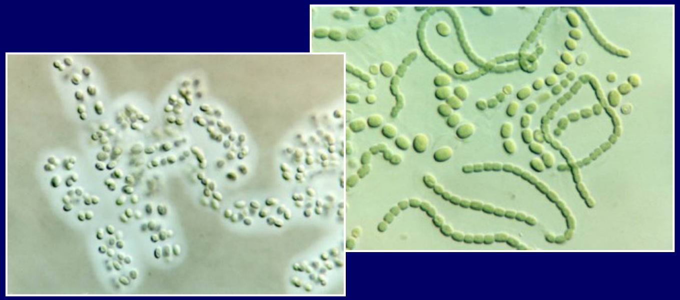
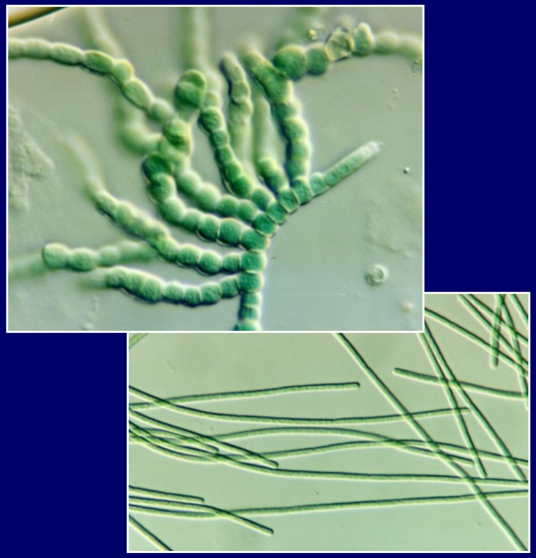
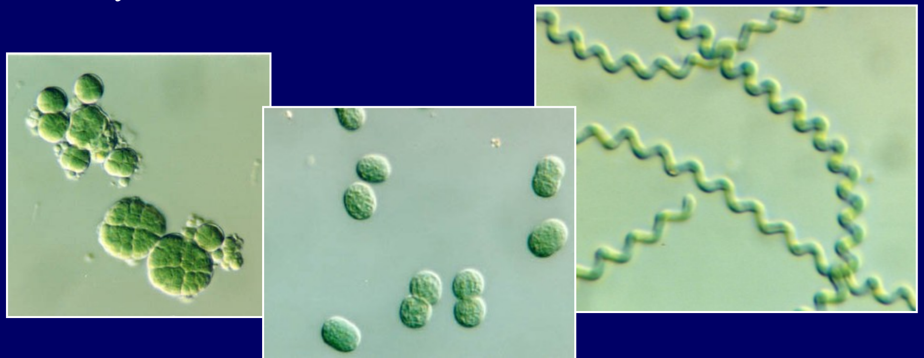


Bioactividad de cianobacterias



Mario Tredici
Dipartimento di Biotecnologie Agrarie
University of Florence



BIOACTIVE SECONDARY METABOLITES (BSM)

✓BSM are compounds produced by cells in stationary or slow growing cultures.

✓The content of BSM in the algal biomass is generally very low (‰).

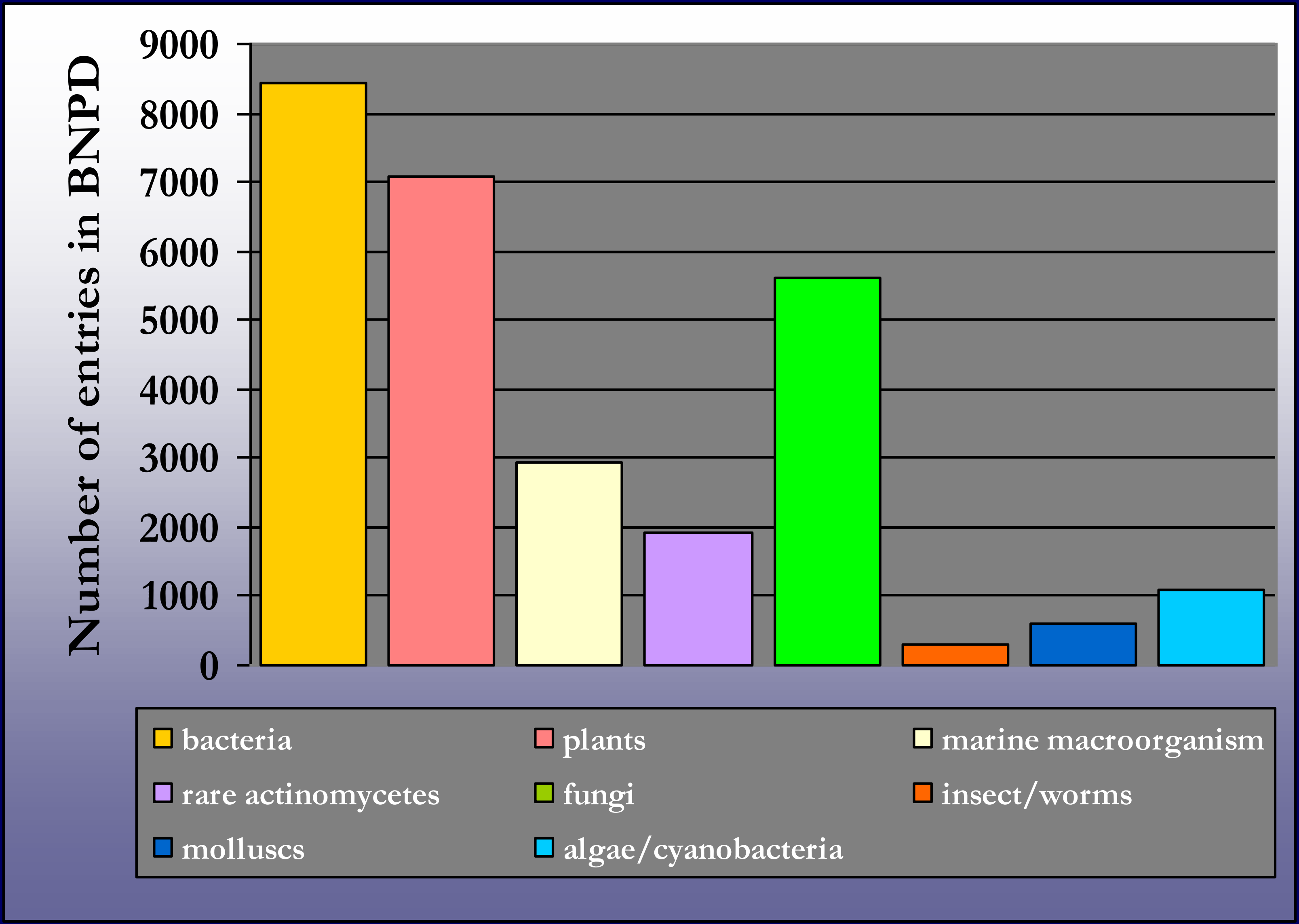
✓BSM tend to differ among organisms and include compounds that act as antibiotics, antitumorals, hormones, toxins (Carmichael, 1992).

✓BSM are often inhibitory to other types of organisms likely to occupy the same ecological niches and are important in competition.

✓BSM have been shown to have important applications in medicine and agriculture.

✓There is urgent need to discover new BSM for the pharmaceutical and agrochemical industries as the rate of discovery has decreased steadily over the past decades.

BIOACTIVE NATURAL PRODUCTS DATABASE



MAIN CHEMICAL CLASSES OF BIOACTIVE COMPOUNDS FROM CYANOBACTERIA

Chemical class	Compound	Activity
Alkaloids	Anatoxin-a Anatoxin (s) Saxitoxin Lyngbyatoxin A	Neurotoxic Antibiotic Anti-inflammatory
Macrolides	Scytophycins Tolytoxin Aplysiatoxin	Antibiotic Cytotoxic
Peptides	Microcolyns Microcystins Nodularin Microginin Mirabimids Anabaenopeptilides Cyanopeptolins **Cryptophycins** Majusculamide C	Antibiotic Antibacterial Antifungal Antimalararial Anti-HIV Cytotoxic Antineoplastic Enzyme inhibitor Hepatotoxic
Various	Curacins Malyngolide Cyanovirins Tubercidin Aulosirazole Sulfolipids	Antibiotic Cytotoxin Enzyme inhibitor Insecticides

POTENTIAL APPLICATIONS OF CYANOBACTERIAL AND MICROALGAL BSM

Medicine

- ✓antibiotics (antifungal, antibacterial, antimalarial, antialgal, etc)
- ✓antiviral compounds
- ✓antitumor agents
- ✓anti-inflammatory agents

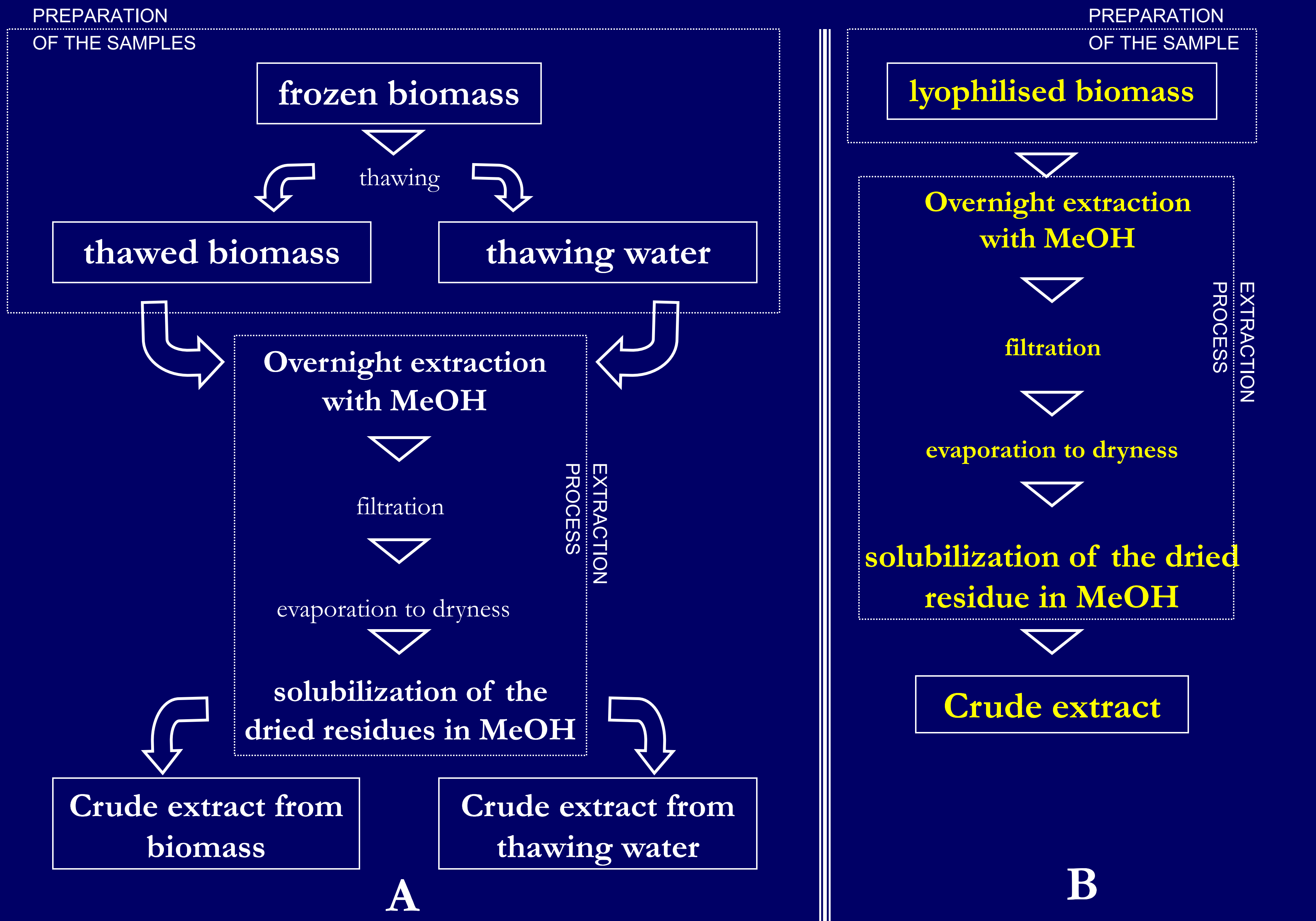
Agriculture

- ✓antifungal products
- ✓antibacterial products
- ✓insecticides and nematocides
- ✓herbicides
- ✓hormones

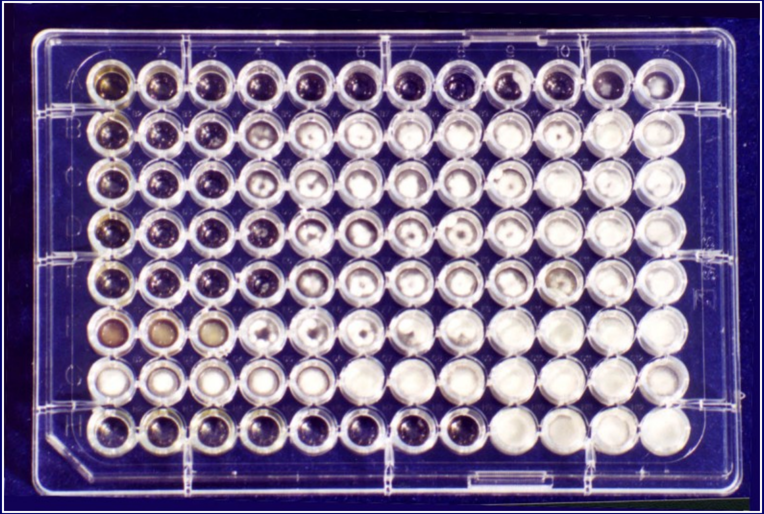
Biocontrol

- ✓control of toxic blooms

Methods: EXTRACTION PROCEDURES



Methods: ANTIFUNGAL ACTIVITY – MICROTITER…



- ✓ Introduction of an aliquot (2-200 µl) of the crude extract in the first well of the plate.
- ✓Evaporation to dryness.
- ✓Resuspension of the extract with DMSO (10% in water).
- ✓Serial dilution of the crude extract (final concentration of DMSO 10% in water).
- ✓Inoculation of each well with the fungus. 5 x 10^4 conidia mL^{-1} or a piece of micelium suspended in 90 µl PDB (Potato Dextrose Broth).
- ✓Final volume in each well: 100 µl.
- ✓Control with 10 µl of DMSO 10% and 90 µl of the fungus in PDB.
- ✓Incubation of the plate at 25 °C for three days.
- ✓Evaluation of activity as capacity of the extract to inhibit fungal growth (of at least 75% with respect to the control), after 72 h of incubation.

…and TEST TUBES

Methods: ANTIFUNGAL ACTIVITY – PETRI DISH

- ✓Introduction of 30 mL of PDA (Potato Dextrose Agar) in a Petri dish.
- ✓Plating of the fungal inoculum.
- ✓Deposition of sterile paper filters on the plate.
- ✓Deposition of the extract onto the filters.
- ✓Deposition of the solvent (control) on the filter.
- ✓Incubation at 25 °C for three days.
- ✓Measurement of the inhibition areas.

Methods: ANTIBACTERIAL ACTIVITY

✓Same as antifungal activity but using higher concentrations of the inoculum, different media (Nutrient Agar) and shorter times of incubation (48h at 30 °C).

Methods: INSECTICIDAL ACTIVITY ("needle injection assay")

✓Injection of 5 µL of cyanobacterial extract under the skin of the larva.

✓Distribution of six larvae in small Petri dishes containing 1 g of pabulum.

✓Daily monitoring of larvae vitality for 20 days against the control (larvae injected with the sole solvent).

Methods: INSECTICIDAL ACTIVITY ("feeding assay with surface contamination")

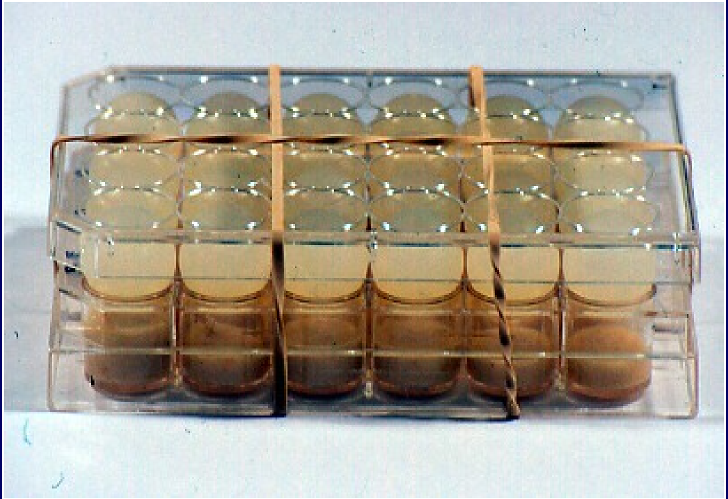
✓Distribution of 2 ml of agarized pabulum in each well of a 24 well plate.

✓Distribution of the extract on the surface of the pabulum and drying to evaporate the solvent.

✓Introduction in each well of a 24h old larva.

✓Incubation a 25 °C under a light/dark cycle.

✓Daily control of larvae vitality and measurement of their weight at the 8th day.



Methods: NEMATOCIDAL ACTIVITY

✓Distribution of 2 mL of agarized medium in each well of a 6 well plate.

✓Distribution of the cyanobacterial extract on the surface of the agarized medium and evaporation of the solvent.

✓Inoculation of the medium with a culture of *Escherichia coli* and incubation overnight at 30 °C to let the bacteria grow.

✓Addition in each well of 6-9 larvae at the 1° stage of development.

✓Incubation at 22 °C and daily observation under the microscope up to 15th day, (developmental stage, presence of adults, eggs, worm motility).

Methods: CITOTOXIC ACTIVITY (test organism *Artemia salina*)

✓Serial dilution of the extract (evaporation of methanol and resuspension in DMSO 10%) in 12 mL tubes with 2 mL of medium and 20 artemia nauplii (24h old).

✓Addition of *Nannochloropsis* sp. cells as feed for the larvae and incubation at 25 °C.

✓Observation after 24 and 48 h of the vitality of the nauplii.

✓The extract is considered active when the mortality is at least 75% higher with respect to the control.

BIOACTIVITY OF 50 *NOSTOC* STRAINS (Piccardi et al., 2000)

	Activity against:		
Origin	fungi	bacteria	*A. salina*
Simbiont with:			
Cicas (12)	1	2	1
Lichens (6)	3	1	3
Briofite	1	0	1
Azolla	1	2	1
Gunnera	0	0	0
Free:			
Ricefield	4	2	2
Soil	1	0	2
Fresh water	1	0	0
Sea water	0	0	0
others	3	1	2

- ✓15 strains were active against one of the two fungi tested
- ✓4 strains were active against both the fungi
- ✓8 strains were active against bacteria
- ✓12 strains were toxic against *A. salina*
- ✓ only one strain showed activity against fungi, bacteria and *A. salina*

Methods: PHYTOHORMONAL ACTIVITY (bioassay using plant cotyledons)

1. Evaluation of citokininic activity
2. Evaluation of auxinic activity

✓ Resuspension in water of the lyophilized biomass and sonication.

✓ Distribution of five day old cotyledons on a paper filter disk watered with the biomass suspension.

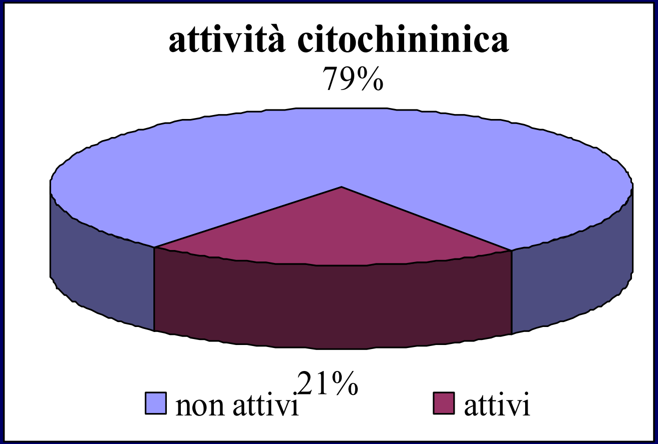
✓ Citokininic activity: incubation at 25 °C for three days and measurement of cotyledons wet weight.

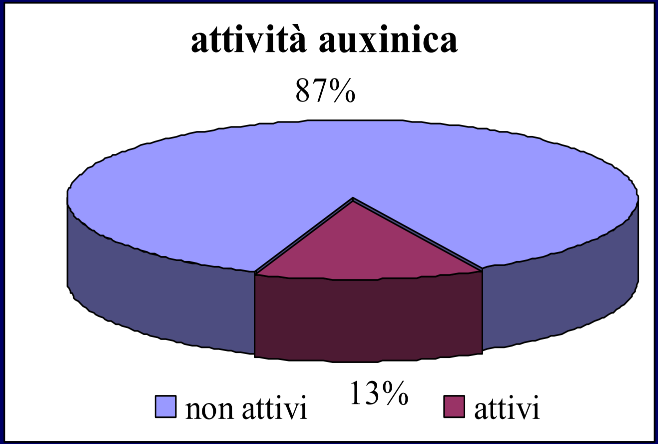
✓ Auxinic activity: incubation at 25 °C for five days and determination of roots number.

Auxinic activity: cotyledons of cucumber treated with different biomass concentrations.

PHYTOHORMONAL ACTIVITY OF CYANOBACTERIA

Ordog (2001). International Symposium on Microalgae and seaweed products in PlantSoil Systems, Mosonmagyarovar, Ungheria, 20-22/06/2001





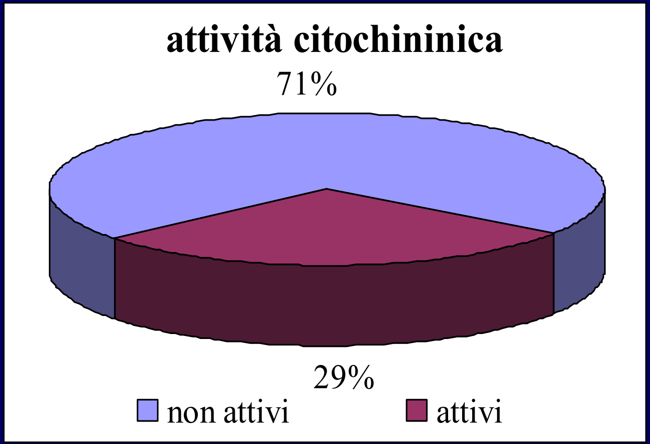
194 strains tested:

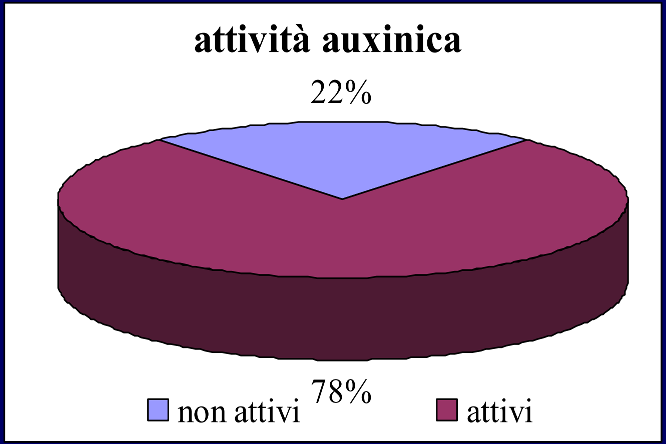
14% Chroococcales,

63% Nostocales,

23% Oscillatoriales

DiBA, University of Florence, unpublished data





86 strains tested :

7% Chroococcales,

5% Pleurocapsales,

57% Nostocales,

31% Oscillatoriales

Sources of bioactive cyanobacterial biomass

1. Harvest from nature of active biological material.
2. Cultivation of the bioactive organism.

COLLECTING BIOACTIVE CYANOBACTERIA FROM THE WILD

- ✓ *Arthrospira platensis* (500-700 tons/year)
- ✓ *Aphanizomenon flos-aquae* (500 tons/year)
- ✓ *Nostoc flagelliforme* (400 tons/year)

Arthrospira platensis

REVIEW ARTICLE

The Potential Application of *Spirulina* (*Arthrospira*) as a Nutritional and Therapeutic Supplement in Health Management

Amha Belay, PhD*
Scientific Director, Earthrise Nutritionals Inc., Calipatria, California

INTRODUCTION

Spirulina, now named *Arthrospira*, is a microscopic and filamentous cyanobacterium (blue-green alga) that has a long history of use as food. Its name derives from the spiral or helical nature of its filaments (Fig 1). There are reports that it was used as food in Mexico during the Aztec civilization some 400 years ago. It is still being used as food by the Kanembu tribe in the Lake Chad area of the Republic of Chad where it is sold as dried bread called "dihe".[1] *Spirulina* has been produced commercially for the last 20 years for food and specialty feeds.[2-4] Commercial algae are normally produced in large outdoor ponds under controlled conditions (Fig 2). Some companies also produce directly from lakes. Current production of *Spirulina* worldwide is estimated to be about 3,000 metric tons. Sold widely in health food stores and mass-market outlets throughout the world, *Spirulina's* safety as food has been established through centuries of human use and through numerous and rigorous toxicological studies.[5-8]

Early interest in *Spirulina* focused mainly on its rich content of protein, vitamins, essential amino acids, minerals, and essential fatty acids. *Spirulina* is 60-70% protein by weight and contains a rich source of vitamins, especially vitamin B_{12} and provitamin A (β-carotene), and minerals, especially iron. One of the few sources of dietary γ-linolenic acid (GLA), it also contains a host of other phytochemicals that have potential health benefits.

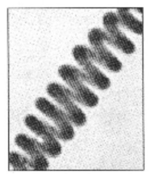


Figure 1. Microscopic view of *Spirulina* (*Arthrospira*) *platensis*

The objectives of this paper are 1) to review the available literature on the potential health effects of *Spirulina* and its extracts, 2) to provide insight into the potential implications of the studies reviewed in the context of possible nutritional and therapeutic applications in health management, and 3) to identify areas of interest for future research.

IMMUNOMODULATION EFFECTS

In a 1993 review of the potential health benefits of *Spirulina*, Belay *et al.*[9] presented the limited published information on this alga and called the attention of researchers to the particular areas of immune enhancement and cancer. Numerous studies have been published since then. The evidence for immune modulation of *Spirulina* in various animal models is so striking that structure function claims have already been applied to some *Spirulina* products.

A summary of the major studies on immunomodulation properties of *Spirulina* is given on Table 1.

Hayashi *et al.*[10] were the first to publish detailed studies on immunomodulatory properties of dietary *Spirulina* in mice. According to their results, 1) mice fed *Spirulina* showed increased numbers of splenic antibody-producing cells in the primary immune response to sheep red blood

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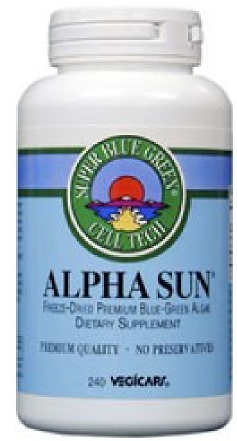
Nutrition

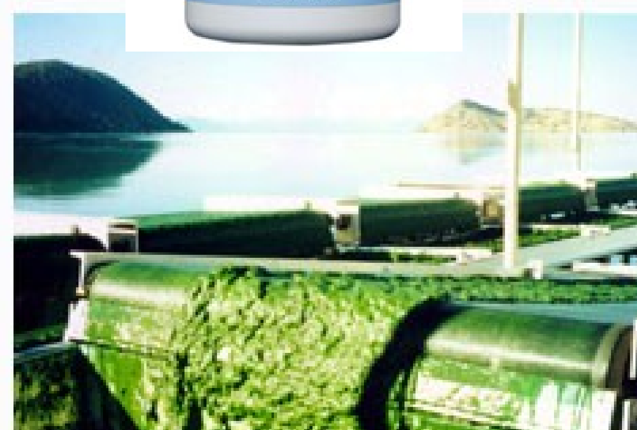
- ✓highly absorbable source of natural beta carotene,
- ✓mixed carotenoids and other phytonutrients,
- ✓B vitamins,
- ✓gamma linolenic acid (GLA),
- ✓protein and essential amino acids

Health

•It has been shown to be effective in the treatment of allergies, anemia, cancer, high cholesterol, elevated blood sugar, viral infections, inflammatory conditions, liver damage, immunodeficiency, cardiovascular diseases, and other conditions ... In a 2002 Japanese study, 12 adult males were administered an oral hot water extract of spirulina, and the number and activity of their natural killer (NK) cells was measured before and after treatment. (NK cells destroy tumor cells by binding to them and delivering lethal chemicals that kill on contact.) At the study's end, there was a significant increase in the production and cancer-killing ability of these subjects' NK cells ... Spirulina also shows potential for decreasing the adverse effects of both chemotherapy and radiation"

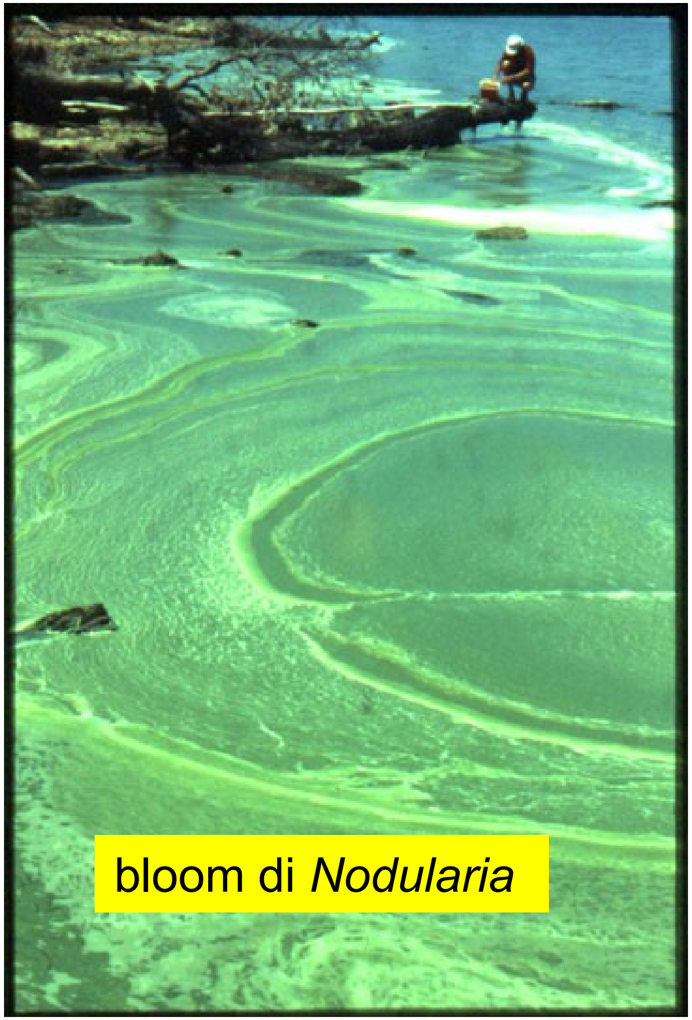
JANA (2002), vol. 5, 27-48



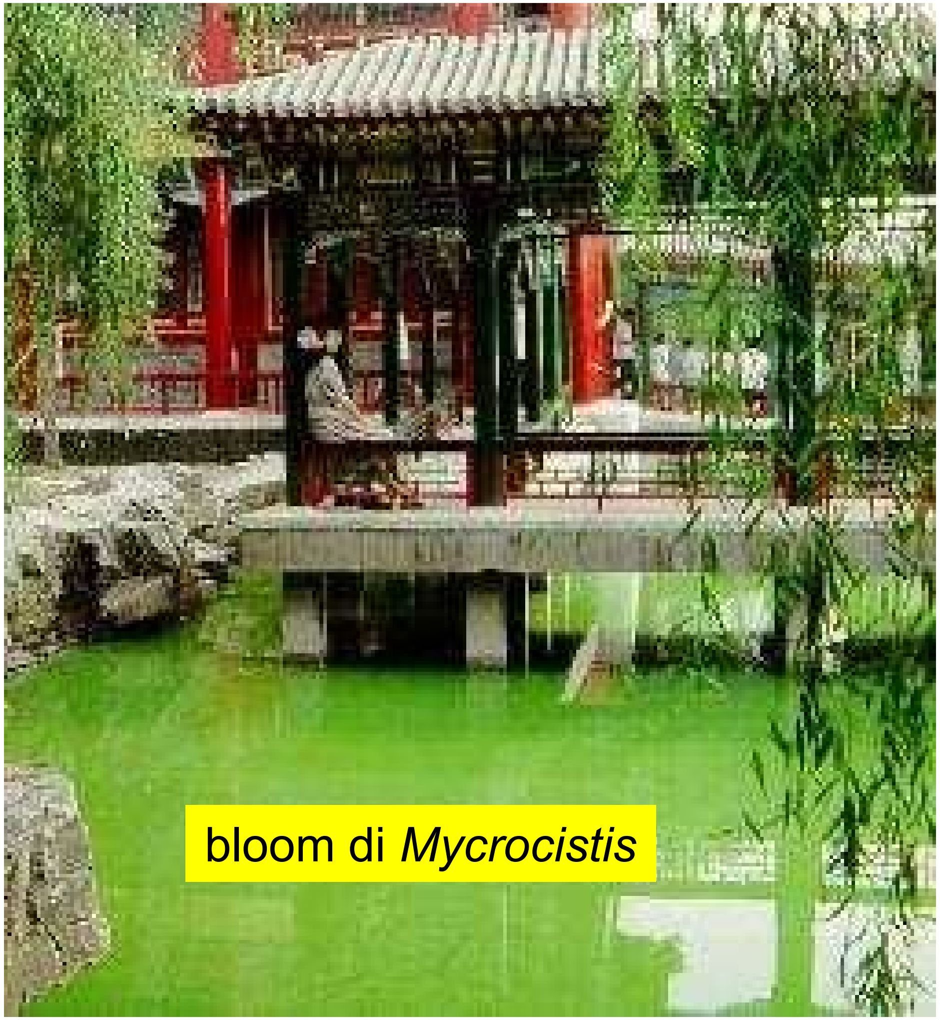


Aphanizomenon flos-aquae

Blooms tossici



bloom di *Nodularia*



bloom di *Mycrocistis*

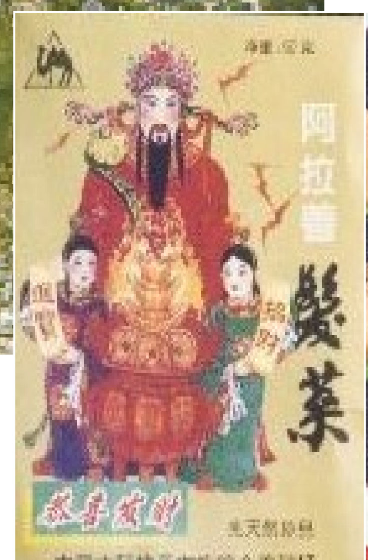
Cianobatteri del suolo utilizzati tradizionalmente come alimento

Località	**Specie**
Bolivia	*Nostoc commune*
Cina	*Nostoc flagelliforme, N. edule*
Ecuador	*Nostoc commune, N. ellipsosporum*
Fiji	*Nostoc sp.*
Java	*Nostoc commune*
Giappone	*Nostoc commune, Aphanotece*
Messico	*Nostoc commune, Phormidium tenue*
Mongolia	*Nostoc edule, Nostoc commune*
Peru	*Nostoc pruniforme*
Tailandia	*Nostoc verrucosum*
Russia	*Nostoc edule*

Jassby, 1988 (mod.)

Nostoc flagelliforme

"fa-cai"



"Fat Choy"

長春社Since 1968

The Conservancy Association

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Add.: 9/F Breakthrough Centre, 191-197 Woosung Street, Kowloon, Hong Kong.
電話 Tel.: (852) 2728 6781 傳真Fax: (852) 2728 5538
電子郵箱E-mail address: cahk@conservancy.org.hk 網址Website: www.conservancy.org.hk

To: the Editor
From: The Conservancy Association
Date: 29 January 2003

Green Group campaign for stop consuming "Fat Choy" And urges Government to ban import and trading

The Conservancy Association appeals to the public, companies and restaurants to stop consuming "Fat Choy" (*Nostoc flagelliforme*) and urges the Government to ban the import and trading of the plant which help to prevent desertification. The group found that many restaurants have included "Fat Choy" in their menu for the Chinese New Year, despite the fact that the Central Government has already banned the trading of the food since 2000.

"Fat Choy" grows in arid area, mainly in Inner Mongolia, Ningxia, Qinghai and Xinzhiang Provinces. When it is removed from the ground, grass and their roots will be ripped off from the ground, exposing the surface soil to wind erosion. This is one of the main cause of desertification. In 2002, a report by Chinese Government to the United Nations indicated that the total desertified area in China reached 2.7 million km^2, or 28% of total land area. It was reported that desertification is taking place at a rate of 10,000 km^2 per year (about the size of 10 Hong Kong. In the last 20 years, in Inner Mongolia alone, the harvest of "Fat Choy" has turned 2,000 km^2 of grassland to desert every year (about the size of 2 Hong Kong).

The Central Government has estimated that over 400 million people (one third of Chinese total population) are directly affected, incurring economic loss of HK$50.7 billion. In recent year, impact of desertification is increasing and leads not only to thousands of ecological refugees, but also to sandstorm in northern part of China.

The harvest of 1 tael of "Fat Choy" will destroy about 1/4 ha of land, or two standard swimming pool. Even if each person in Hong Kong eats "Fat Choy" once a year (about 0.04 tael or 1.5 g), 700 km^2 of grassland will be turned into desert.

The Association urges the SAR government to pass law to ban the import and trading of "Fat Choy" that leads to desertification, in compliance with the law in Mainland China. Before such legislation is in place, Hong Kong Customs should step up its measures to illegal import of "Fat Choy". The group also suggests that the Consumer Council should regularly inspect the Fat Choy available in the market to avoid citizens being deceived. The group also pledges citizens, companies and restaurants to stop consuming "Fat Choy" and suggests to replace "Fat Choy" by lettuce which in Cantonese is "Shang Choy" – literally meaning "Creating Wealth".

For further enquiries, please contact Gordon Ng, Chief Executive of the Association at 6077 5765 or 2272 0322.

PROBLEMS WITH FIELD-COLLECTED MATERIAL

✓Very few bioactive cyanobacteria can be collected in large amounts.

✓Collecting from the environment requires considerable time and effort.

✓Harvesting of large quantities requires the consent of the country where the collection is made and must be carefully evaluated not to adversely impact the collection site.

✓Lack of reproducibility:
Secondary metabolite production in field material is unpredictable:
- many cyanobacteria prove to be non active on recollection;
- bioactivity may vary within a few meters at the collection site.

Research and development of BSM from microalgae and cyanobacteria can not rely on field collected material.

ADVANTAGES OF CULTURING

- ✓Between 1 and 10% of microalgae and cyanobacteria are cultivable by current techniques.

- ✓ Some active strains may be very rare in the field and thus their bioactivity is overlooked. We can find them through enrichment, isolation and cultivation.

- ✓ Synthesis of BSM is dependent on culture conditions (temperature, pH, light, nutrients). We can stabilise production of the active molecule by controlling culture conditions. Genetic manipulation is also possible.

Very few attempts have been made at mass cultivation of bioactive cyanobacterial strains.

- ✓ In several cases scale-up has been achieved by a number of small (15-30 L) square pans or carboys (Patterson et al., 1999, Rossi et al., 1997).
- ✓Cytotoxin production by a marine *Lyngbya* strain in a 250 L bioreactor (Armstrong et al., 1991).
- ✓Cultivation of *Nodularia harveyana* in a 80-L tubular reactor outdoors (Pushparaj et al., 1994).
- ✓Cultivation of two cytotoxin producing strains in a low-cost 800-L PE cylindrical tank (Bolis et al., 1999).
- ✓Cultivation of three bioactive *Nostoc* strains in 120-L annular columns (Rodolfi et al., 2001, 2002).

Annular columns

Microalgae cultivated

Nannochloropsis

Pavlova

Monodus

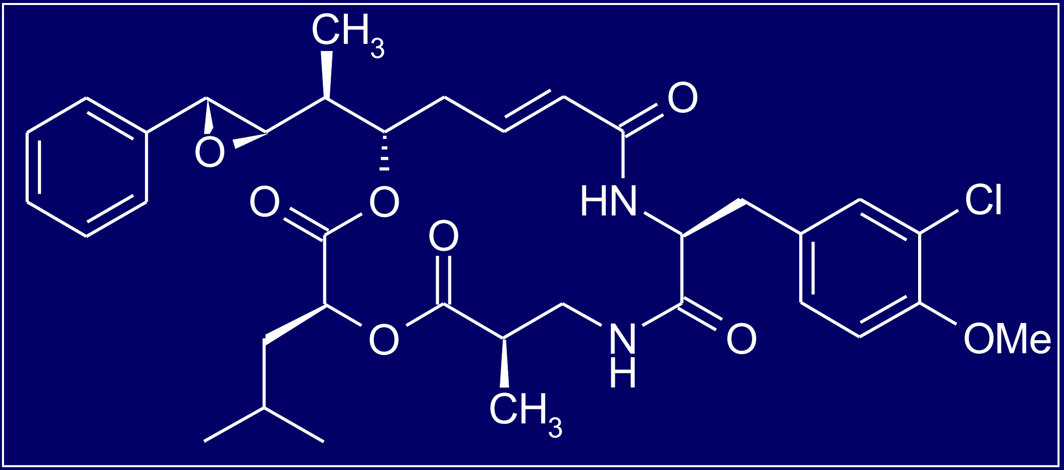
Phaeodactylum

***Tetraselmis* spp.**

Nostoc (bioactive strains)

(Florence, 1994)

Cryptophycin 1



✓Isolated in the 1980s by a group at Merck from *Nostoc* ATCC 53789 and recognized as a potent fungicide.

✓Cryptophycin analogues are extensively studied as potent chemotherapeutic agents against solid tumors and are in phase II clinical trials being run by Eli Lilly.

✓Cryptophycins are obtained exclusively through chemical synthesis (32 steps)

✓The molecular complexity of the compound is modest, but producing enough material to supply clinical trials (i.e. multi-kilogram quantities) is not an easy task.

PROBLEMS IN MASS CULTIVATION OF BIOACTIVE PHOTOTROPHS

GENERAL

✓Low productivity

✓Contamination (maintaining axenicity and monospecificity)

✓Control of parameters (temperature, pH, nutrients, light)

✓Oxygen accumulation

✓Biofouling

✓Polysaccharide production

SPECIFIC

✓Defining conditions for maximum BSM production in culture

✓Loss, alteration or decrease of secondary metabolite production

✓Toxicity against operators and allergenic effects

✓Treatment of the exhaust medium

FUTURE ACTIONS

✓Screening programs must be extended to new areas

✓Understand the physiology of BSM synthesis in mass cultures to stabilise and optimise production.

✓Determine the chemical structure of as many BSM as possible and their mode of action (biochemical target).

✓Develop efficient reactors for mass cultivation of bioactive strains and efficient harvesting and separation techniques.

Bioprocess intensification: optimisation of fermentation yields via media composition and feed strategies, control of physical conditions, induction, genetics, immobilisation and bioreactor engineering (Marwick et al., 1999)

PRODUCTION OF BSM BY CULTURED CYANOBACTERIA

Cryptophycin from *Nostoc* sp. ATCC 53789

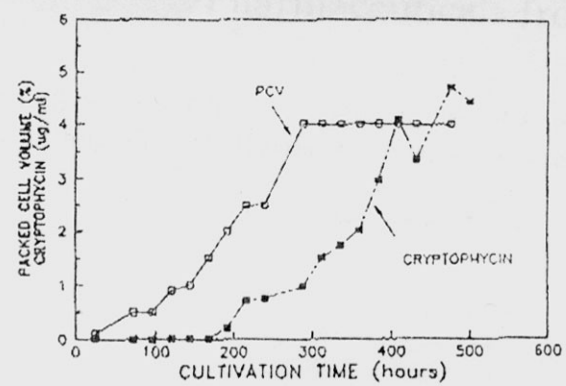
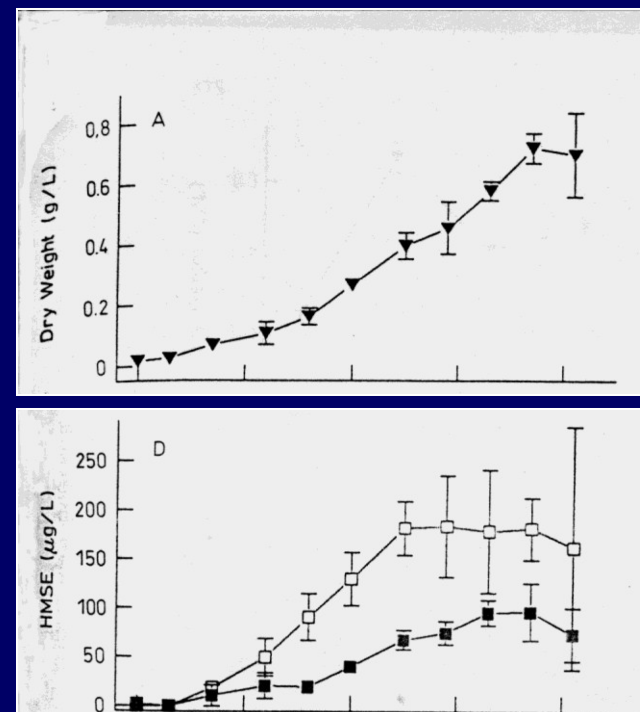


Fig. 6. Time course for *Nostoc* sp. growth and cryptophycin production in a fermentor.

Schwartz et al., 1990

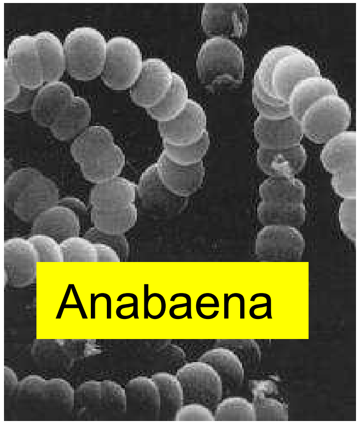
Scytophycin from *Scytonema ocellatum*



Patterson and Bolis, 1993

Cianobatteri

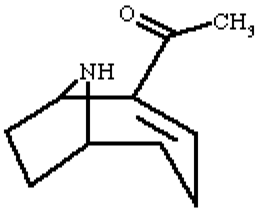
Tossine dei cianobatteri



- **Neurotossine (alcaloidi)**
- Sassitossine
- Anatossine

(Very fast death factor- letale in 4 minuti)

- **Epatotossine (ciclope**
- Microcistine
- Nodularine



ANATOXIN-A

12 generi produttori di tossine

Anabaena

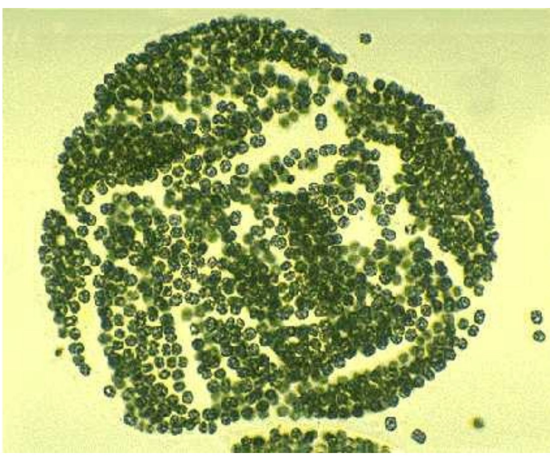
Microcystis

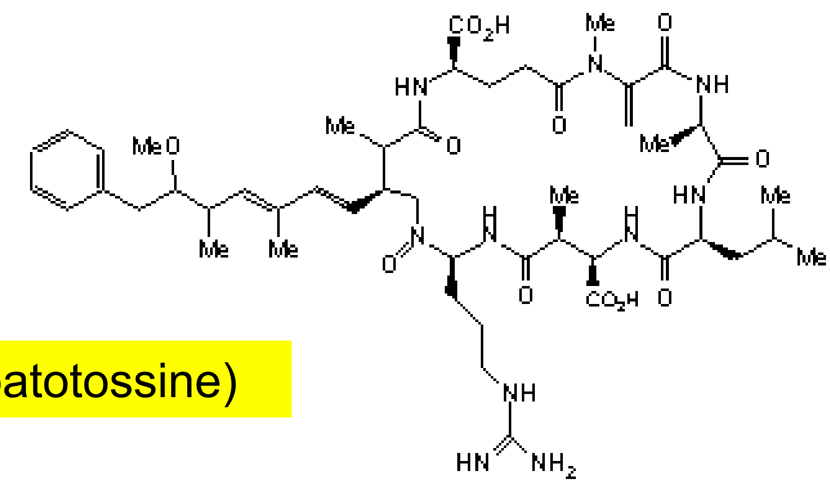
Aphanizomenon

Nodularia

Microcystis

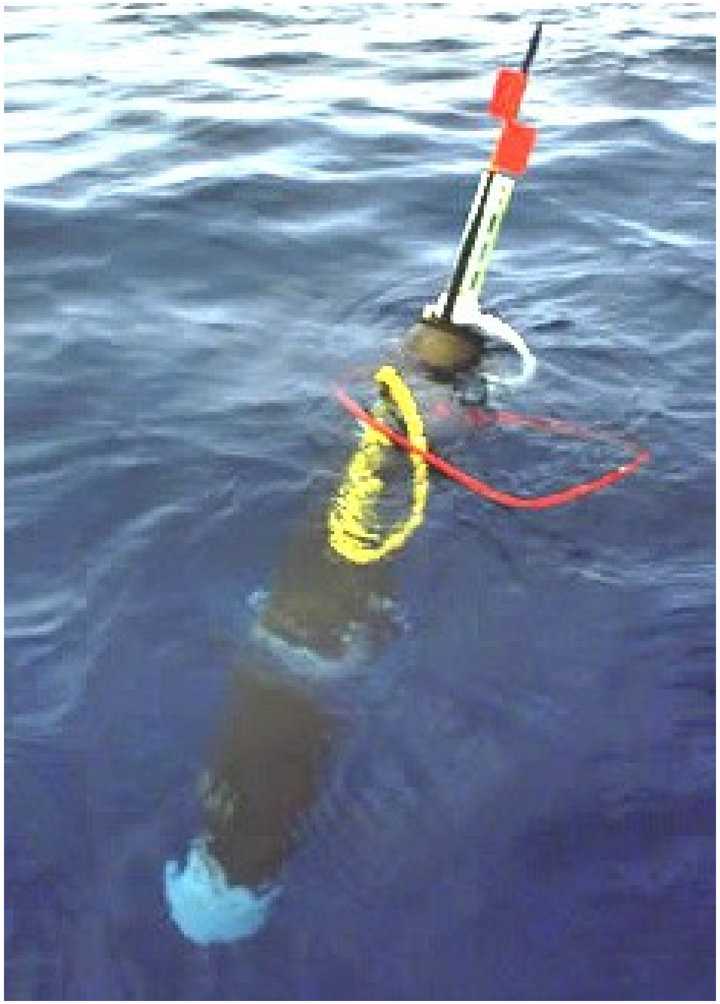
Cellule singole, coloniali, ampia diffusione in acque dolci





Microcistine (potenti epatotossine)

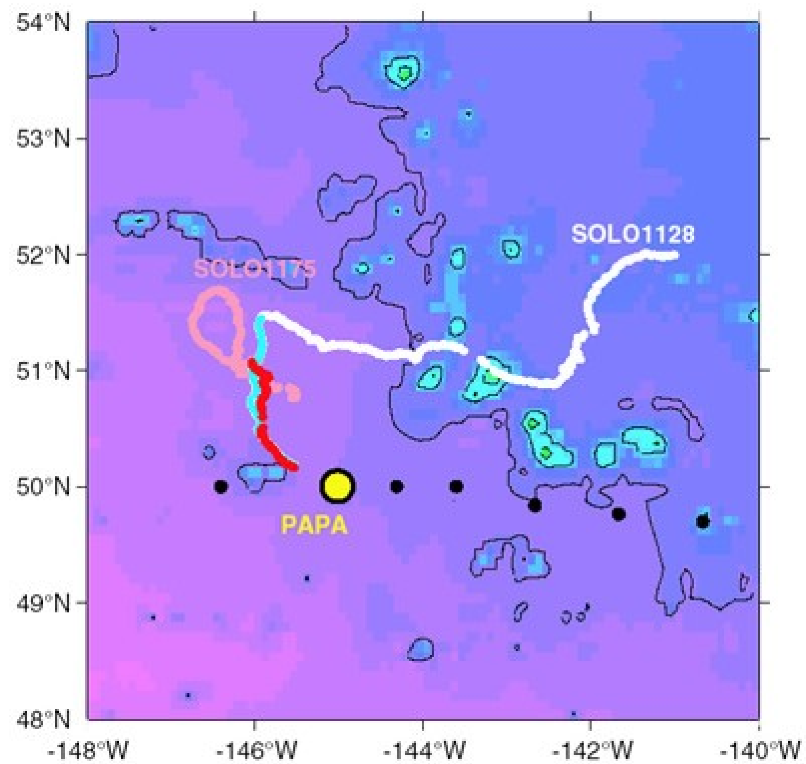
Asian dust storm causes plankton to bloom in the North Pacific. Robotic Carbon Explorers test the "iron hypothesis" in nature *(Science, October 24, 2002)*.



Le sonde si immergono e ritornano periodicamente in superficie per inviare i dati al satellite.

Nella primavera del 2001, due sonde Carbon Explorers (sonde SOLO modificate) vengono rilasciate nel Nord Pacifico.

La crescita del fitoplancton nella zona è limitata da carenza di ferro.

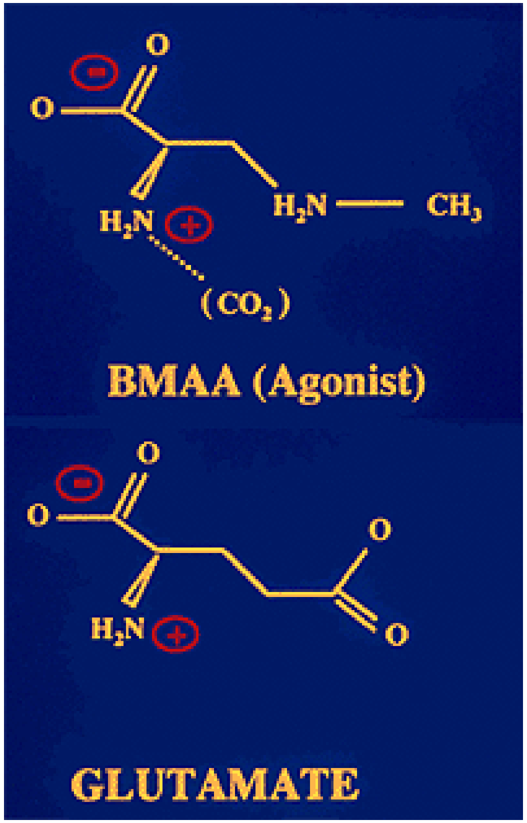


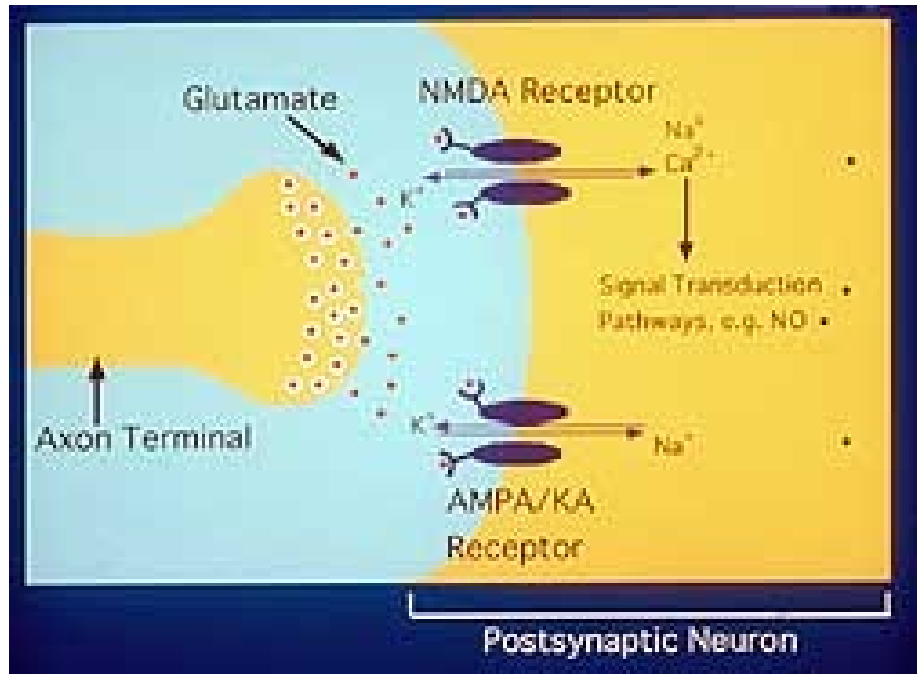
La sclerosi laterale amiotrofica (SLA) e il complesso SLA/Demenza-Parkinson di Guam (SLA-PD)

1. La SLA si manifesta con debolezza generale che progredisce fino a completa paralisi delle braccia, le gambe ed il tronco. I pazienti muoiono dopo 2-6 anni dai primi sintomi per incapacità a deglutire e/o respirare. L'autopsia del midollo e del tessuto cerebrale rivela la morte dei neuroni motori
2. Colpisce gli adulti (prevalentemente l'uomo)
3. Ultimamente si è riscontrato un aumento di incidenza di SLA (oltre 20 volte rispetto alla popolazione) tra i calciatori
4. E' spesso associata ad ambiente rurale e traumi
5. La SLA-PD è endemica tra la popolazione Chamorro dell'isola di Guam nel Pacifico
6. Sarebbero entrambe causate da una neurotossina, la BMAA, fino a poco fa ritenuta presente solo nelle cycas
7. La BMAA sarebbe implicata anche in altre malattie degenerative del SNC (Alzheimer, Parkinson)

La BMAA (β-N-metilammino-L-alanina)

La BMAA è un aminoacido non proteico con azione neurotossica (agonista del glutamato)





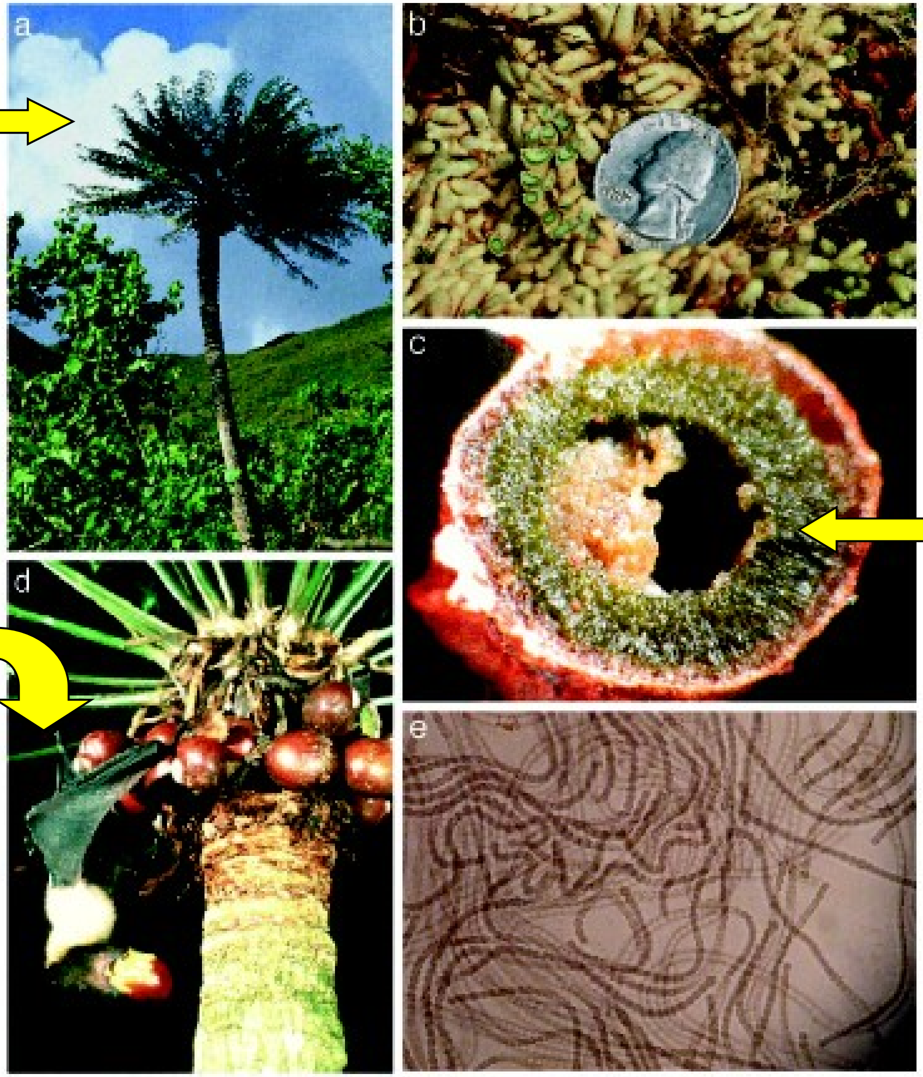
Nel 1966, Vega e Bell identificano una neurotossina, la BMAA, in *Cycas micronesia.* Allora venne escluso che potesse essere implicata in malattie degenerative del SNC (tipo SLA-PD) perché, vista la sua presenza limitata a specie arboree tropicali e le basse concentrazioni, non si ritenne possibile l'ingestione in quantitivi tossici (Charlton, 1992)

(Cox et al., PNAS, 2003)

Anche le foglie contengono BMAA (sapore amaro deterrente contro erbivori?)

Le volpi volanti si nutrono dei semi di cicas che contengono BMAA.

Sono al loro volta cibo dei Chamorro che le mangiano, in occasione di festività, bollite in latte di cocco.



I nostoc vivono in simbiosi nelle radici coralloidi. Le radici coralloidi contengono la BMAA.

Le radici non colonizzate non hanno BMAA.

Fig. 2. *C. micronesica* Hill. (*a*) Habit in South Guam as a 4-m-tall unbranched tree. (*b*) Positively geotropic coralloid roots with tips cut to show zone of cyanobacterial invasion. (*c*) Cross section of coralloid root showing green ring of cyanobacterial growth. (*d*) *P. mariannus* feeding on fleshy sarcotesta of seed (photo courtesy of Merlin Tuttle, Bat Conservation International). (*e*) Cyanobacteria of the genus *Nostoc* cultured from the coralloid roots.

(Cox et al., PNAS, 2005)

PNAS
Proceedings of the National Academy of Sciences of the United States of America

E' di qualche mese fa (5.04.05) la pubblicazione di un articolo su PNAS online che ha fatto in breve il giro del mondo.

Tutti i cianobatterici (non solo i simbionti) possono produrre BMAA

Proc Natl Acad Sci U S A. 2005 April 5; 102(14): 5074–5078.
doi: 10.1073/pnas.0501526102. Published online 2005 April 4.

Ecology

Diverse taxa of cyanobacteria produce β-*N*-methylamino-L-alanine, a neurotoxic amino acid

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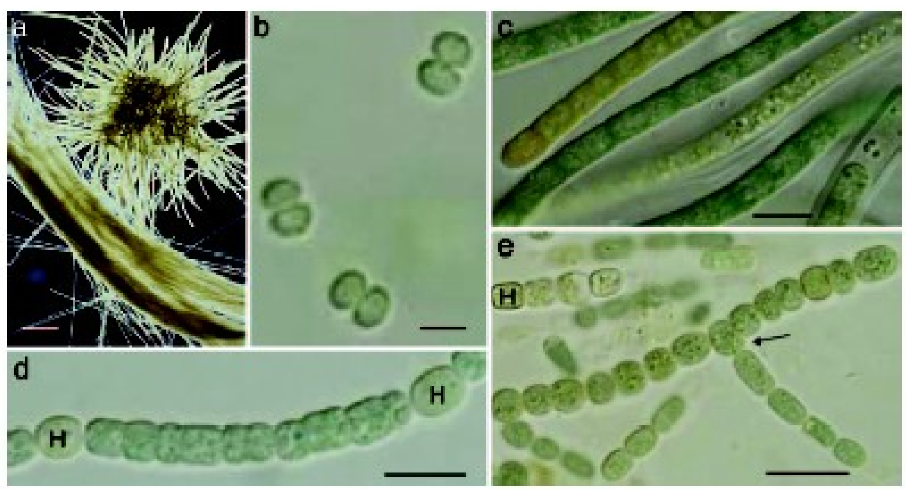

Fig. 1. Cyanobacterial strains that produce BMAA representing different morphological sections. (*a*) The bloom-forming, filamentous, and colony-forming *Trichodesmium thiebautii* (section III). (Scale bar: 100 μm.) (*b*) The unicellular *Synechococcus* PCC 6301 (section I). (Scale bar: 1 μm.) (*c*) The filamentous *Symploca* PCC 8002 (section III). (Scale bar: 10 μm.) (*d*) The filamentous, nonbranching, and heterocystous (H) *Nostoc* PCC 7107 (section IV). (Scale bar: 10 μm.) (*e*) The filamentous, heterocystous (H) and branching (arrow) *Fischerella* PCC 7521 (section V). (Scale bar: 15 μm.)

29 ceppi positivi su 30 testati

Table 2. BMAA in free-living cyanobacteria

Cyanobacterial species/strain	Section*	Habitat	Origin	Free BMAA, μg/g	Protein BMAA, μg/g
Microcystis PCC 7806	I	Freshwater	The Netherlands	4	6
Microcystis PCC 7820	I	Freshwater	Scotland	6	12
Prochlorococcus marinus CCMP1377	I	Marine	Sargasso Sea	32†	57†
Synechocystis PCC 6308	I	Freshwater	U.S.A.	ND	ND
Synechococcus PCC 6301	I	Freshwater	U.S.A.	25	ND
Chroococcidiopsis indica GQ2-7	II	Marine coral	Unknown	435	76
Chroococcidiopsis indica GT-3-26	II	Marine rock	Unknown	1,306	5,415
Myxosarcina burmensis GB-9-4	II	Marine coral	Marshall Islands	79	1,943
Myxosarcina concinna GT-7-6	II	Marine coral	Unknown	1,501	960
Lyngbya majuscula	III	Marine	Zanzibar	32	4
Planktothrix agardhii NIES 595	III	Freshwater	Northern Ireland	318	30
Plectonema PCC 73110	III	Unknown	Unknown	155	150
Phormidium	III	Unknown	Unknown	11	270
Symploca PCC 8002	III	Marine, intertidal	U.K.	3	262
Trichodesmium thiebautii	III	Marine	Caribbean	145	8
Trichodesmium CCMP1985	III	Marine, coastal	North Carolina	13†	17†
Anabaena PCC 7120	IV	Unknown	U.S.A.	32	ND
Anabaena variabilis ATCC 29413	IV	Freshwater	U.S.A.	35	ND
Aphanizomenon flos-aquae	IV	Marine	Baltic Sea	ND	866
Cylindrospermopsis raciborskii CR3	IV	Freshwater	Australia	6,478	14
Nodularia spumigena	IV	Brackish water	Baltic Sea	16‡	50‡
Nodularia harveyana CCAP 1452/1	IV	Marine	Unknown	20	11
Nostoc 268	IV	Brackish Water	Baltic Sea	34	274
Nostoc PCC 6310	IV	Freshwater	Israel	42	ND
Nostoc PCC 7107	IV	Freshwater	U.S.A.	27	1,772
Nostoc sp. CMMED 01	IV	Marine	Hawaiian Islands	1,243	1,070
Calothrix PCC 7103	IV	Unknown	Unknown	13‡	92‡
Chlorogloeopsis PCC 6912	V	Soil	India	758	ND
Fischerella PCC 7521	V	Yellowstone, hot spring	U.S.A.	44	175
Scytonema PCC 7110	V	Limestone cave	Bermuda	ND	1,733

ND, not detected.

*Morphological groupings are as defined in ref. 1. Section I, unicellular cyanobacteria that reproduce by binary fusion or budding; section II, unicellular cyanobacteria that reproduce by multiple fission or by both multiple fission and binary fission; section III, filamentous, nonheterocystous cyanobacteria that divide in one plane; section IV, filamentous, heterocystous cyanobacteria that divide in only one plane; section V, heterocystous, filamentous cyanobacteria that divide in more than one plane.

†Estimate of concentration based on <1 mg dry weight of sample.

‡BMAA was not detected in all samples of this isolate.

Cox et al. PNAS, 2005

Se si dimostrasse con certezza la relazione tra BMAA e SLA e le altre malattie degenerative, i risultati dell'indagine di Cox et al. (2005) aprirebbero scenari preoccupanti:

1. La produzione di BMAA non è limitata alle sole cycas o alle simbiosi cianobatteriche, ma si estende a tutti gli ambienti colonizzati da cianobatteri (dai deserti ai laghi nordici, dai tropici all'Antartide)
2. Se si confermano i dati di concentrazione ritrovati nei cianobatteri liberi, dobbiamo pensare a milioni di tonnellate di BMAA introdotti nell'ambiente dai cianobatteri
3. I cianobatteri sono alla base di molte catene alimentari e quindi è possibile la biomagnificazione, come dimostra il caso di Guam. Ci sono ungulati che si alimentano quasi esclusivamente di licheni come *Peltigera*
4. Trova spiegazione il caso dei Canadesi morti di Alzheimer?
5. Vi sono altri microrganismi potenziali produttori?