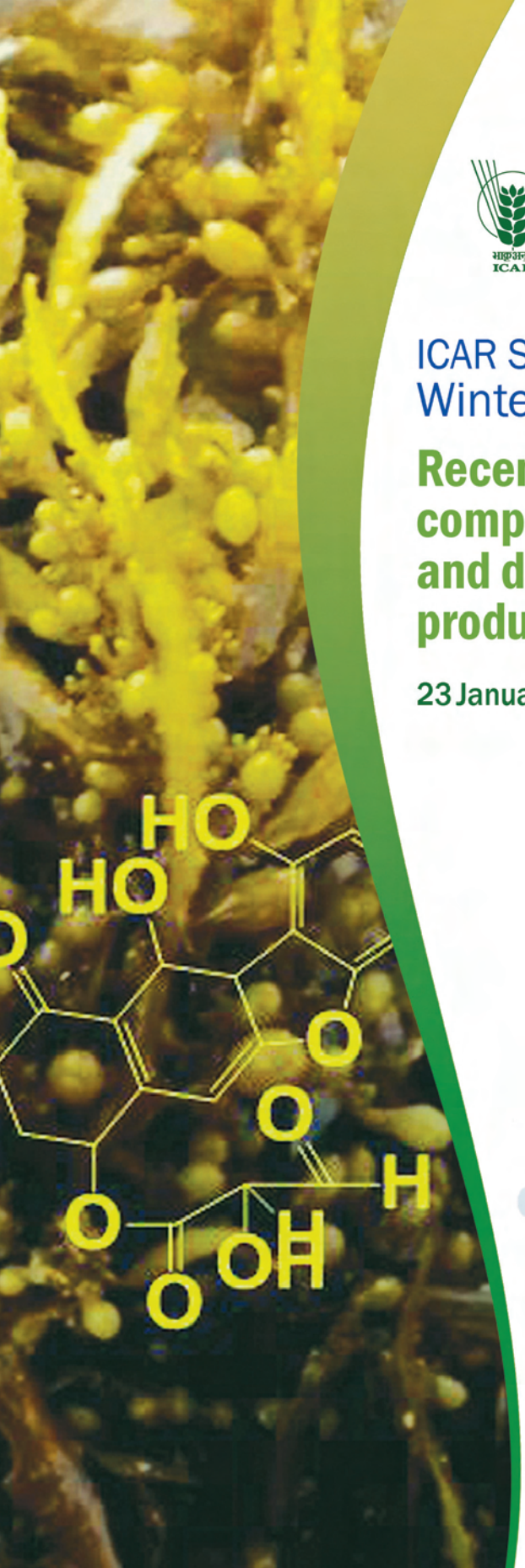
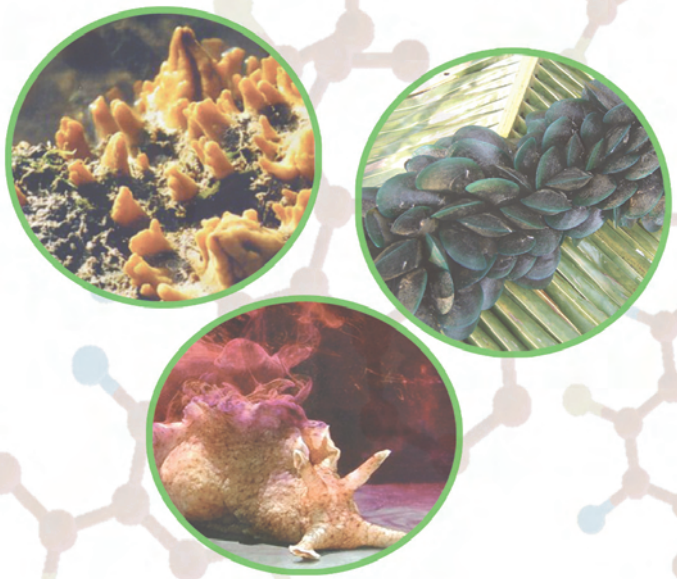


ICAR Sponsored Winter School on

Recent advances in bioactive compounds from marine organisms and development of high value products for health management

23 January to 12 February 2018



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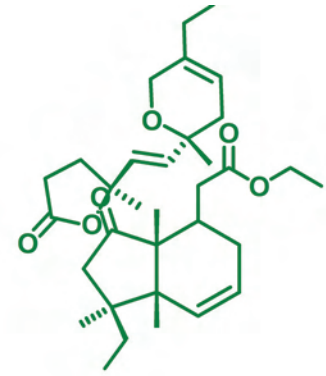
ICAR-Central Marine Fisheries Research Institute
Post Box No. 1603, Ernakulam North P.O., Kochi-682 018, Kerala, India



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Course Manual

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Recent advances in bioactive compounds from marine organisms and development of high-value products for health management

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ICAR-Central Marine Fisheries Research Institute,
23 January - 12 February, 2018

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Edited by Foxit Reader

FOREWORD

There has been a growing interest in the marine derived bioactive compounds in the recent years, and the functional foods, enriched with natural ingredients have been proved to provide beneficial action for human health. Marine derived bioactive components and the functional food ingredients demonstrated to possess potential health benefits. High value secondary bioactive metabolites from the marine organisms are attracting attention because of the growing demand for new compounds of 'marine natural' origin, having potential applications in pharmaceutical fields, and concerns about the adverse effects by synthetic drugs and their derivatives. The pioneering R & D works at ICAR-Central Marine Fisheries Research Institute on marine bioprospecting envisaged a systematic approach involving chemical profiling of major species of marine organisms for bioactive pharmacophore leads for activity against various diseases, and a library of molecules with bioactive potential. The research work in this institute developed protocols to prepare various pharmaceutical leads, nutraceuticals/ functional food supplements enriched with lead molecules with different properties against various drug targets for use against various life-threatening diseases.

ICAR-Central Marine Fisheries Research Institute is the pioneering marine research institute in India to work in the frontier area of bioactive molecule discovery from marine organisms as promising therapeutic agents against various diseases, aquatic food product technology, and development of high value products for health management. This prestigious research institute of Indian Council of Agricultural Research is working in the broad national interest of producing high value bioactive leads from the marine organisms, which would provide promising therapeutic agents against various diseases. This institute has developed and commercialized the nutraceutical products Cadalmin™ Green Algal extract (Cadalmin™ GAe) and Antidiabetic extract (Cadalmin™ ADe) as green alternatives to synthetic drugs to combat rheumatic arthritic pains and type-2 diabetes, respectively to a leading biopharmaceutical company in India. The anti-inflammatory nutraceutical Cadalmin™ Green Mussel extract (Cadalmin™ GMe) from Asian green mussel Perna viridis has been commercialized with Amalgam Group of Companies. Cadalmin™ Antihypercholesterolemic extract (Cadalmin™ ACe) has been developed from seaweeds to combat dyslipidemia leading to obesity, and the product was out-licensed to a leading Indian MNC in wellness and obesity management. Antimicrobial therapeutic product from marine bacteria as oral applicant has been developed and the product is in pipeline for commercialization. Seaweed-derived natural template inspired synthetic derivatives as potential pharmacophores were designed and developed. Several nutraceutical and cosmeceutical products from marine organisms are in pipeline, and are being commercialized.

The objective of the National level ICAR Winter School on "Recent advances in bioactive compounds from marine organisms and development of high-value products for health management" is to provide up-to-date information and acquaint the participants with the latest technologies on isolation and characterization of marine natural products of pharmaceutical importance from marine organisms, general and advanced methods of isolation procedures by chromatography, classification of organic compounds and their characterization by advanced spectroscopic experiments. This program further aims to give exposure to the chemical perspectives of marine organisms, primary and secondary bioactive metabolites from fish and marine organisms to develop bioactive compounds and high-value functional food products. Theory and practical classes will be conducted in these areas to provide the participants a hands-on experience.

This ICAR Winter School is organized with the full funding support from ICAR, New Delhi, and the twenty-five participants from various parts of India who are attending this programme were selected after scrutiny of their applications based on their bio-data. They are serving as academicians, such as Professors/Scientists, and in similar posts. The faculties include the knowledgeable scientists and professors from various parts of India and abroad. This training will enable the participants to efficiently carry out their academic programmes, and to plan research on bioactive molecule discovery in their respective laboratories and institutes so that they can formulate the strategies for research.

The Winter School on "Recent advances in bioactive compounds from marine organisms and development of high value products for health management" is very ideal for the current scenario of increasing lifestyle diseases and human health. Understanding the importance of natural products in the health care system of India, ICAR-Central Marine Fisheries Research Institute has reasonably contributed in the various aspects. The Manual released on this occasion covers all aspects of marine natural products prepared by the experts in their respective fields. I congratulate the Course Director of this programme, Dr. Kajal Chakraborty and Head of the Marine Biotechnology Division, Dr. P. Vijayagopal, along with other staff members of Marine Biotechnology Division and Central Marine Fisheries Research Institute for their sincere efforts in bringing out the manual in time, and to arrange the programme in a befitting manner.

A. Gopalakrishnan
Director, ICAR-Central Marine Fisheries Research Institute
Kochi, Kerala

PREFACE

Marine-derived bioactive components and the functional food ingredients with potential health benefits are an emerging area of research. The rich diversity of flora and fauna in the marine and coastal habitats of the Indian subcontinent represent an untapped reservoir of bioactive compounds with valuable pharmaceutical and biomedical use. Considering the underutilization of these groups of marine organisms, exploring bioactive compounds and development of any biologically useful products have benefits as health products. Comprehensive analyses demonstrated that during the last decade the average proportion of bioactive compounds among the new compounds is declining, though there are a large number of marine natural products yet to be explored. This may indicate that the research level of bioactivity is not keeping up with the discovery of new compounds. Thus, the research tools and methods for finding bioactivity need to be improved. The first improvement is about methods of spectral and bioactivity-guided separation and purification of marine-derived secondary metabolites, which combine the discovery of new compounds. These improvements in technology are dependent upon the automation in spectroscopy, which also allows the study of the functions of new compounds extracted from the target marine organisms. Second, for the discovery of new lead compounds and artificial intelligence for drug development evolved to a more mechanistic approach that targets specific molecular lesions. Combined with high-throughput screening through a large number of drug targets, bioactivity research against various life-threatening diseases will be effective in revealing the potentially useful biological properties of marine natural products. Furthermore, the discovery of new bioactive compounds from marine metabolites will form the basis for new drug leads. Thus, the new compounds will absolutely compose an abundant resource for future bioactivity research and drug development. Various medicinal and biomedical products from marine flora and fauna provide a myriad of benefits for human health and multiple life-threatening diseases, and therefore, are the attractive options for the food and pharmaceutical industry. The increasing interest in marine-based functional food ingredients and nutraceutical formulations in the last decade along with increased number of patents filed/granted have appropriately demonstrated the possibilities of bioactive from marine organisms to maintain and improve human health and well-being.

The present ICAR Winter School on "Recent advances in bioactive compounds from marine organisms and development of high-value products for health management" is designed to acquaint the participants with the advances in marine bioactive compounds with emphasis on the latest technologies on isolation and characterization of marine natural products of pharmaceutical importance. The course is planned in such a way that it covers both theoretical and practical aspect of recent advances in bioactive compounds from marine organisms. This programme will strengthen the knowledge of participants with regard to

the general and advanced methods of isolation procedures by chromatography, and their characterization by advanced spectroscopic experiments aspects.

I wish to thank the Education Division of Indian Council of Agricultural Research for giving us an opportunity to organize this ICAR Winter School. We are grateful to Dr. A. Gopalakrishnan, Director, ICAR-Central Marine Fisheries Research Institute, for his guidance, continuous interest in the course and providing all necessary facilities. I am highly obliged to Dr. P. Vijayagopal, Head, Marine Biotechnology Division for his guidance and support for the programme. All the scientists of Marine Biotechnology Division, technical staff, supporting staff and research scholars supported us in organizing the ICAR Winter School. I recall with gratitude the marvellous effort and help in preparing this manual by Minju Joy, Research Scholar of Marine Biotechnology Division. I take this opportunity to thank all the faculty members who have devoted their valuable time and contributed material for the preparation of the manual. I am confident that the Course Manual would aid the participants to enhance their knowledge and competence in the area of marine bioactive compounds and their applications for the development of high-value products for health management.

Kajal Chakraborty
Course Director

January, 2018

CONTENTS

CHAPTER

06

BIOACTIVE MARINE NATURAL PRODUCTS - A REVIEW

Dr. Meledath Govindan[1], Kajal Chakraborty[2], Minju Joy[2]

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Fitchburg State University, Fitchburg, Massachusetts, USA
[2]ICAR-Central Marine Fisheries Research Institute, Kochi

For thousands of year's natural products have played a key role in the development of cures for diseases. Extensive literature reviews by Gordon Cragg and David Newman of the U.S. National Institutes of Health and others have shown that over 60% of all drugs sold in the market are of natural products origin. In the area of cancer chemotherapy this figure is close to 67%. Even though many of these are of terrestrial plant or microbiological origin, marine organisms have become targets of drug discovery efforts since 1960's. With the advent of SCUBA and availability of sophisticated separation and structure elucidation technologies the field of marine natural products has blossomed in the past few decades,

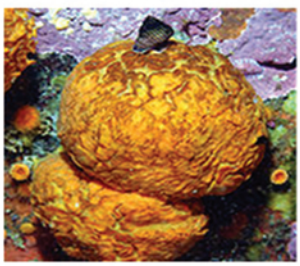
WHY MARINE NATURAL PRODUCTS?

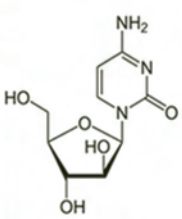
The marine flora and fauna remain largely unexplored. Approximately 71% of the molecular entities listed in the *Dictionary of Marine Natural Products* have novel molecular structures compared to ~40% of those in the *Dictionary of Natural Products*. In NCI preclinical cytotoxicity screen, marine organisms show higher incidence of anti-tumor potential: 1% vs. 0.1% for terrestrial organisms. Number of new marine compounds reported each year is increasing >1000 compounds.

EXAMPLES OF PROMINENT GROUPS OF MARINE NATURAL PRODUCT DRUGS

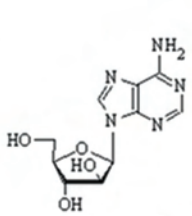
Ara C, Ara A, and AZT

Ara C is an anti-leukemic agents sold by Pharmacia (formerly Upjohn) and Glaxo SmithKline as Cytosar-U. Ara A (vidarabine) was a drug sold in the US and elsewhere as an antiviral agent. AZT, is the first effective drug against AIDS. These were designed based on the discovery of spongothymidine and spongouridine isolated from the Caribbean sponge *Tethya crypta* by Bergmann in 1950's.

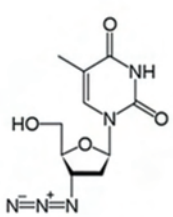




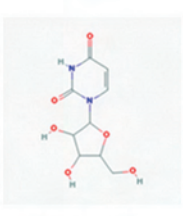
Ara C



Ara A



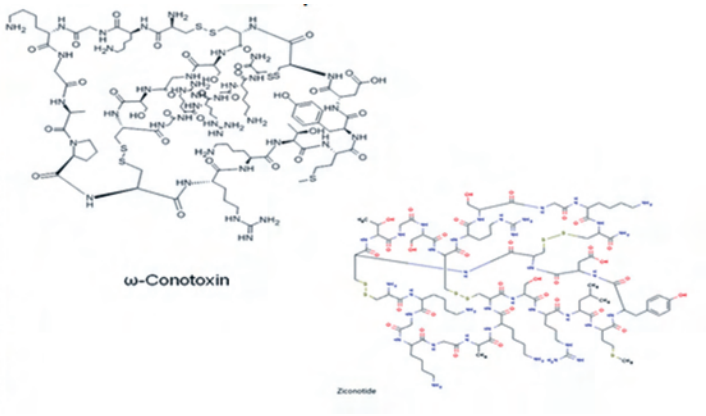
AZT



Spongiouridine

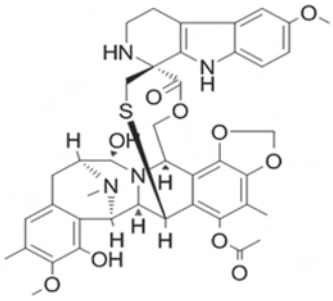
ù-Conotoxin

ù-Conotoxin MVIIA was first isolated in 1979 by Oilvera and co-workers from the Pacific piscivorous marine snail *Conus magus*. It is a linear 25 amino acid, polycationic peptide containing six cysteine residues linked by three disulfide bridges that stabilize its well-defined three dimensional structures. It inhibits N-type voltage-dependent calcium channels – 1000 times more powerful than morphine. Its complete chemical synthesis was achieved in 1987. After more than two decades of research and development, ziconotide, a synthetic form of ù-conotoxin MVIIA under the trade name Prialt, is being used for the specific indication of chronic pain.



Trabectedin - Ecteinascidin 743

Originally isolated from *Ecteinascidia turbinata* in 1969 by A.J. Weinheimer et al. *E. turbinata* is a mangrove tunicate, a colonial ascidian. Structure was elucidated in 1990 independently by Ken Rinehart et al. of Illinois and Amy Wright et al. of Harbor Branch Oceanographic Institution, Florida. Sold by Zeltia and Johnson and Johnson under the brand name Yondelis. Approved for use in Europe and South Korea for the treatment of advanced soft tissue sarcoma and relapsed ovarian cancers. Undergoing clinical trials for the treatment of breast, prostate, and pediatric sarcoma - cancer that begins in the muscle, fat, fibrous tissue, blood vessels, or other supporting soft tissues of the body. US FDA approved the drug in 2015 for soft tissue sarcomas - liposarcoma and leiomyosarcoma.



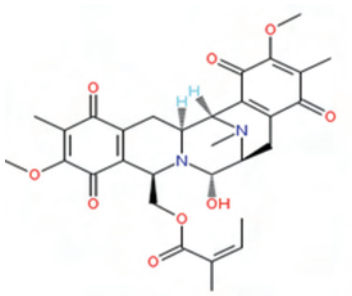
PM01183 (Lurbinectedin)

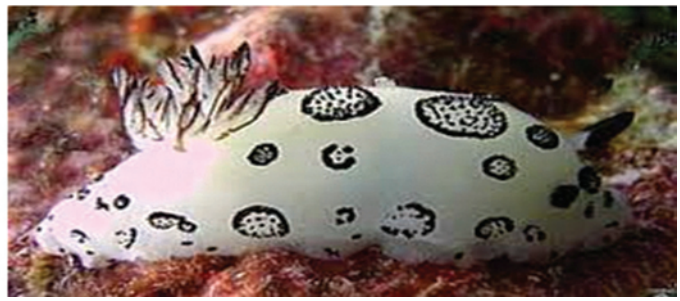
An analog of trabectidin is undergoing Phase III clinical evaluations against metastatic breast cancer. It was isolated

from symbiotic microbacteria growing on the tunicate. Drug is being developed by ParmaMar, S.A. It blocks trans-activated transcription, induces DNA double-strand breaks and modulates tumor microenvironment.

Jorumycin (Zalypsis)

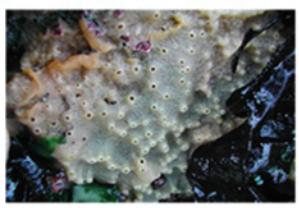
Isolated from nudibranch *Jorunna funebris* collected in India by Fontana et al. in 2000. Developed by Pharmamar as a treatment for lung and colon cancer as well as melanoma. Structurally related to ecteinascidin 743



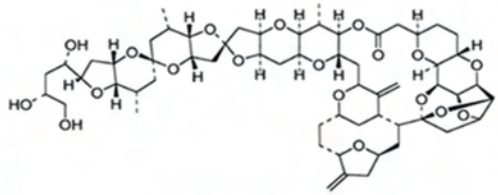


Halichondrin B

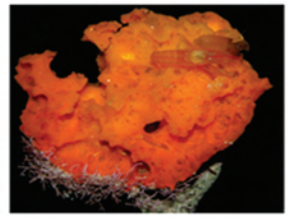
One of a series of compounds originally isolated in the 1980's from *Halichondria okadai* and subsequently from other sponges, including *Lissodendoryx sp*. Synthesized by Professor Kishi of Harvard University and the synthetic analog (eribulin mesylate) produced by Eisai Research Institute (MA) is an FDA approved as a drug against advanced or metastatic breast cancer previously treated with anthracyclines and taxanes.



H. okadai



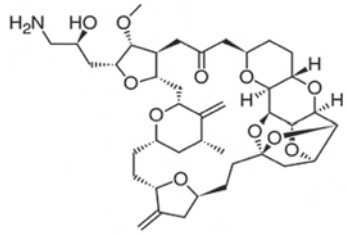
Halichondrin B

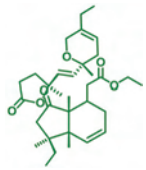


Lissodendoryx sp.

Eribulin Mesylate

The FDA approved the microtubule inhibitor Halaven,® eribulin mesylate, a derivative of halichondrin to treat metastatic breast cancer. It essentially contains the macrocyclic ring portion. It acts by a novel microtubule targeting mechanism where it aggregates tubulin and selectively blocks microtubule growth and inhibits mitosis.



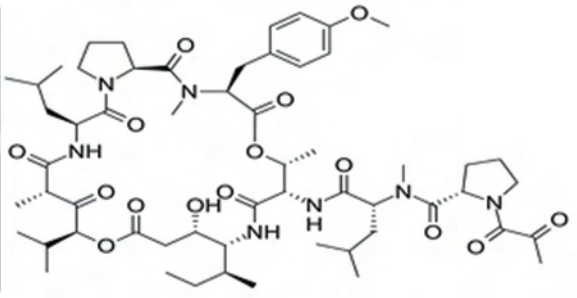


Didemnin B

Isolated from Carbbean tunicate *Tridemnum solidum* by late Professor Ken Rinehart of Univ. of Illinois. Displayed antiviral and in vivo cytotoxic activities at nanomolar concentrations. Reached Phase II clinical trials against cancer. Did not make it to Phase III because of its toxicity.

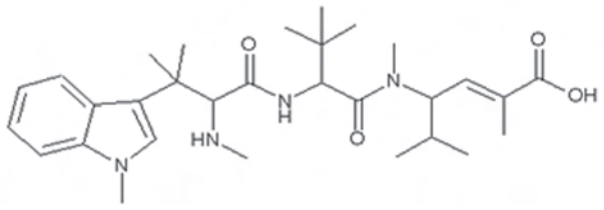
Aplidine (Plitidepsin)

Extracted from the ascidian *Aplidium albicans* by Rinehart group. Differs from didemnin B only in replacement of the *N*-lactyl side chain with a pyruvyl group. Pharmamar (Spanish company) is conducting a randomized, multicenter, open-label, Phase III study of plitidepsin in combination with dexamethasone vs. dexamethasone alone in patients with relapsed/ refractory multiple myeloma. Has been given orphan drug status by WHO



HTI-286 - A Hemiasterlin derivative

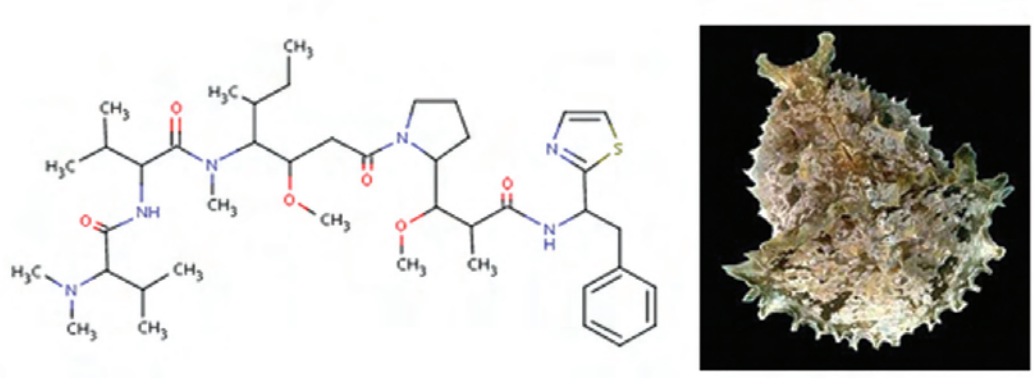
Hemiasterlin, a cytotoxic peptide was first isolated from S. African sponge *Hemiasterella minor* by Y. Kashman et al., (Tel Aviv) in 1994. Related isomers hemiasterlin A & B, were reported by Raymond Andersen and co-workers from sponges of the genus Auletta and Cymbastella in 1995. HTI-286 is a synthetic analog made by Anderson and Wyeth labs - their partner in an NIH supported research program. Work by E. Hamel (2008 Nobel Laureate) showed that it interacts with tubulin to produce microtubule depolymerization similar to vinblastine. Unfortunately it was withdrawn from further development during phase-II clinical trials for the treatment of non-small cell lung cancer



Dolastatin 10

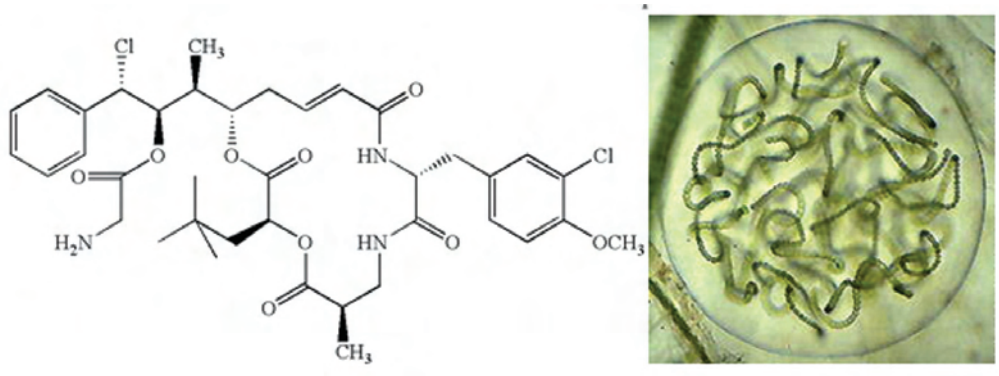
Cytotoxic peptide from Indian Ocean mollusk *Dolabella auricularia* by Prof. George Pettit of University of Arizona. Underwent Phase II trials against metastatic or recurrent liver,

bile duct, colorectal, gallbladder, and prostate ancer but is not move on to the next phase. Dolastatin 10 exhibited a unique interaction with tubulin. Three other dolastatin derivatives are also currently progressing through clinical trials as a single agent against prostate adenocarcinoma188, NSCLC 189, melanoma 190, colorectal cancer 191, soft-tissue sarcomas 192, breast cancer 193, and pancreatic cancer.



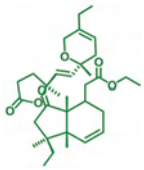
Cryptophycins

Derived from filamentous blue-green alga (cyanobacterium) by late Richard Moore of University of Hawaii. A synthetic analogue of Crp-1, cryptophycin-52 was developed by Eli lilly to improve hydrolytic stability and formulation. Underwent clinical trials against non-small cell lung cancer (NSCLC) with advanced tumor but was withdrawn. However, new analogs cryptophycin-309 and cryptophycin-249, have undergone preclinical efficacy studies and may soon enter clinical trials.



Spongistatin

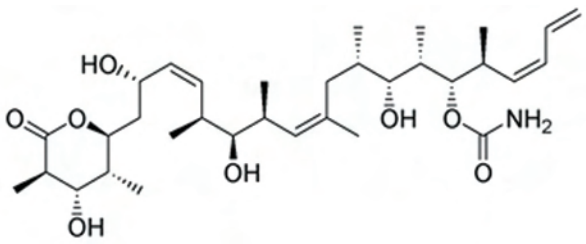
- Derived from a marine sponge *Spirastrella spinispirulifera* species from Eastern Indian Ocean near Maldives.



- Extremely potent activity against selected human tumor cell types in the U.S. National Cancer Institute's primary screen.
- Inhibits mitosis by binding in the *Vinca* alkaloid domain of tubulin thus preventing tubulin assembly.
- Being tried in combination with vincristine as potential anticancer agent.

Discodermolide

- Isolated by Harbor Branch chemist and my friend, Dr. Sarath Gunasakera from the deep water Caribbean sponge *Discodermia dissoluta*.
- Initially was found have immunosuppressive property but subsequently found to have stronger tubulin binding property than Taxol.
- Effective in paclitaxel and in epothilone-resistant cancer cells.
- Underwent clinical trials as an antitumor agent against colorectal cancers but dropped after Phase I clinical trials due to toxicity.
- Analogs are being looked at and combination therapy with paclitaxel is also a possibility.



At this point it might be important to give an overview of the drug development process, especially the clinical trials. These are carried out after the pre-clinical development work that includes animal testing to evaluate toxicity, pharmacology and pharmacokinetics. Typically, formulation and stability studies are also carried out in parallel. The formulated drug candidate is used in clinical trials.

CLINICAL TRIALS

- **Phase I** trials are the first stage of testing in human subjects.
  - Normally, a small (20-100) group of healthy volunteers will be selected.
  - Designed to assess the safety (pharmacovigilance), tolerability, pharmacokinetics, and pharmacodynamics of a drug
  - Often conducted in an inpatient clinic, where the subject can be observed by full-time staff.
  - Phase I trials most often include healthy volunteers.

- In some circumstances real patients are used, such as patients who have end-stage disease and lack other treatment options
- Volunteers are paid for their inconvenience

- **Phase II**
  - performed on larger groups (20-300) and are designed to assess how well the drug works
  - development process for a new drug often fails during Phase II trials when the drug is discovered not to work as planned, or to have toxic effects.
  - Phase II studies are sometimes divided into Phase IIA and Phase IIB.
- Phase IIA is specifically designed to assess dosing requirements (how much drug should be given),
- Phase IIB is specifically designed to study efficacy (how well the drug works at the prescribed dose(s)).
  - Some trials combine Phase I and Phase II, and test both efficacy and toxicity.
- **Phase III** studies are randomized controlled multicenter trials on large patient groups - 300-3,000 or more depending upon the disease/medical condition studied
  - Aimed at being the definitive assessment of how effective the drug is, in comparison with current treatments.
  - Because of their size and comparatively long duration, Phase III trials are the most expensive, time-consuming and difficult trials to design and run, especially in therapies for chronic medical conditions.
  - Most drugs undergoing Phase III clinical trials can be marketed under FDA norms with proper recommendations and guidelines, but in case of any adverse effects being reported anywhere, the drugs need to be recalled immediately from the market.
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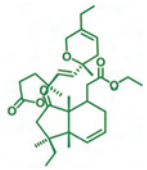
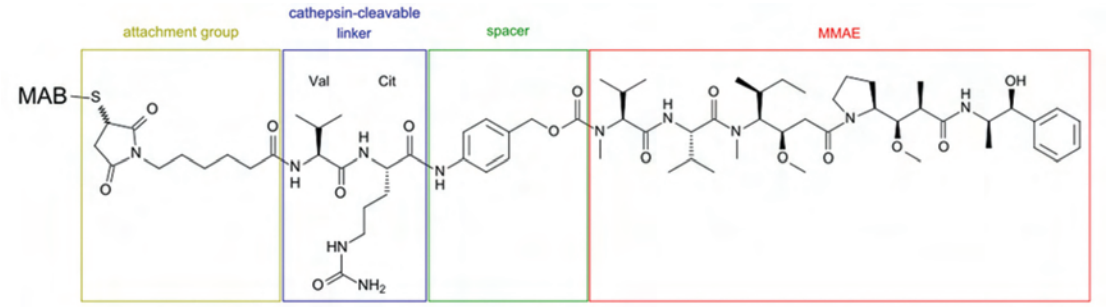


- Most drugs undergoing Phase III clinical trials can be marketed under FDA norms with proper recommendations and guidelines, but in case of any adverse effects being reported anywhere, the drugs need to be recalled immediately from the market.

- **Phase IV** studies (aka post marketing surveillance trials) are conducted after a drug has been approved for consumer sale
- The objectives include:
  - to compare a drug with other drugs already in the market
  - to monitor a drug's long-term effectiveness and impact on a patient's quality of life
  - to determine the cost-effectiveness of a drug therapy relative to other traditional and new therapies.
  - Phase IV studies could result in a drug being taken off the market or restrictions of use could be placed on the product.

Auristatin Derivatives

Currently, over 78 antibody drug conjugates (ADCs) are in clinical trials and employ auristatins as warheads (payloads). One such study has led to the U.S. FDA approval of ADC, brentuximab vedotin (Adcetris®, Seattle Genetics) to treat relapsed or refractory Hodgkin lymphoma and systemic anaplastic large cell lymphoma. It was earlier approved by European Medicine Agency and in Japan. It contains monomethyl auristatin E (MMAE)



Auristatins in Clinical Trials

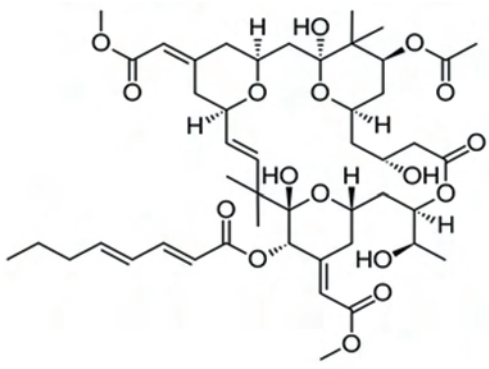
Newman and Cragg reports that as of March 2017, the following auristatin containing ADC's are being studied.

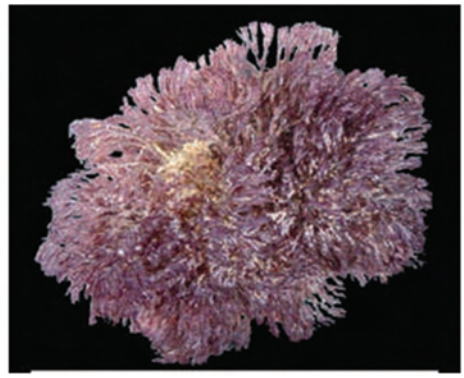
- Phase III: seven (six being directed against various lymphomas with multiple drug regimens, and one being a comparative trial).

- Phase II: 53 (52 against various lymphomas with 15 only studying brentuximab vedotin, 35 having a variety of other drug treatments in addition to the ADC, and one where the ADC alone is being tested against mesothelioma).
- Phase I: 28 (27 against lymphomas and leukemias, with one against mycosis fungoides/Sezary Syndrome. One trial has brentuximab vedotin as the sole agent studying Graft versus Host Disease following allogenic stem cell transplantation).

Bryostatins

- Bryostatins were isolated from the bryozoan, *Bugula neritina,* by Pettit group. Many analogs have been isolated.
- It was one of the promising marine natural products.
- Bryostatin 1 went through Phase II clinical trials as an anticancer agent but did not proceed into Phase III due to adverse side effects.
- As of 2013 it was being tested in Phase II clinical trials as a treatment for Alzheimer's disease.

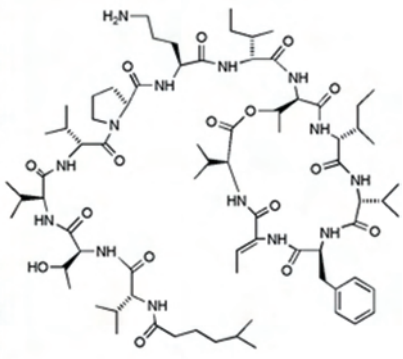




Kahalalide

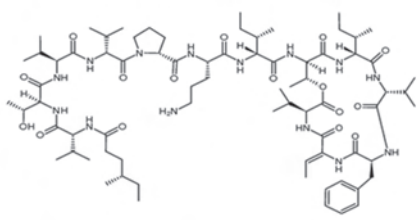
- Cyclic depsipeptide isolated by Prof. Paul Scheuer's group at U. of Hawaii from the sacoglassan mollusk *Elysia rufescens* – apparently comes from the alga *Bryopsis sp.* on which it grazes.
- Kahalalide F (KF) is the largest and the most biologically active of the 13 natural peptides isolated from *E. rufescens.*
- KF was subsequently synthesized by Spanish researchers using peptide synthesis methodology.

- KF is being evaluated in phase II clinical trials for the treatment of prostate, breast and liver cancers.



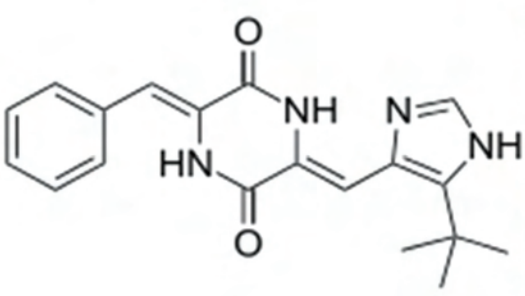
Elisidepsin - A Kahalalide F derivative

- Elisidepsin (Irvalec®) is a synthetic cyclic analog of kahalalide F.
- Currently in phase II clinical trials in patients with advanced/metastatic non-small cell lung, esophageal and gastric cancers.



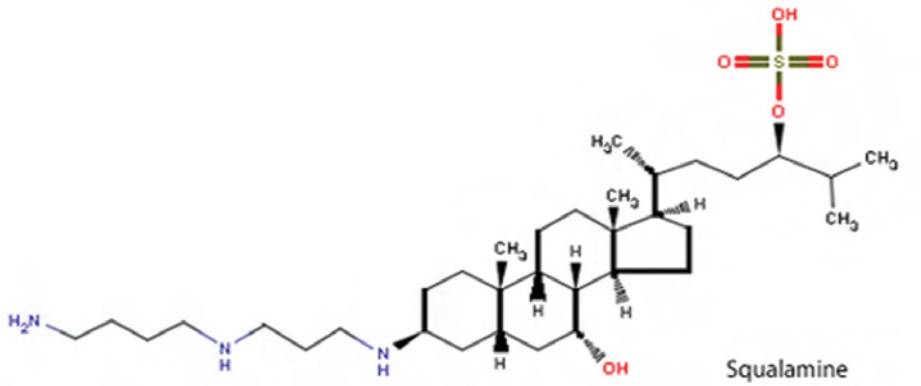
Plinabulin

- Plinabulin is a small molecule under development by BeyondSpring Pharmaceuticals, and is in a world-wide Phase III clinical trial for non-small cell lung cancer.
- A synthetic analogue of the diketipiperazine phenylahistin, a natural product isolated from a marine and terrestrial fungus, *Aspergillus sp.*
- It selectively binds to the colchicine-binding site of tubulin. This disrupts mitotic spindle assembly leading to cell cycle arrest at M phase and blockage of cell division.



Squalamine

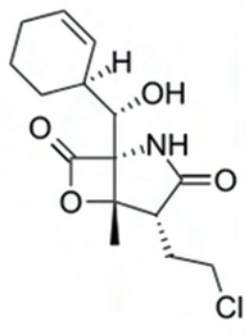
- Simple amino sterol isolated from a dogfish shark, *Squalus acanthias*, collected off New England coast.
- Undergoing Phase II clinical trials against ovarian cancer, NSCLC, and prostate cancer.
- Squalamine exhibits anti-angiogenic activity under certain conditions (angiogenesis is the formation and differentiation of blood vessels).

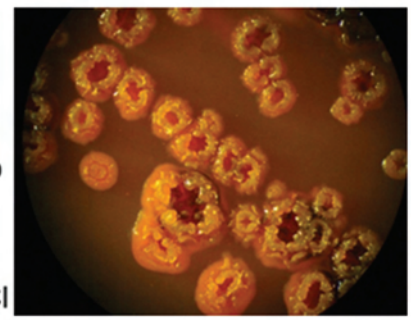


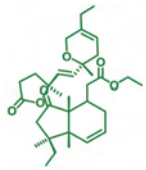
Squalamine

Salinosporamide A

- A potent proteasome inhibitor isolated from the marine bacteria *Salinispora tropica* and *Salinispora arenicola*, which are found in ocean sediment.
- Has been given orphan drug approval (Marizomib) for the treatment of multiple myeloma and being evaluated as treatment for other cancers.
- Possess a highly functionalized ã-lactam-â-lactone bicyclic core. Unique activity - irreversibly inhibits the three major catalytic activities of the 20S core of the ubiquitin-26S proteasome.
- Scripps Institute scientists led by Fenical and Moore have sequenced the 5,183,331 bp genome and analyzed all identifiable gene clusters to establish the biosynthetic pathways for the metabolites.

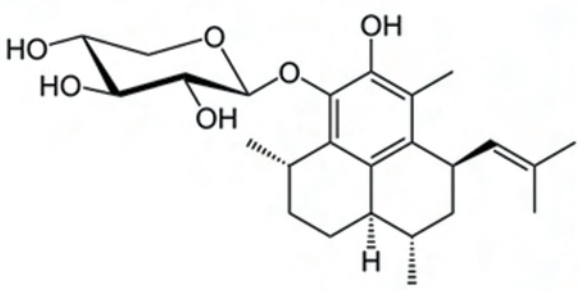






Pseudopterosins

- Pseudopterosins are a group of diterpene glycosides primarily extracted from the octocoral of the genus *Pseudopterogorgia*.
- They possess an array of potent biological activities including anti-inflammatory and analgesic, wound-healing, anti-bacterial, anti-cancer, anti-viral, anti-malarial, and anti-tuberculosis in both *in vitro* and *in vivo* assays with a novel mechanism of action.
- In Phase II clinical trials, pseudopterosins were found to augment re-epithelialization process with qualitative enhancement in the early wound repair process.
- Pseudopterosins are now a constituent of the cosmetic "anti-wrinkle cream" sold by Estee Lauder under the brand name "Resilience."



Compounds undergoing pre-clinical evaluation

- Salicylhalimide from the Western Australian sponge *Haliclona* sp.
  - Potential antitumor agent as well as use as bone resorption agent
- Thiocoraline from an actinomcyete (rod-shaped gram positive bacteria)
  - Showed potential as an anticancer agent in NCI 60-cell line screen
  - Inhibits DNA polymerase a
- Dictyodendrins from Japanese sponge *Dictyodendrilla verongiformis*
  - telomerase inhibitors for potential treatment against Alzheimer's disease

DMBX-A (GTS-21) - A possible treatment Alzheimer's disease

- A synthetic derivative of naturally occurring anabaseine derived from a marine worm, *Amphiporus lactifloreus*

- 3-(2,4-Dimethoxybenzylidene)-anabaseine (DMXBA; also called GTS-21), is an alpha7 acetylcholine receptor (á7AChR) agonist.
- Undergoing Phase II clinical trials for the treatment of Anzheimer's disease as well as schizophrenia

CONCLUSIONS

The field of marine natural products continues to flourish as seen by the number papers published despite the diminished financial support by pharmaceutical companies. Most of the major multinational phama companies dropped their natural products drug discovery sections in the 1990's and 2000's but governmental support in the US continued for the most part until this decade. The focus has been shifting from traditional bioassay-guided separations followed by structure determination to novel dereplication methods using the power of LC-MS, MS-MS, and the emerging technology of LC-NMR. Molecular biology and metabolomics are also beginning to emerge as a tool to discover and produce natural products of interest. As stated by Newman et al. in their 2010 article in Cell Press. Opinions from leaders in the field of marine natural products all agree that the potential of these compounds to significantly contribute to the pharmacopeiais still on the horizon. With the eminent development of more marine natural products from those in the current pipeline, the contribution of marine natural products to the future pharmacopeia seems to be promising. New technologies and efficient collaborations between academic and industrial scientists will be essential to ensure the future success of marine natural products as new and novel therapeutic entities that can make a significant contribution to the treatment of human disease."

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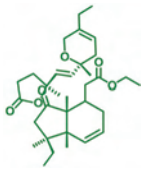

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Inauguration of winter school 2018 by Padma Bhushan Dr. Manju Sharma

Photo with Dr. K. Gopakumar, Formerly DDG ICAR (Fy)

Field visit to India Sea Foods

Field visit to BOS Naturals

Field visit to Accelerated Freeze Drying Co. Ltd

Photo with Dr. Meledath Govindan

Lectures and Interactive Sessions

Practical Sessions


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WELCOME
Sitting (L to R) Minimol K.C., Grace Thomas, Kajal Chakraborty (Course Director), P. Vijayagopal (Head, Marine Biotechnology Division), A. Gopalakrishnan (Director), Paulson Mathew, Sathu T., Radhakrishnan E.K.
Standing (L to R) Aswathy Elizabeth Mani, Sreemol C.K., Prima Francis, Soumya Krishnan, Minju Joy, V. Rani, Seeja Thomachan Panjikkaran, Sheneya Festus, Drishya K., Anie Y., Suja Rani S., Sindhu Issac, Teena P. Varghese, Magna Thomas, Santwana Palai, Norma Xavier Chelat, Naheef K., Satya Narayan Sahoo, Jaimin Hareshbhai Bhatt, Ajoy Saha, Senthil Kuppusamy, Kedar Shashikant Damle, Shubhajit Dhara, Midhun Dominic C.D., Manukuttan K.S., Suji Chandru, Tima Antony, Soumya Salas

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