

Biological effects of cyanobacterial peptides – research on human brain cells in culture

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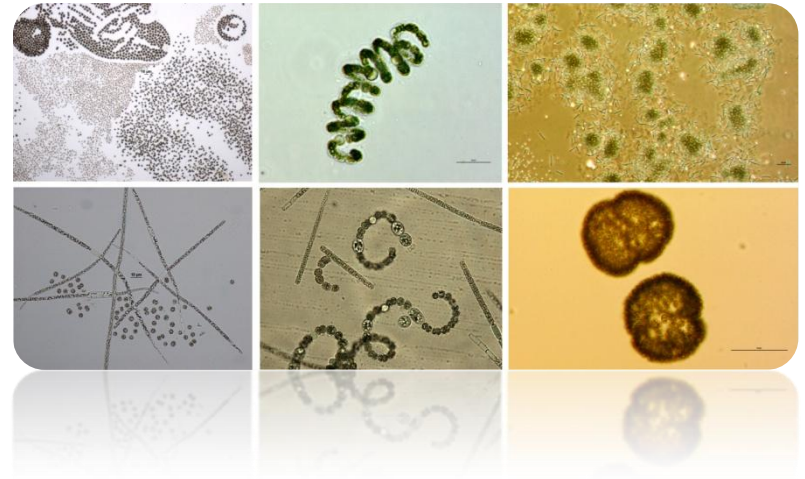
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INTRODUCTION

Cyanobacteria



- cyanobacterial mass occurrences
- production of secondary metabolites with variety of activities

↳ ecological

↳ biochemical

↳ biological

...



Cyclic cyanopeptides (CCP)

• **Microcystins** (MC-LR, MC-RR, ...) → **toxic CCP**

• **Depsipeptides**

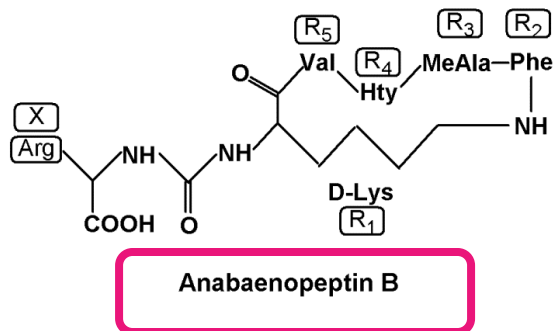
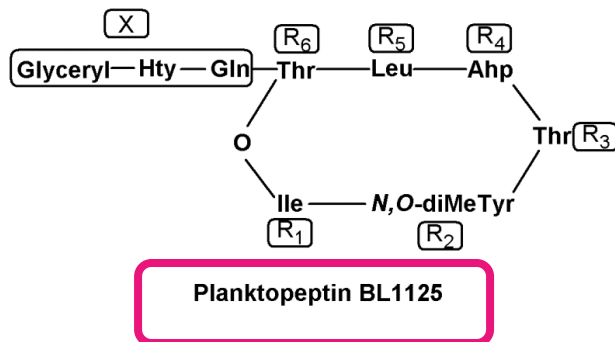
• **Anabaenopeptins**

• **Microviridins**

• **Microginins**

• **Aeruginosins ...**

} **“non-toxic” CCP**



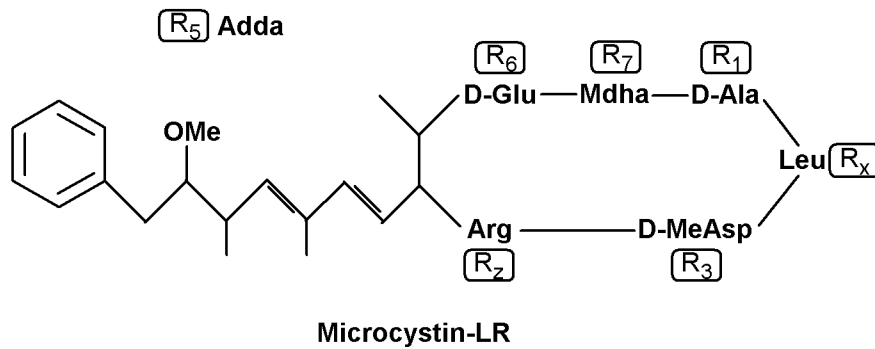
Non-hepatotoxic CCP (n-hCCP):
PP BL1125

AnP B

AnP F

Cyclic cyanopeptides (CCP)

Microcystins



HEPATOTOXICITY

Inhibitor of protein phosphatases 1 and 2a (PP-1, PP-2a) in nM range

Also brain, lungs, kidney, heart,...

Research on human brain cells in culture

n-hCCPs



ASTROCYTES (brain cells *in vitro*)



NORMAL astrocytes

NHA



TUMOR astrocytes

U87




SELECTIVE TOXICITY?



Comparison with MC-LR (hCCP)

Research on human brain cells in culture

- CYTOTOXICITY
- CELL PROLIFERATION
- CELL CYTOSKELETON ORGANIZATION
- EXPRESSION OF CELL CYTOSKELETON ELEMENTS
- EXPRESSION PROFILE OF CELL CYTOSKELETON REGULATORS

 protein phosphatases -1 and -2a inhibitory potential
(inhibition in μM range)

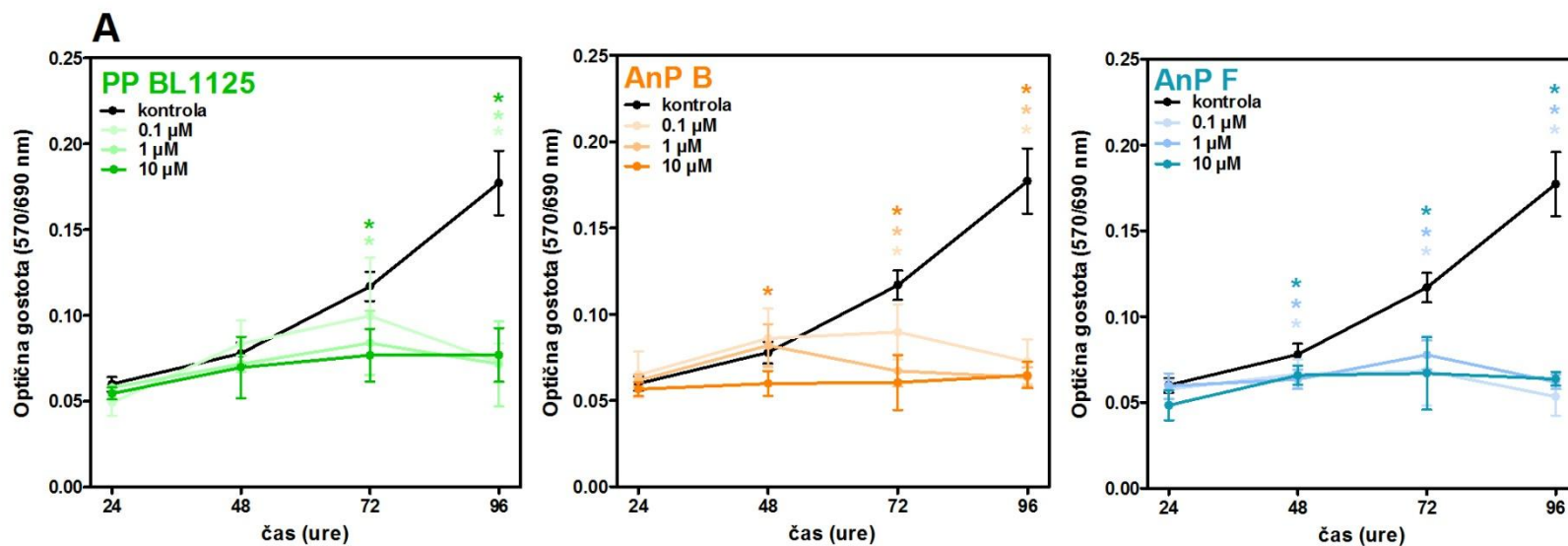
Enzyme	Inhibitor (CCP)	IC ₅₀
PP-1	MC-LR	(5,0 ± 1,6) nM
	PP BL1125	(131,5 ± 87,5) μM
	AnP B	(9,5 ± 0,9) μM
	AnP F	(28,2 ± 3,4) μM
PP-2a	MC-LR	(0,048 ± 0,01) nM
	PP BL1125	(18,2 ± 15,7) μM
	AnP B	(12,3 ± 6,1) μM
	AnP F	(1,04 ± 0,24) μM

RESULTS

NHA \neq U87

- CYTOTOXICITY and CELL PROLIFERATION

- cytostatic effect of n-hCCP on NHA



RESULTS

- **CELL CYTOSKELETON ORGANIZATION** - similar effect on actin, tubulin and intermediate filaments (nestin, GFAP) in both cells, but more pronounced when treated with MC-LR (correlation with PPs inhibition)
- **EXPRESSION OF CELL CYTOSKELETON ELEMENTS** – different effects on mRNA expression (*ACTB*, *TUBA1A*, *NES*, *GFAP*)
- **EXPRESSION PROFILE OF CELL CYTOSKELETON REGULATORS** – all CCPs alter the expression of several genes of the regulatory proteins (NHA > U87)

CONCLUSIONS

- The brain is a very important target for cyanobacterial toxins
- MC-LR and selected n-hCCPs influence the cell cytoskeleton in normal and tumour astrocytes
 - the influence is very complex and involves different signalling pathways, related to protein phosphatases.

It is important to emphasize, that not only MC, but also other CCP can induce damage.



very important for human health, risk assessment and implementation of sanitation measures.