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UNIVERSIDAD DE CHILE



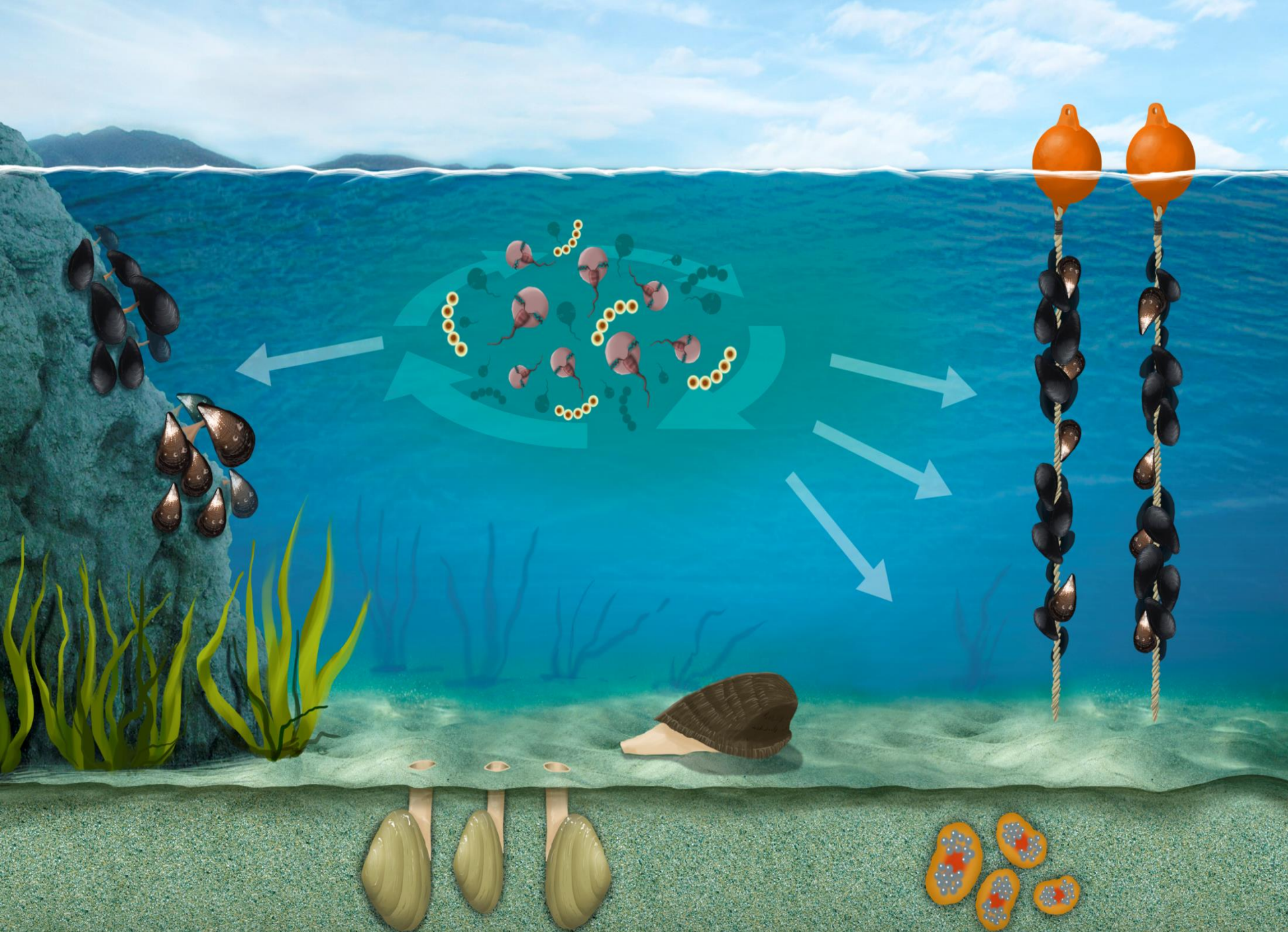
FONDECYT
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“COMPOSICIÓN, DISTRIBUCIÓN Y METABOLISMO DE TOXINAS DEL GRUPO ACIDO OKADAICO Y SAXITOXINAS EN INVERTEBRADOS MARINOS ENDÉMICOS DEL SUR AUSTRAL DE CHILE”

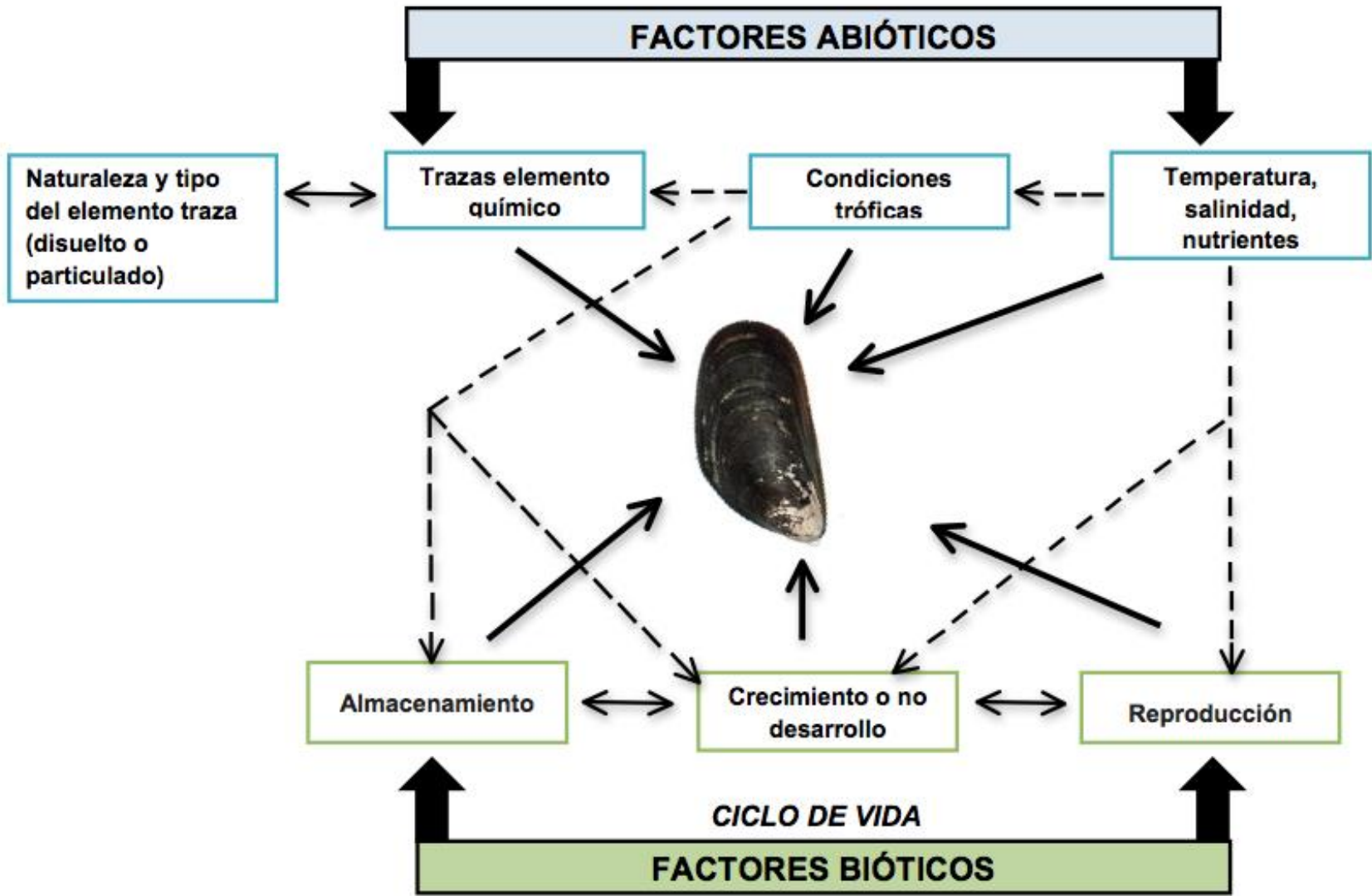
Carlos García M.
P.I. Conicyt/Fondecyt-Regular N° 1160168

Datos de Investigación

- **Área de estudio:** Sector Islas Huichas, Región de Aysén, Chile.
- **Evaluaciones:** 2010, 2012, 2013, 2014, 2015 y 2016.
- **Autorizaciones Sanitarias:** 130, 831, 1178, 1180, 1163 y 413.
- **Aprobación de Comité Bioética.**
- **Unidad de Bioseguridad.**

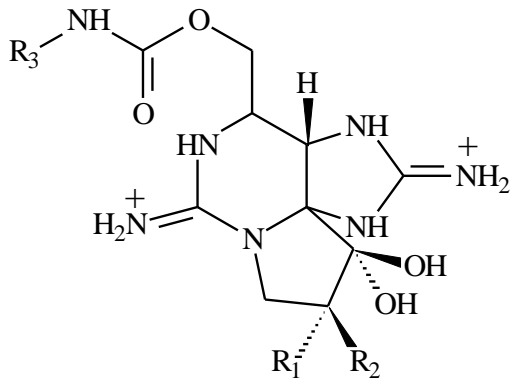


FANs sobre organismos de estratos rocosos, fondos blandos, carnívoros y centros de cultivos (García et al., 2017).



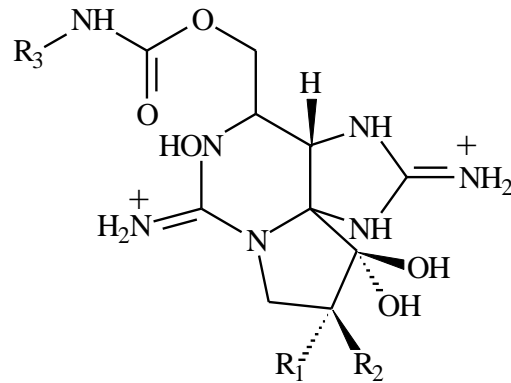


Grupo Saxitoxina (STX).



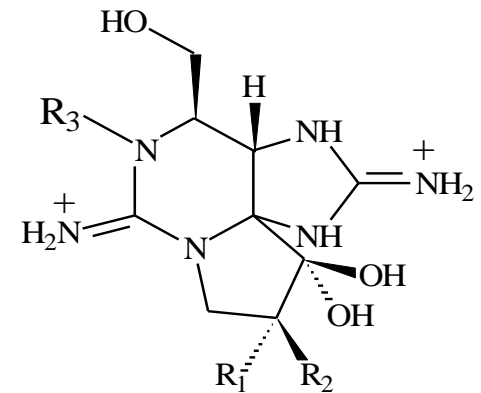
N1-HType

	R ₁	R ₂	R ₃
STX	H	H	H
GTX5	H	H	SO ₃ ⁻
GTX2	OSO ₃ ⁻	H	H
GTX3	H	OSO ₃ ⁻	H
C1	OSO ₃ ⁻	H	SO ₃ ⁻
C2	H	OSO ₃ ⁻	SO ₃ ⁻



N1-OHType

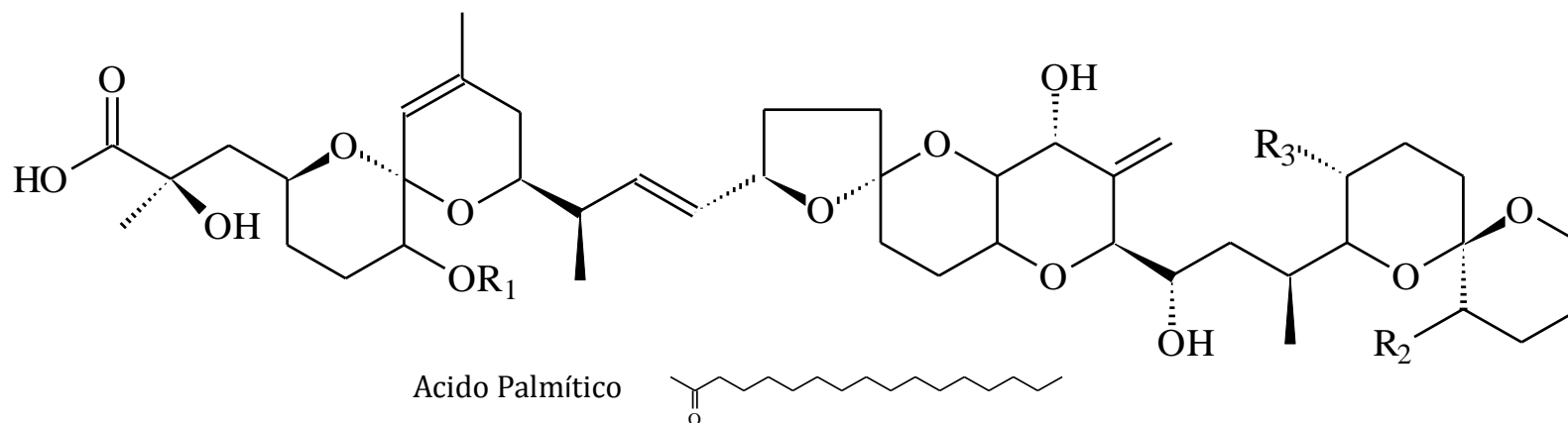
	R ₁	R ₂	R ₃
neoSTX	H	H	H
GTX6	H	H	SO ₃ ⁻
GTX1	OSO ₃ ⁻	H	H
GTX4	H	OSO ₃ ⁻	H
C3	OSO ₃ ⁻	H	SO ₃ ⁻
C4	H	OSO ₃ ⁻	SO ₃ ⁻



Decarbamoyl-PSP-Toxins

	R ₁	R ₂	R ₃
dcSTX	H	H	H
dcneoSTX	H	H	OH
dcGTX1	OSO ₃ ⁻	H	OH
dcGTX2	OSO ₃ ⁻	H	H
dcGTX3	H	OSO ₃ ⁻	H
dcGTX4	H	OSO ₃ ⁻	OH

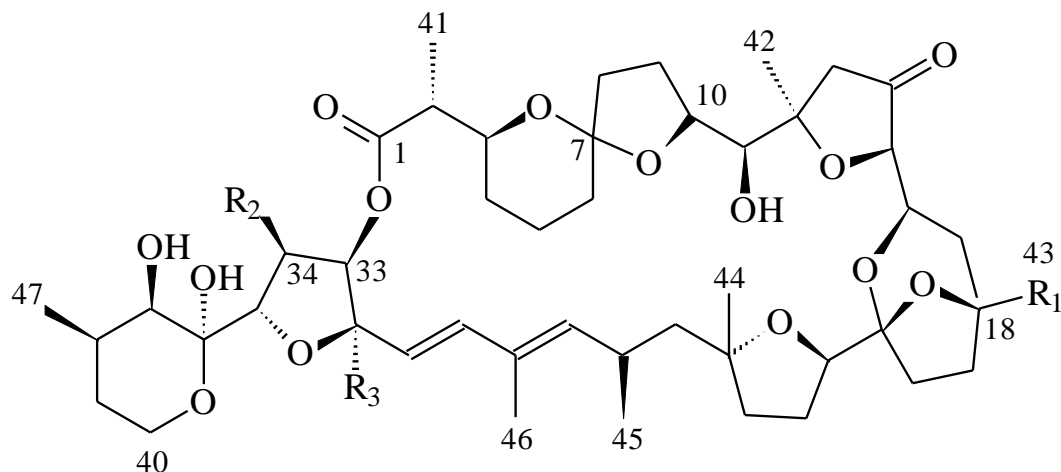
Grupo Ácido Okadaico (AO).



Nombres		R ¹	R ²	R ³
Acido Okadaico	(AO)	H	H	CH ₃
Dinofisistoxina-1	(DTX-1)	H	CH ₃	CH ₃
Dinofisistoxina-2	(DTX-2)	H	CH ₃	H
Dinofisistoxina-3	(DTX-3)	Acyl	CH ₃	CH ₃

Estructuras químicas de toxinas del grupo-AO. R indica la substitución del radical aplicado a cada estructura de acuerdo al nombre de la toxina. Ácido palmítico corresponde al ácido graso de mayor porcentaje detectado en la posición R1 de DTX-3.

Grupo - Pectenotoxinas (PTXs).

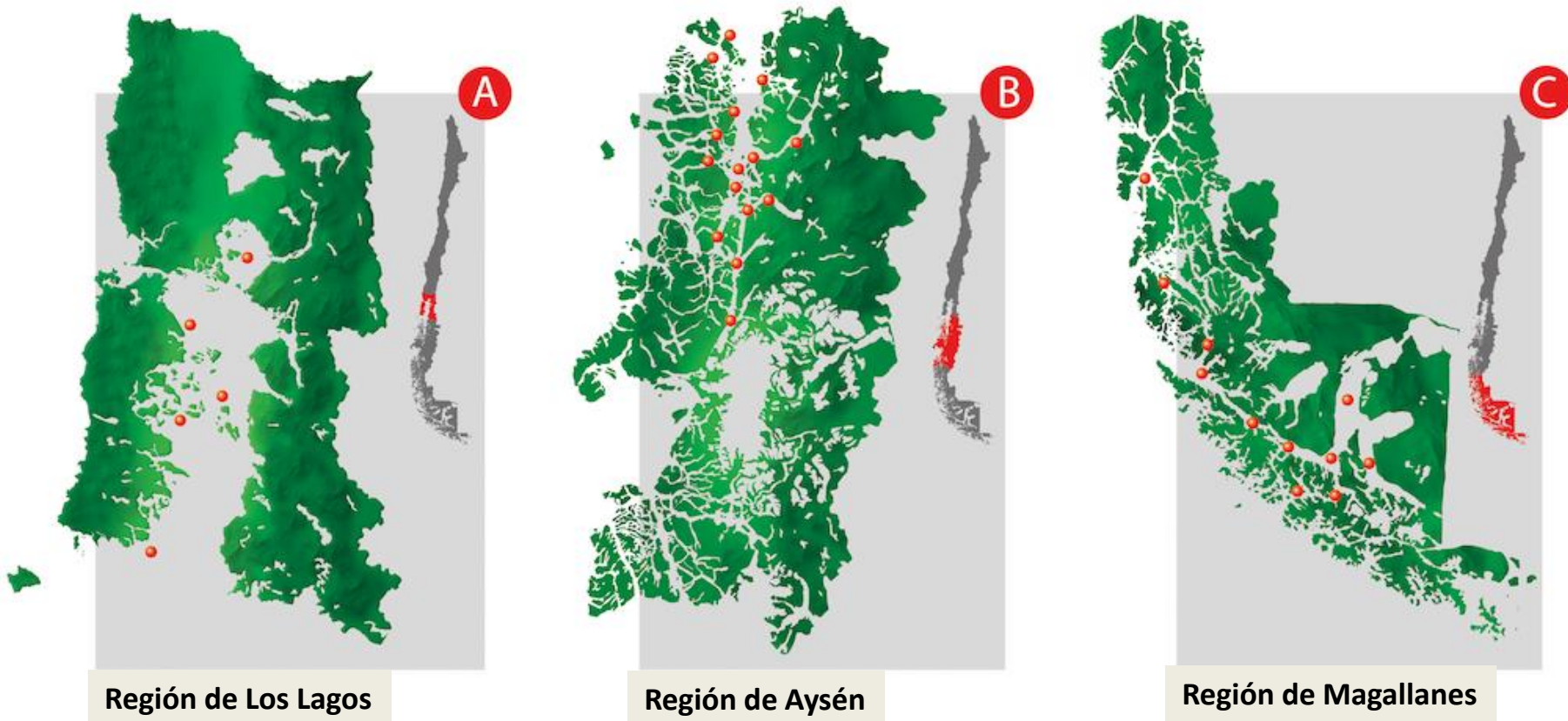


Nombres	R ¹	R ²	R ³	C-7
Pectenotoxina-1 (PTX-1)	CH ₃ OH	H	H	R
Pectenotoxina-2 (PTX-2)	CH ₃	H	H	R
Pectenotoxina-2b (PTX-2b)	CH ₃	H	H	S
Pectenotoxina-3 (PTX-3)	CHO	H	H	R
Pectenotoxina-4 (PTX-4)	CH ₂ OH	H	H	S
Pectenotoxina-6 (PTX-6)	COOH	H	H	R
Pectenotoxina-7 (PTX-7)	COOH	H	H	S
Pectenotoxina-11 (PTX-11)	CH ₃	OH	H	R
Pectenotoxina-11b (PTX-11b)	CH ₃	OH	H	S
Pectenotoxina-13 (PTX-13)	CH ₃	H	OH	R

Estructuras químicas correspondientes al grupo-PTXs.

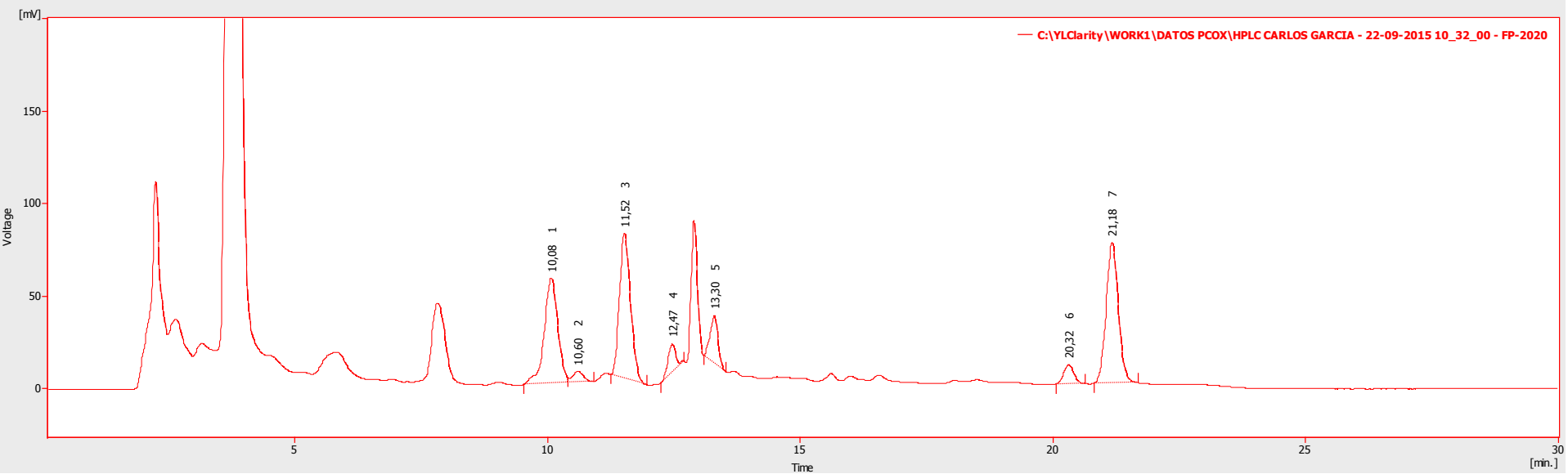
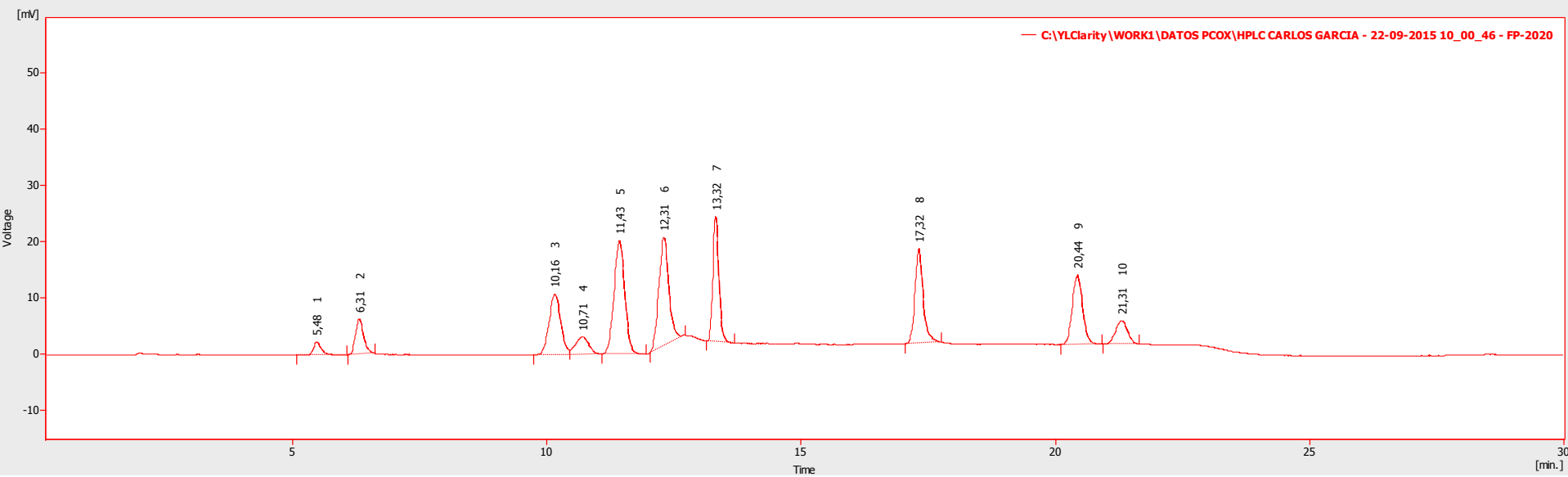
R indica la substitución del radical aplicado a cada estructura de acuerdo al nombre de la toxina.

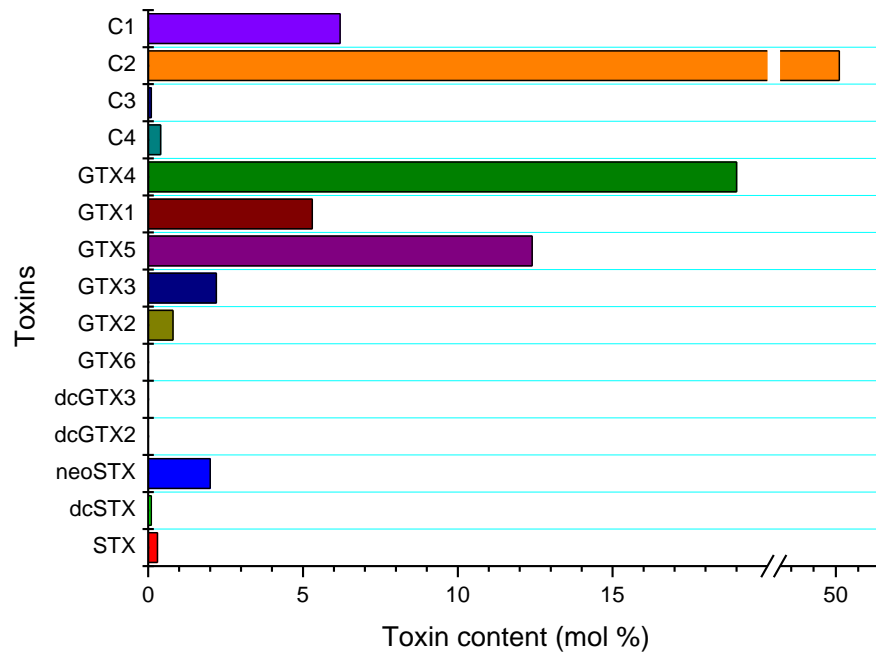
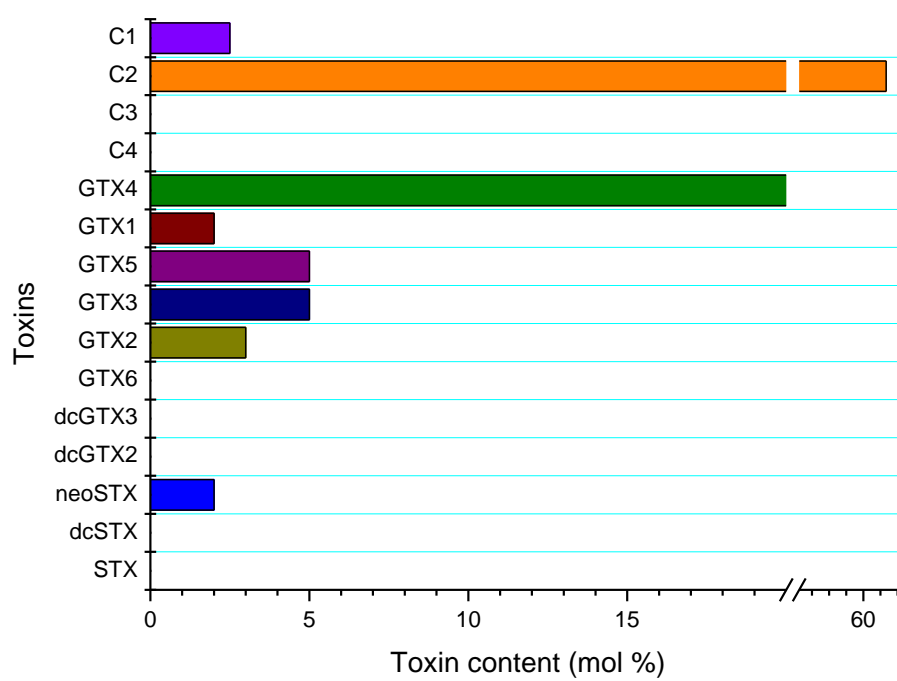
Zonas identificadas en el sur de Chile con FANs

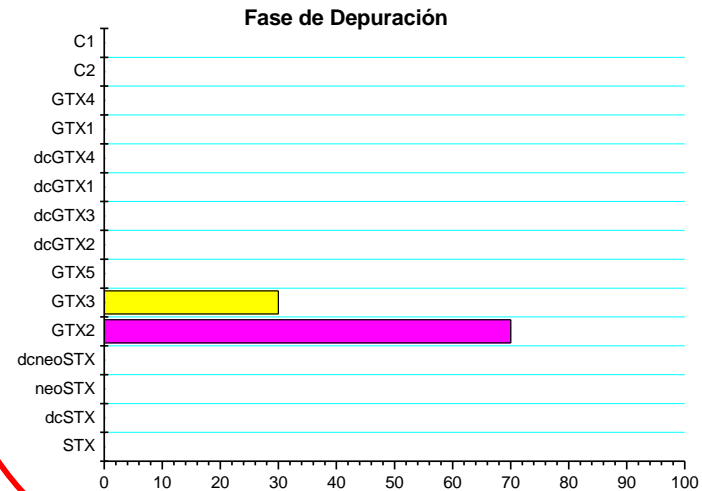
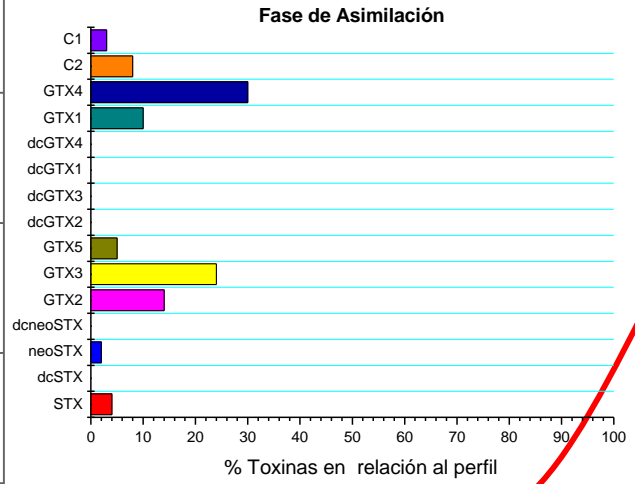
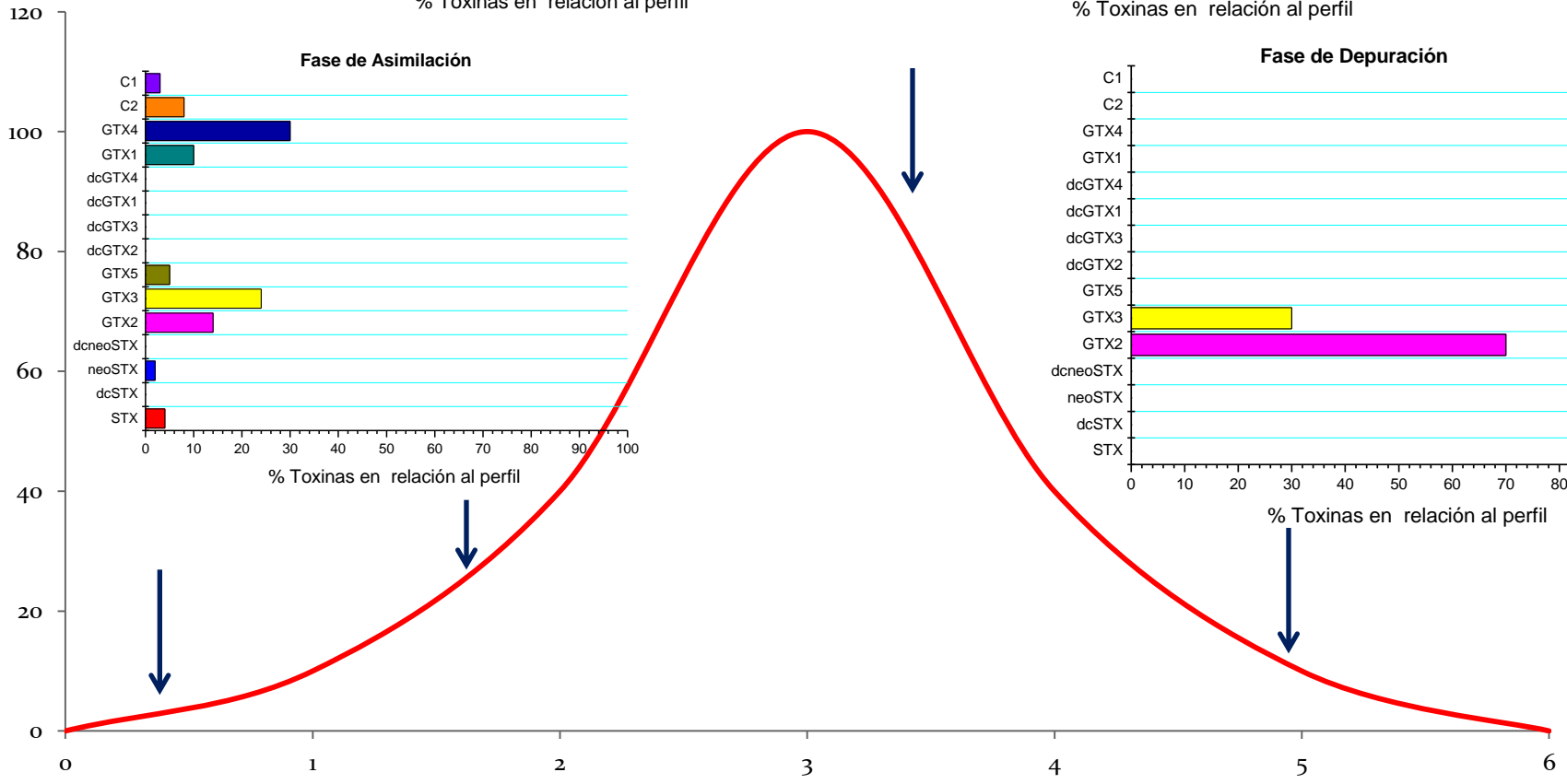
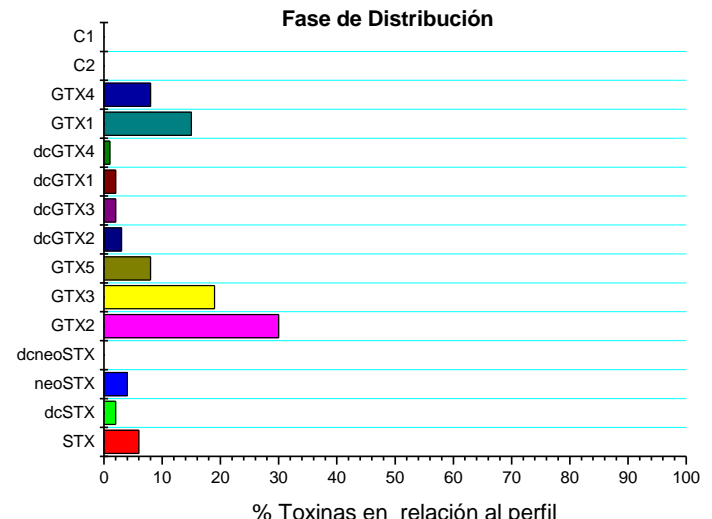
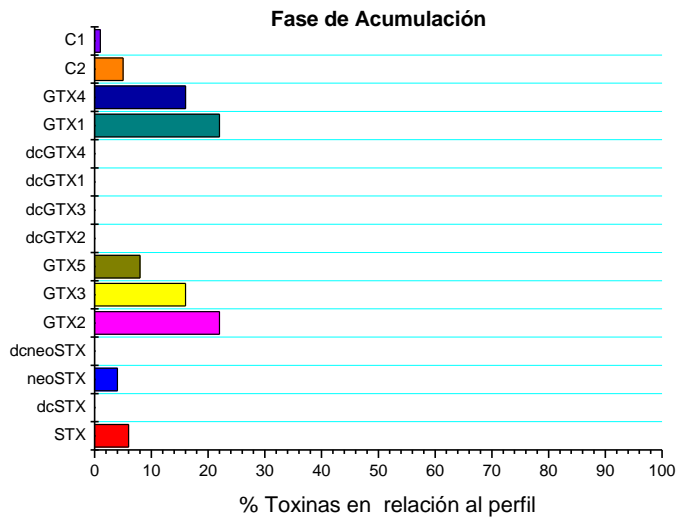


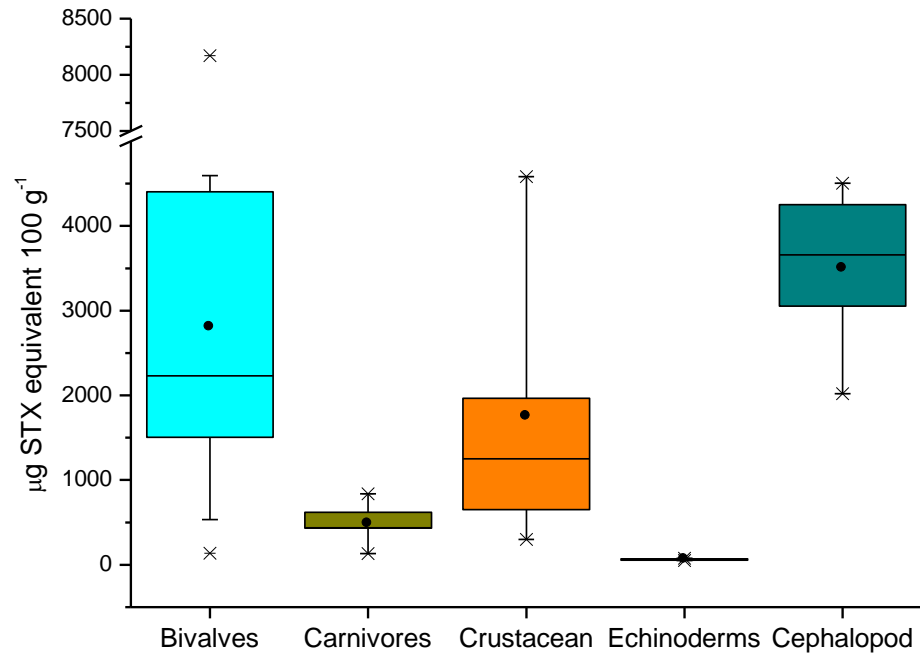
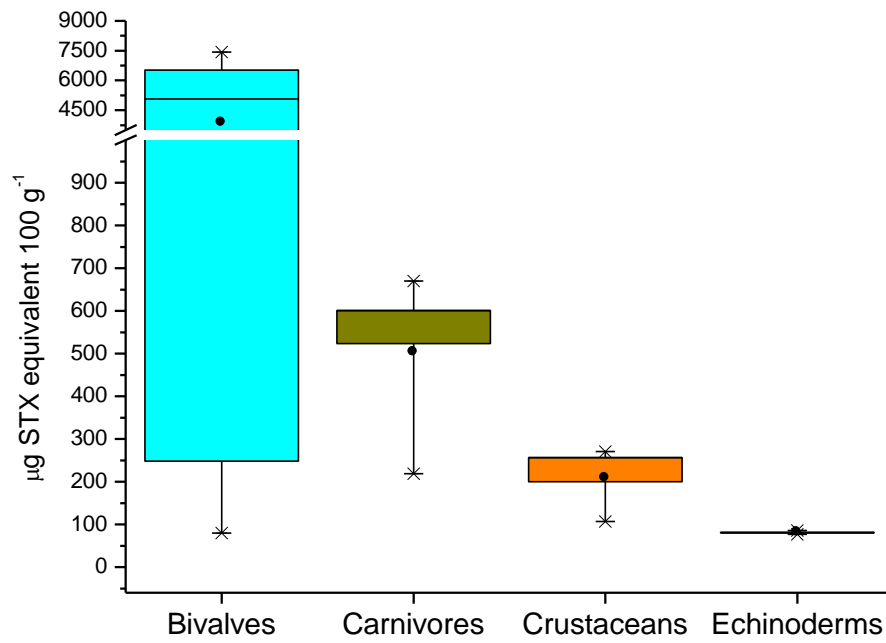
(García et al., 2013).

Grupo	Saxitoxina	Acido Okadaico
Origen	<i>Alexandrium catenella</i> <i>Alexandrium ostenfeldii</i>	<i>Dinophysis acuta</i> <i>Dinophysis acuminata</i> <i>Prorocentrum sp.</i>
Tipo de toxinas	Hidrofílicas	Lipofílicas
Análogos	≈ 50 Saxitoxina neoSaxitoxina Gonyautoxinas	≈ 15 dinofisistoxinas 1-3 acyl-derivados
Métodos de detección	Bioensayo ratón (AOAC 2000) LC-pre-COX (AOAC 2005.06) LC-PCOX (AOAC 2011.02)	LC-MS/MS
Límite regulatorio	80 µg/ 100 g	160 µg kg









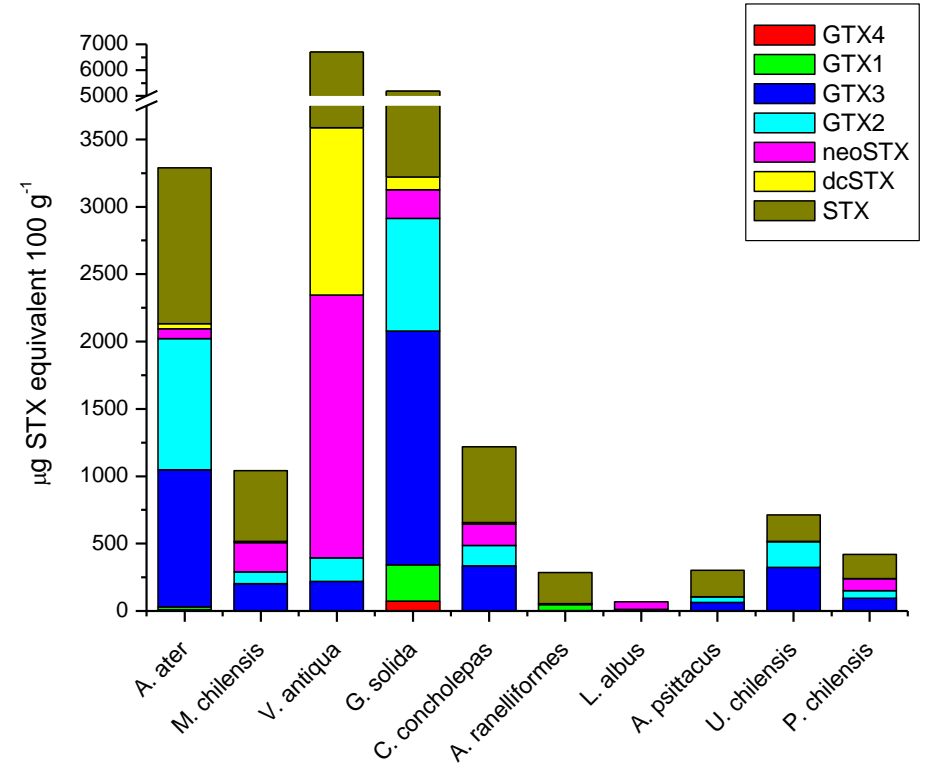
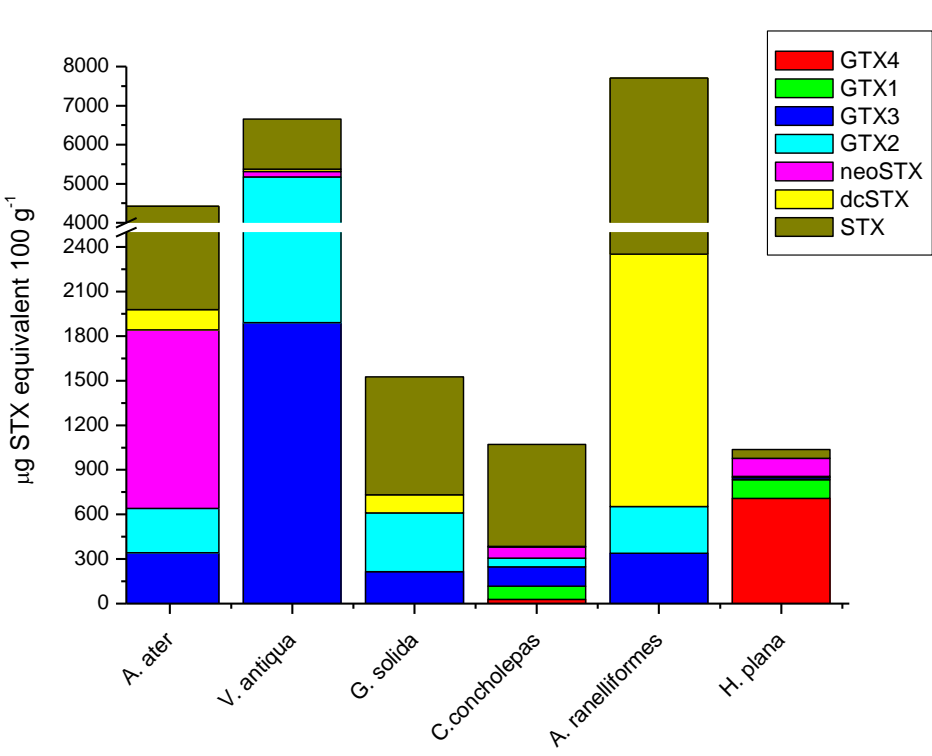
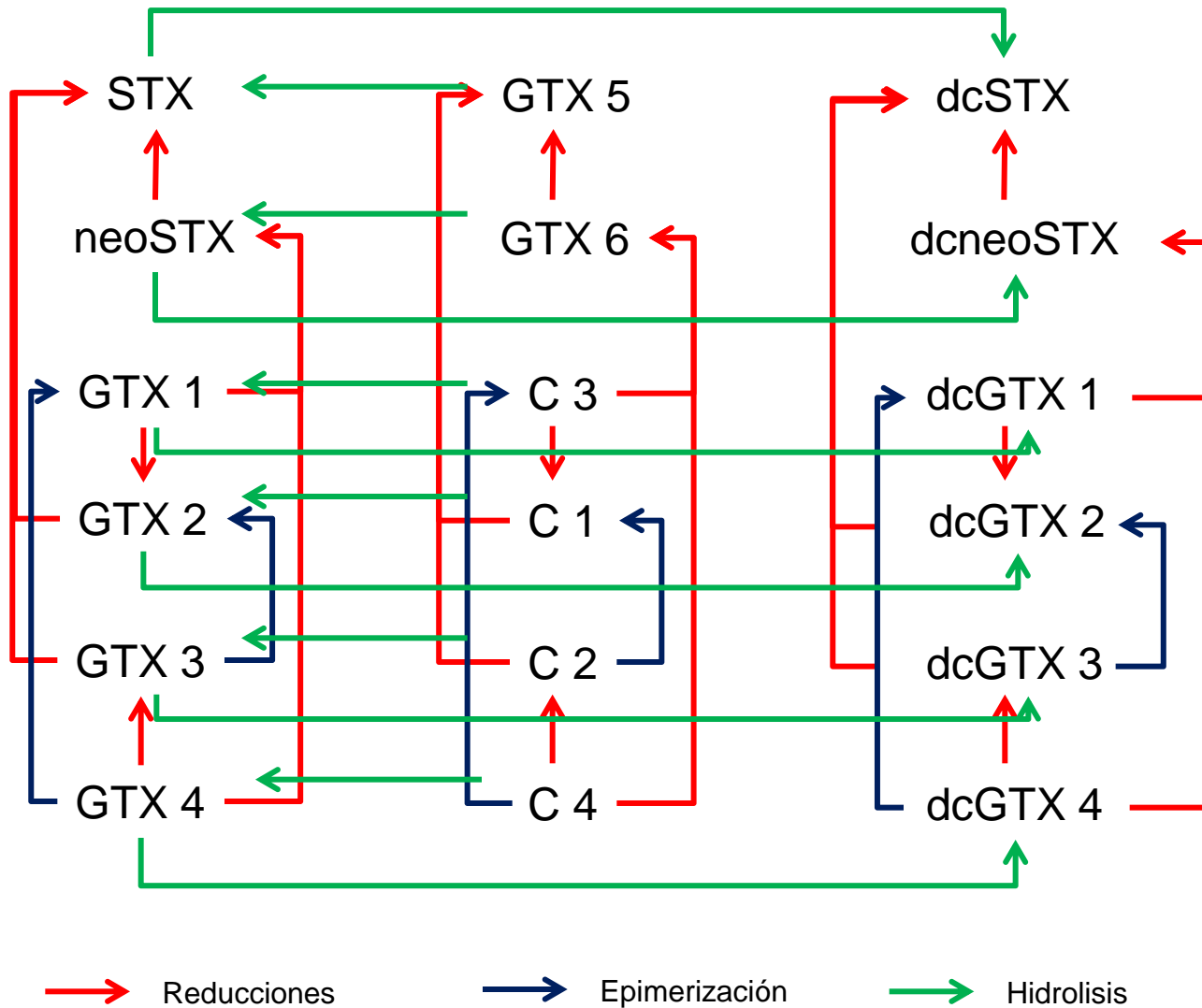


Table 1. STX-group toxin contents in edible parts (visceral and non-visceral tissues) of marine organisms (bivalves and gastropods) collected from Huichas Island, Region of Aysén. Values expressed in $\mu\text{g } 100 \text{ g}^{-1}$ and total toxicity in $\mu\text{g STX eq } 100 \text{ g}^{-1}$. n.d., none detected.

Species/common name	Tissue	Toxins ($\mu\text{g } 100 \text{ g}^{-1}$)							Total
		neoSTX	STX	GTX4	GTX1	GTX5	GTX3	GTX2	$\mu\text{g STX eq } 100 \text{ g}^{-1}$
<i>Venus antiqua</i> /Chilean clam	Adductor muscle	n.d.	n.d.	n.d.	n.d.	28 ± 0.1	n.d.	n.d.	28 ± 0.1
	Foot	n.d.	n.d.	n.d.	n.d.	1.1 ± 0.1	n.d.	n.d.	1.1 ± 0.01
	Digestive gland	n.d.	13.7	1.6 ± 0.1	18.2 ± 0.1	49 ± 0.1	10.9 ± 0.1	1.6 ± 0.1	95 ± 0.1
<i>Gari solida</i> /Pacific clam	Foot	41.1 ± 0.5	n.d.	< LOQ	1.6 ± 0.6	8.3 ± 0.2	< LOQ	0.72 ± 0.1	54 ± 0.4
	Digestive glands	4.4 ± 0.1	9.4	16.7 ± 0.1	142.7	1683.2	622.6	753.5	3232 ± 5.2 *
<i>Tagelus dombeii</i> /razor clam	Foot	n.d.	n.d.	9.9 ± 0.1	96.6 ± 0.7	n.d.	6.6 ± 0.3	1.0 ± 0.1	114 ± 1.2
	Digestive glands	n.d.	n.d.	n.d.	n.d.	147 ± 0.9	< LOQ	0.8 ± 0.5	148 ± 1.4
<i>Aulacomya ater</i> /ribbed mussel	Mantle	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
	Digestive glands	n.d.	n.d.	15.6 ± 0.1	6.3 ± 0.1	n.d.	124.4 ± 0.2	58.9 ± 0.1	205 ± 1.5
	Adductor muscle	n.d.	n.d.	n.d.	n.d.	n.d.	0.50	0.50	1.0 ± 0.01
<i>Mytilus chilensis</i> /blue mussel	Mantle	n.d.	n.d.	196.1 ± 1.1	9.3 ± 0.6	n.d.	n.d.	n.d.	205 ± 1.7
	Digestive glands	n.d.	n.d.	44.6 ± 0.4	354.9 ± 1.5	n.d.	n.d.	n.d.	399 ± 1.9
	Adductor muscle	2472.7 ± 4.9	n.d.	n.d.	n.d.	n.d.	6.3 ± 0.7	16.8 ± 0.8	2495 ± 6.4 *
<i>Choromytilus chorus</i> /giant mussel	Mantle	n.d.	n.d.	7.3 ± 0.1	1.7 ± 0.1	n.d.	n.d.	n.d.	9.0 ± 0.2
	Digestive glands	n.d.	n.d.	n.d.	n.d.	4.3 ± 0.1	< LOQ	12.3 ± 0.1	16 ± 0.2
	Adductor muscle	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
<i>Argobuccinum ranelliformes</i> /top shell	Foot	n.d.	n.d.	16.5 ± 0.1	1.9 ± 0.1	n.d.	1.6 ± 0.1	< LOQ	20 ± 0.3
	Digestive glands	n.d.	n.d.	2885.9	1.5 ± 0.1	288.7	445.4	16.0 ± 0.1	3637 ± 4.2 *
<i>Concholepas concholepas</i> /loco	Foot	n.d.	81 ± 0.7	n.d.	n.d.	n.d.	n.d.	n.d.	81 ± 0.7
	Digestive glands	n.d.	n.d.	17.5 ± 0.5	141.3 ± 0.4	n.d.	11.7 ± 0.2	9.0 ± 0.1	179 ± 1.2



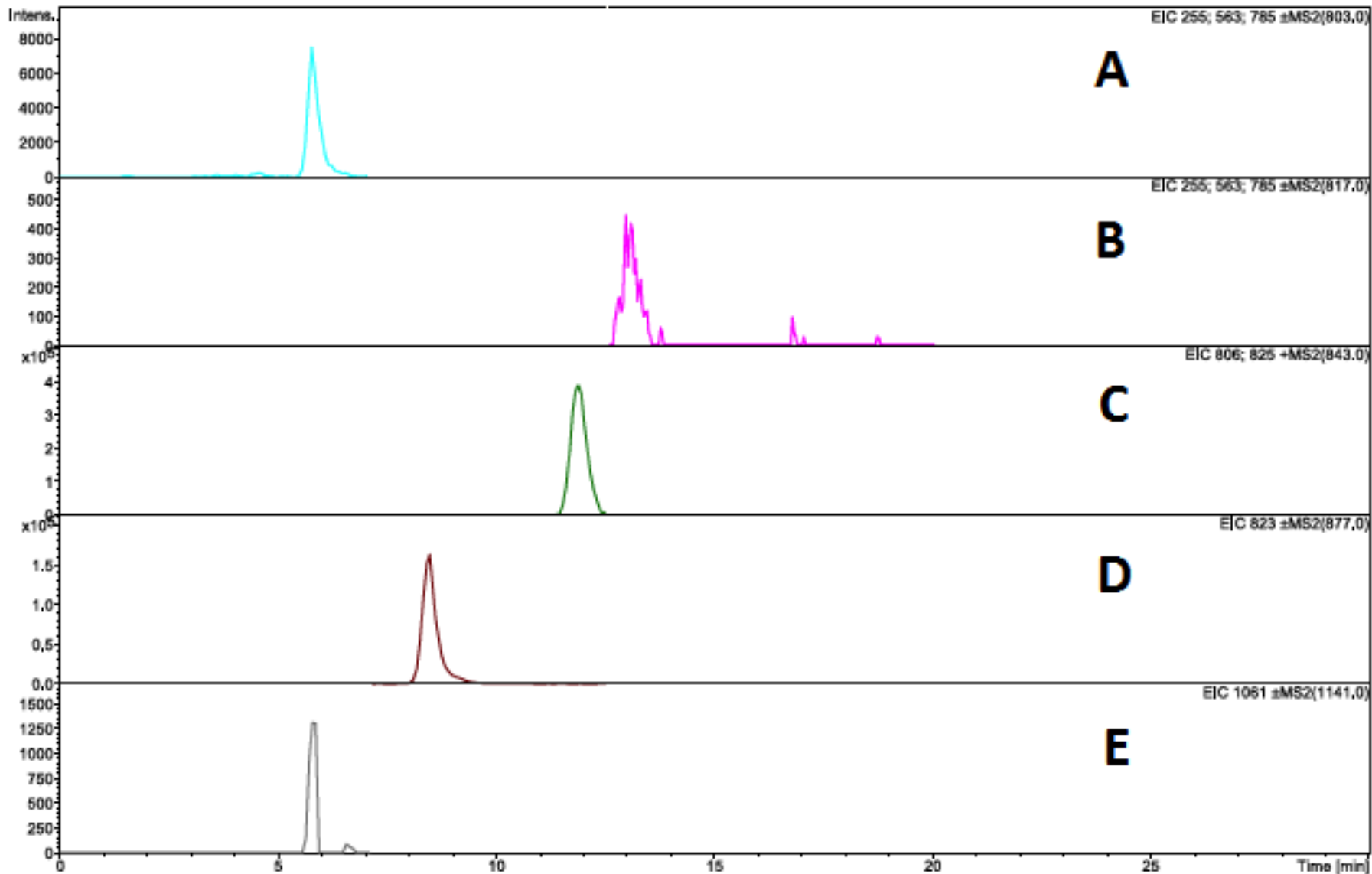
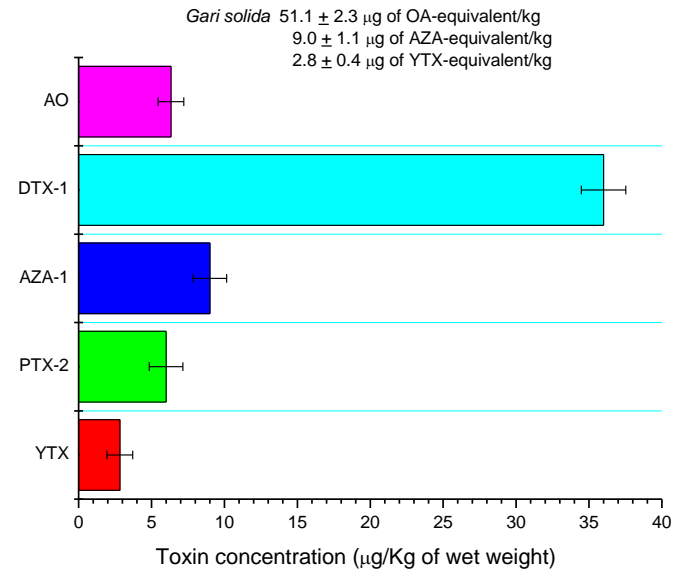
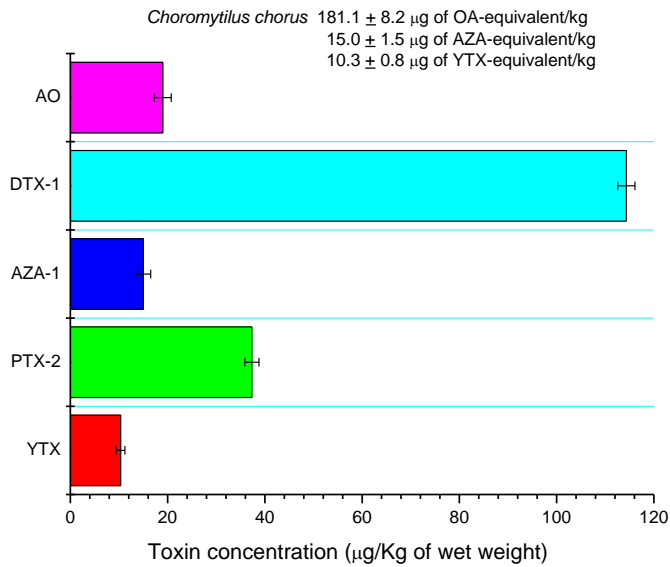
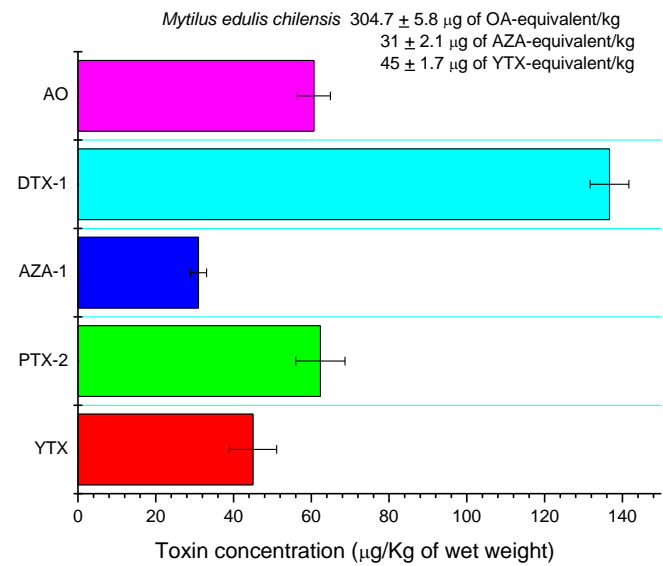
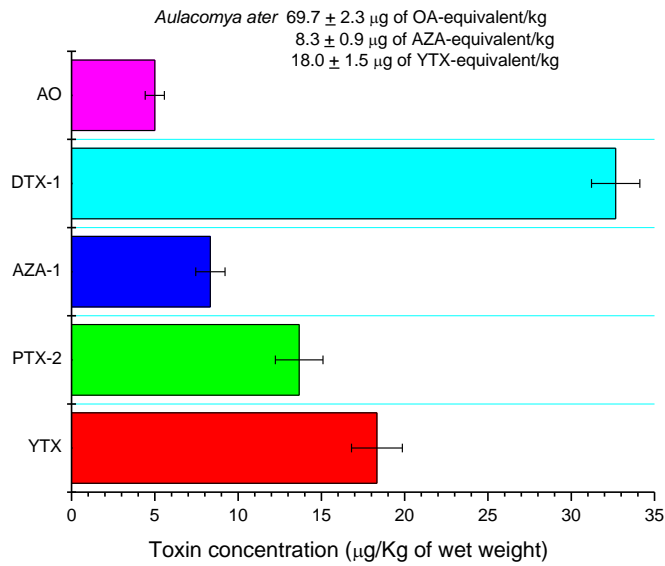
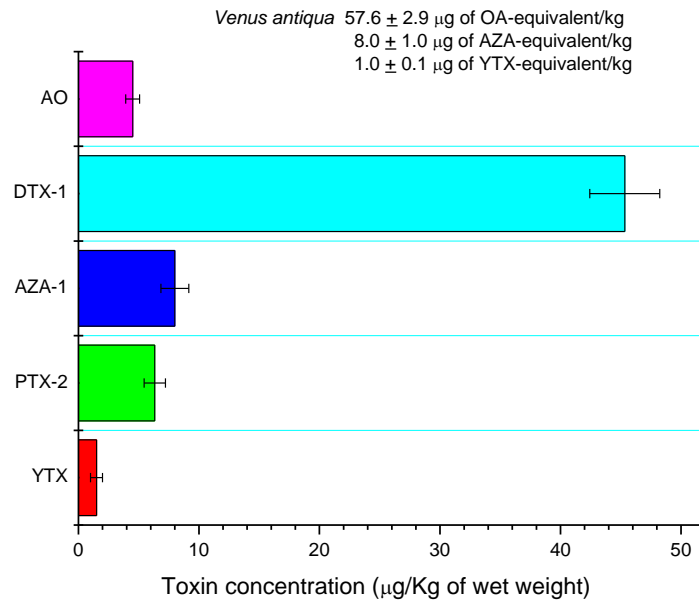
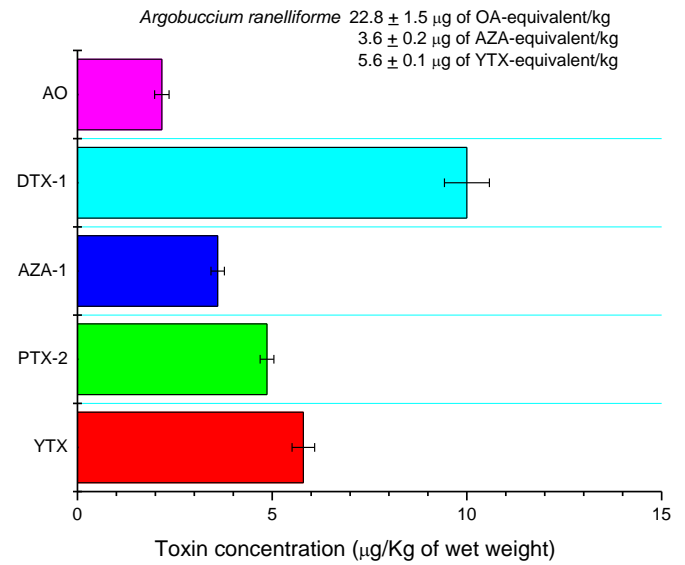
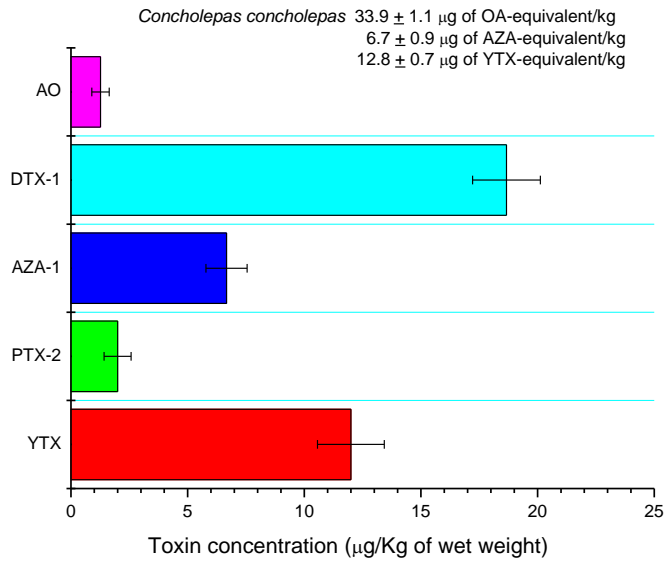


Figura 17. Cromatogramas de HPLC-MS/MS obtenidos desde una mezcla estándar :
(a) ácido okadaico (4.89 μ M), (b) dinofisistoxina-1 (0.62 μ M)(c) azaspirácido-1 (0.8 mM),
(d) pectenotoxina-2 (1.66 mM) y (e) yessotoxina (1.53 mM).





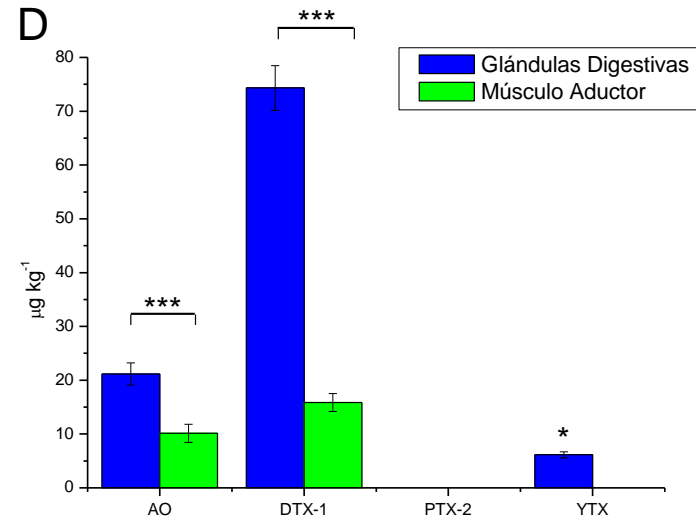
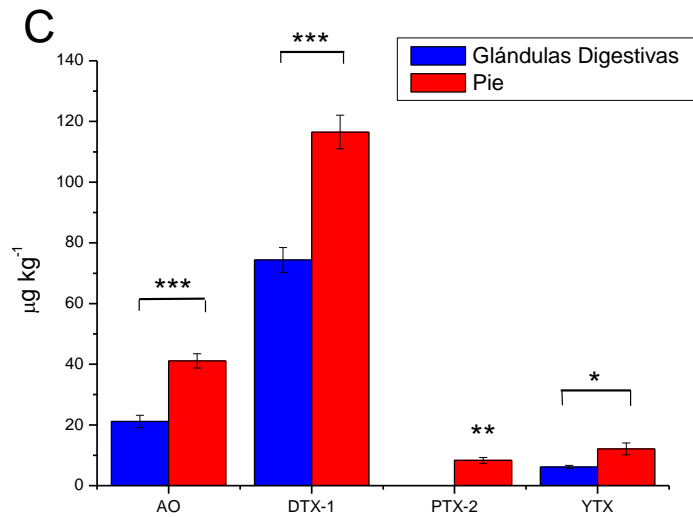
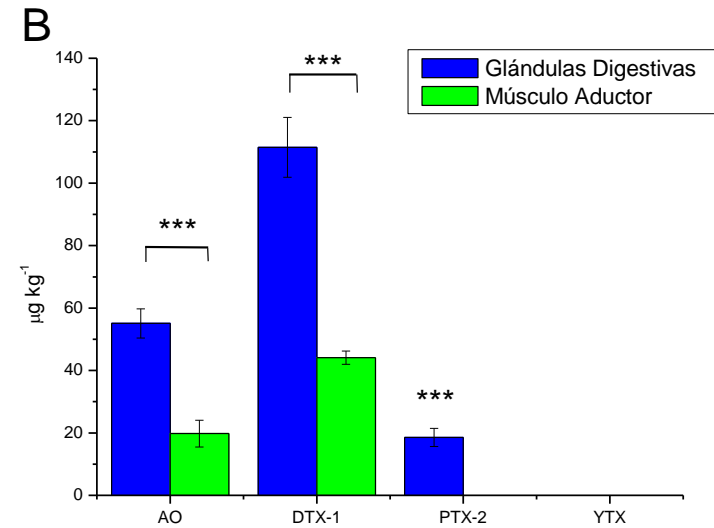
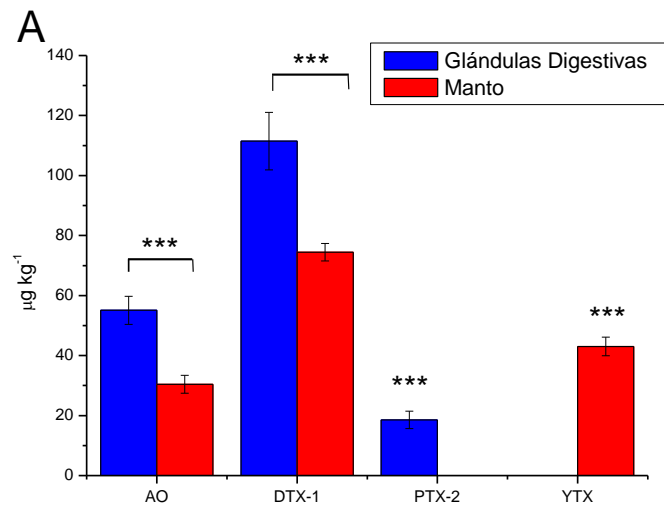
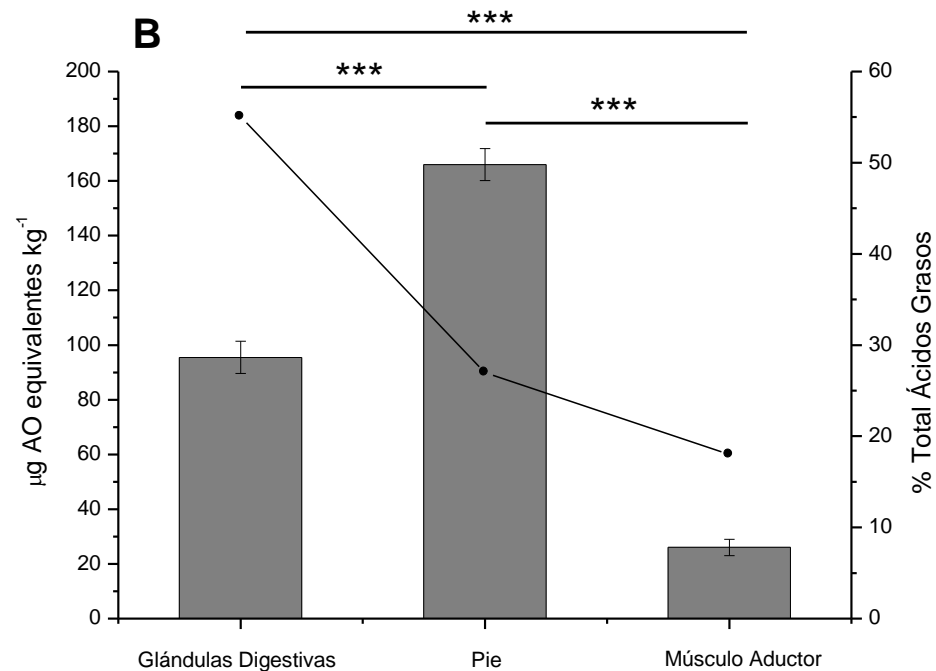
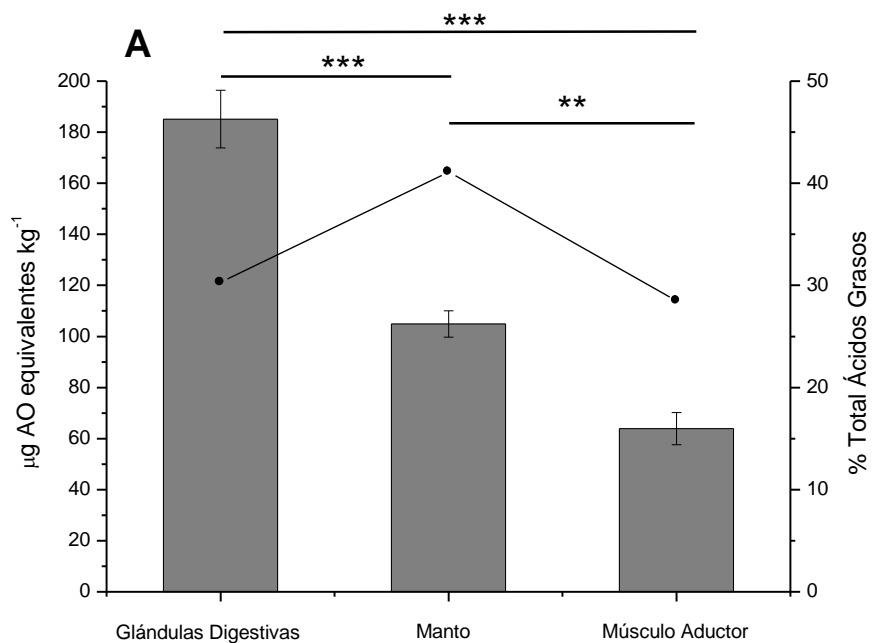
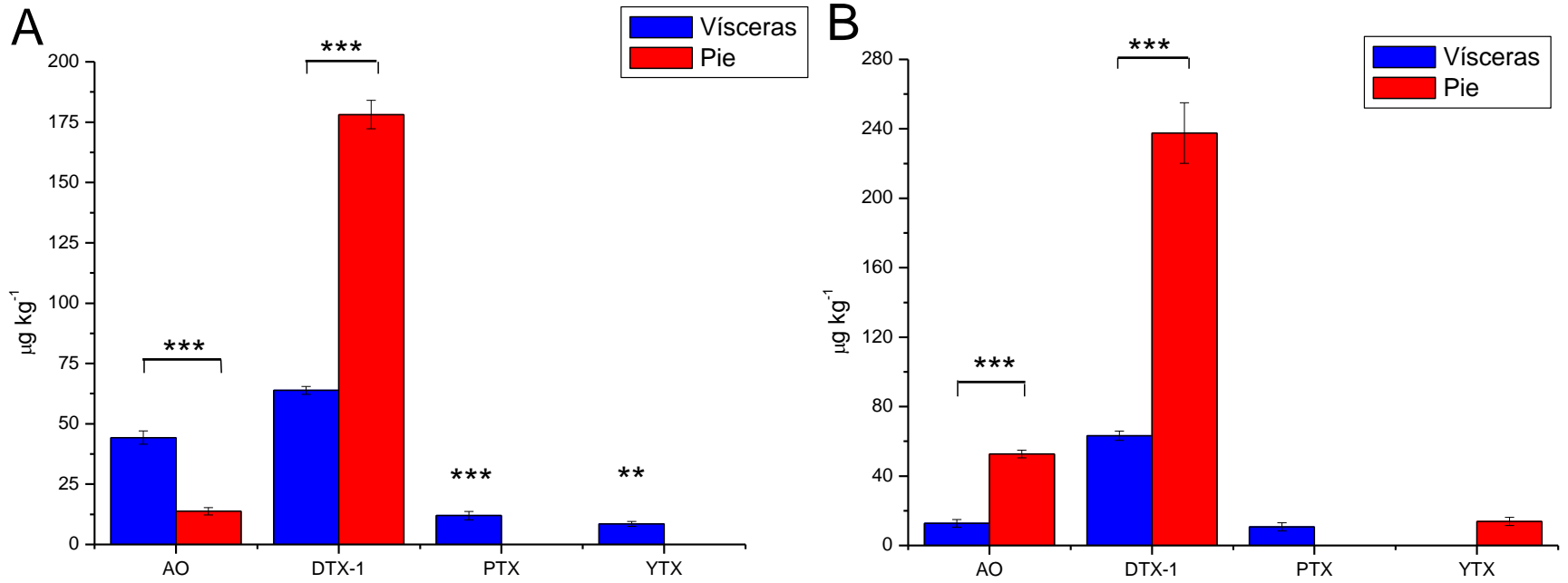


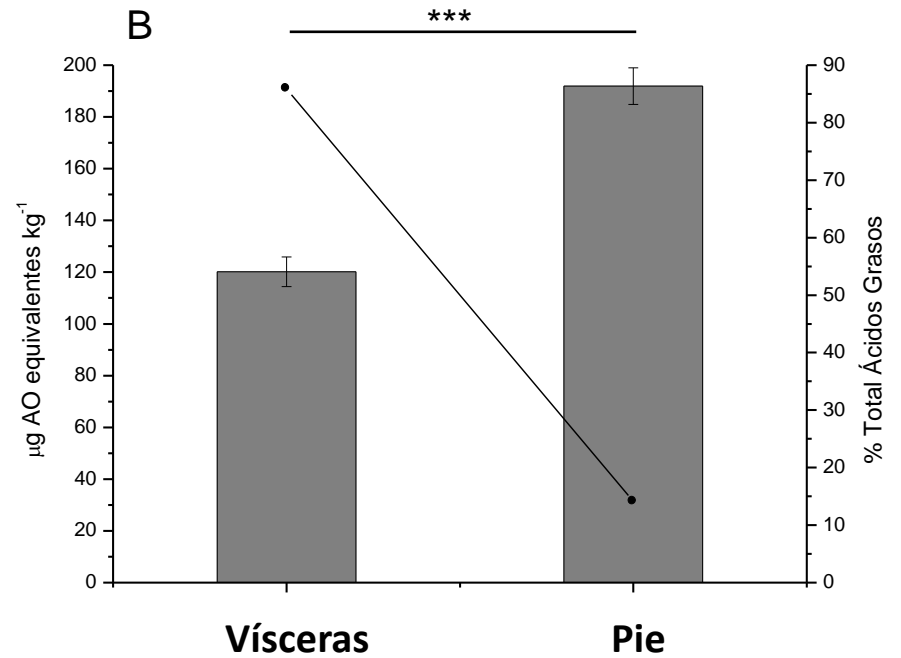
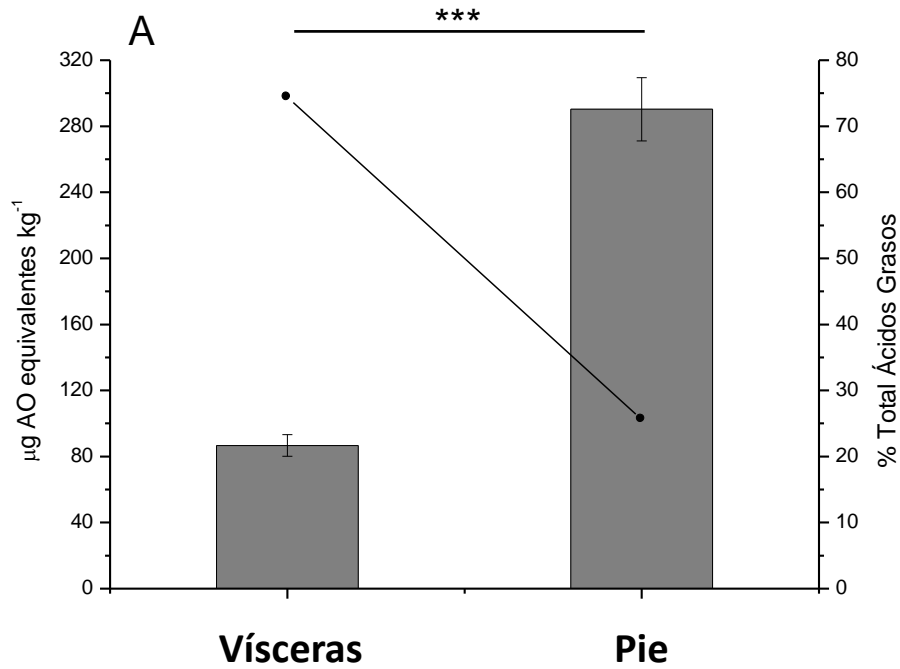
Figura 30. Relación de las concentraciones de toxinas lipofílicas en los tejidos de *Mytilus chilensis* entre glándulas digestivas y manto (a); glándulas digestivas y músculo aductor (b); manto y músculo aductor; y en *Gari solida* (c). Barras representan desviación estándar (** p<0,01; *** p<0,001).



Toxicidades del grupo-AO ($\mu\text{g AO equivalentes kg}^{-1}$) en tejidos viscerales (glándulas digestivas) y no viscerales (manto y músculo aductor) de *Mytilus chilensis* (a) y *Gari solida* (b) (columnas), en relación al porcentaje total de ácidos grasos (●). Barras representan desviación estándar. (** $p < 0,01$; *** $p < 0,001$).

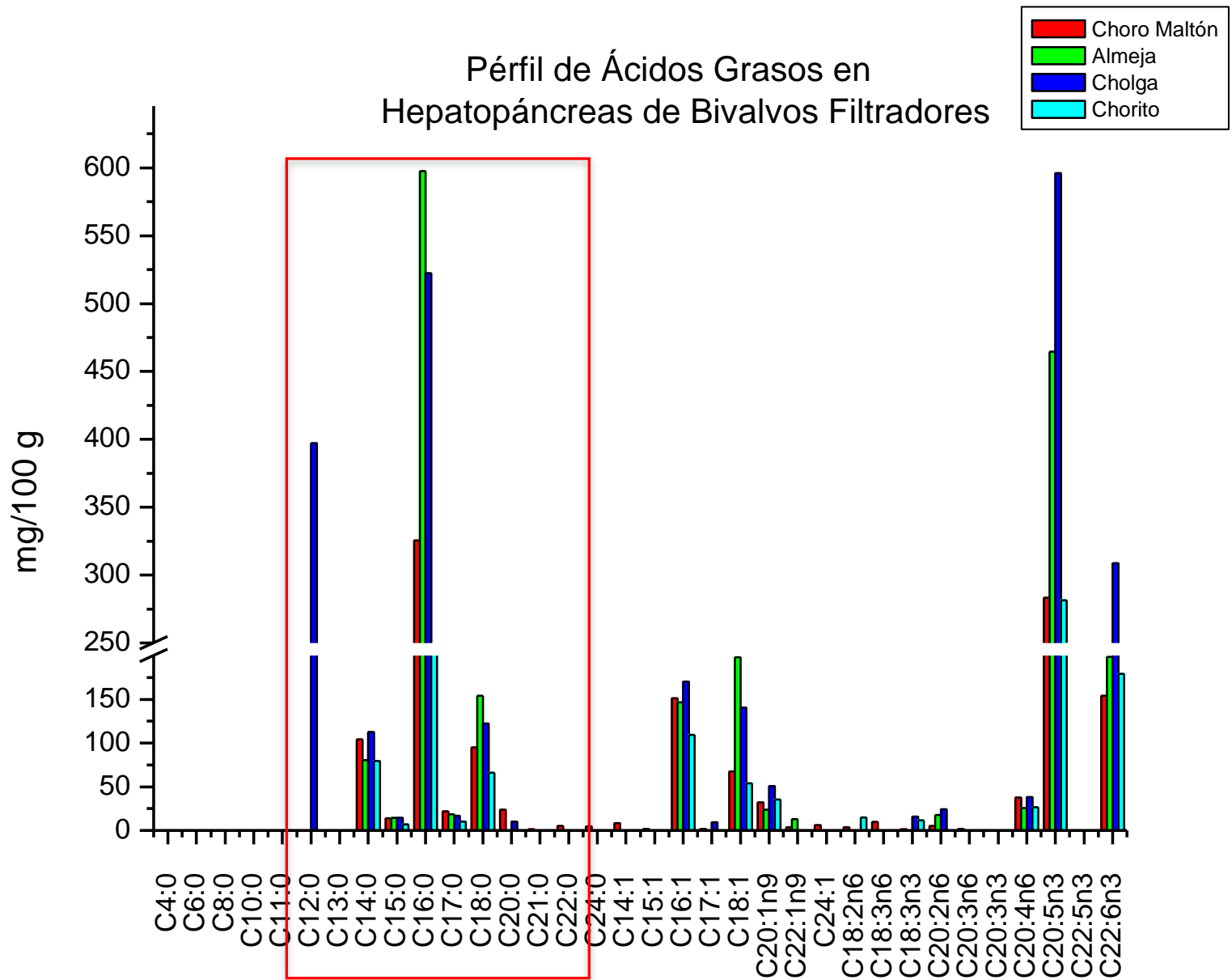


Relación de las concentraciones tóxicas de toxinas lipofílicas en los tejidos de carnívoros gastrópodos. (a) Visceras y pie en *Concholepas concholepas* y (b) Visceras y pie en *Argobuccinum ranelliformes*. Barras representan desviación estándar. (** $p < 0,01$; *** $p < 0,001$).

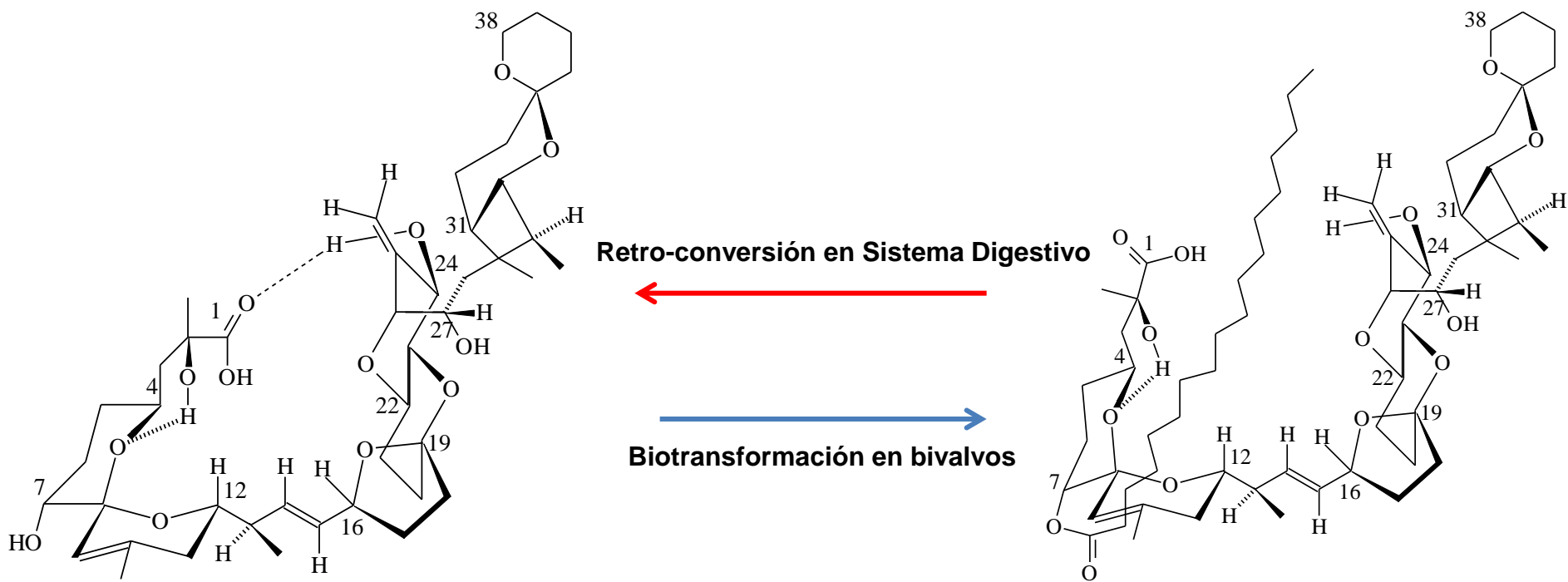


Toxicidades del grupo-AO ($\mu\text{g AO equivalentes kg}^{-1}$) en vísceras y pie de *Concholepas concholepas* (a) y *Argobuccinum ranelliformes* (b), en relación al porcentaje total de ácidos grasos detectados (●). Barras representan desviación estándar. (***) $p < 0,001$.

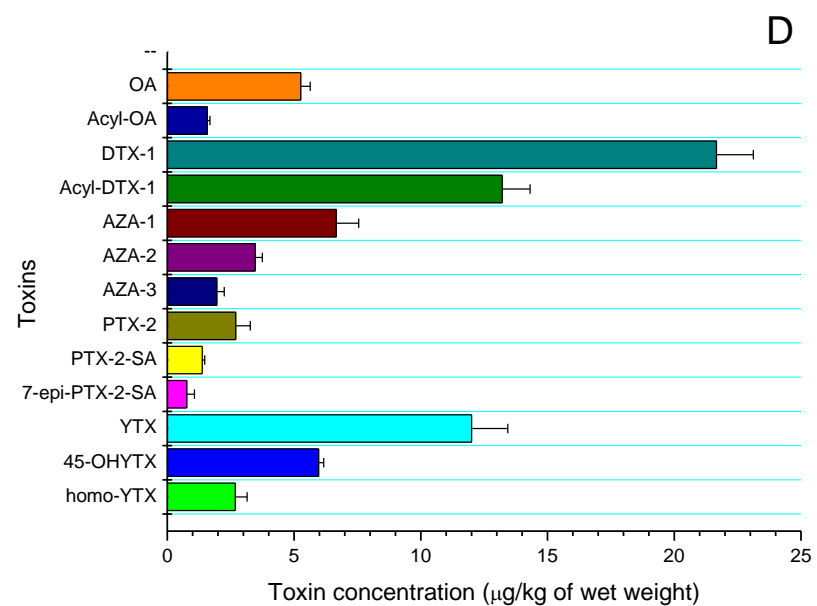
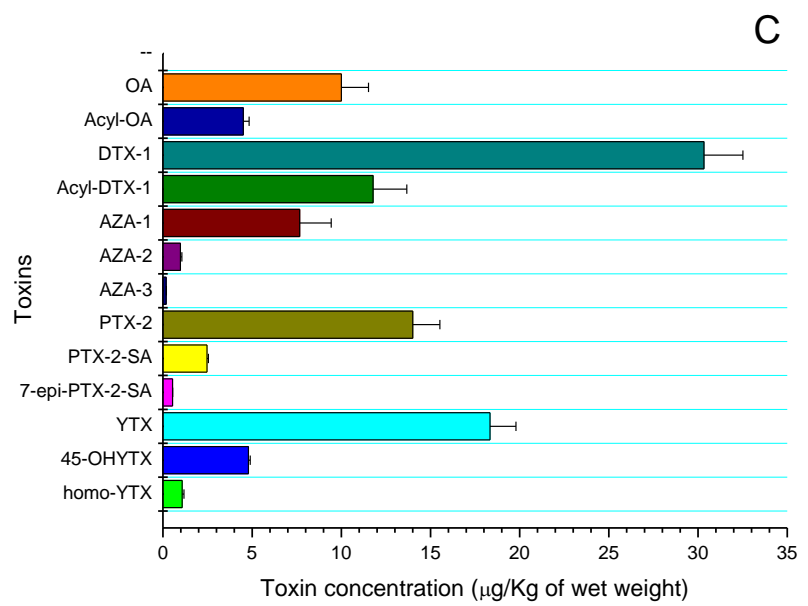
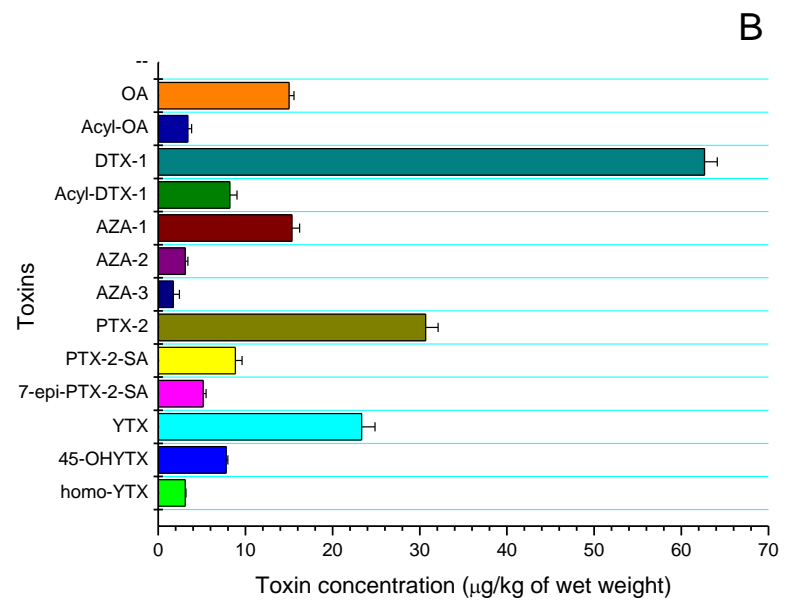
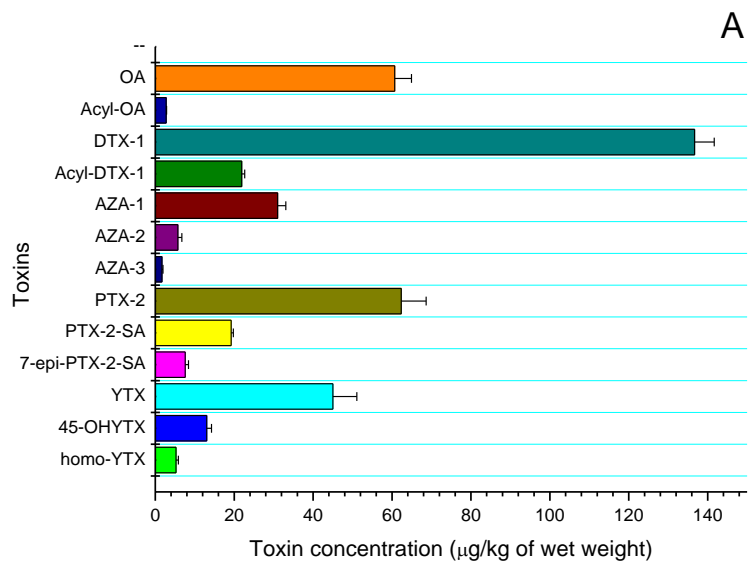
Perfil de Ácidos Grasos en Hepatopáncreas de Bivalvos Filtradores



Perfil de ácidos grasos (saturados, monoinsturados y poliinsaturados) en Hepatopáncreas de Choro-zapato (*Choromytilus chorus*), Almeja (*Venus antiqua*), Cholga (*Aulacomya ater*) y Chorito (*Mytilus chilensis*).

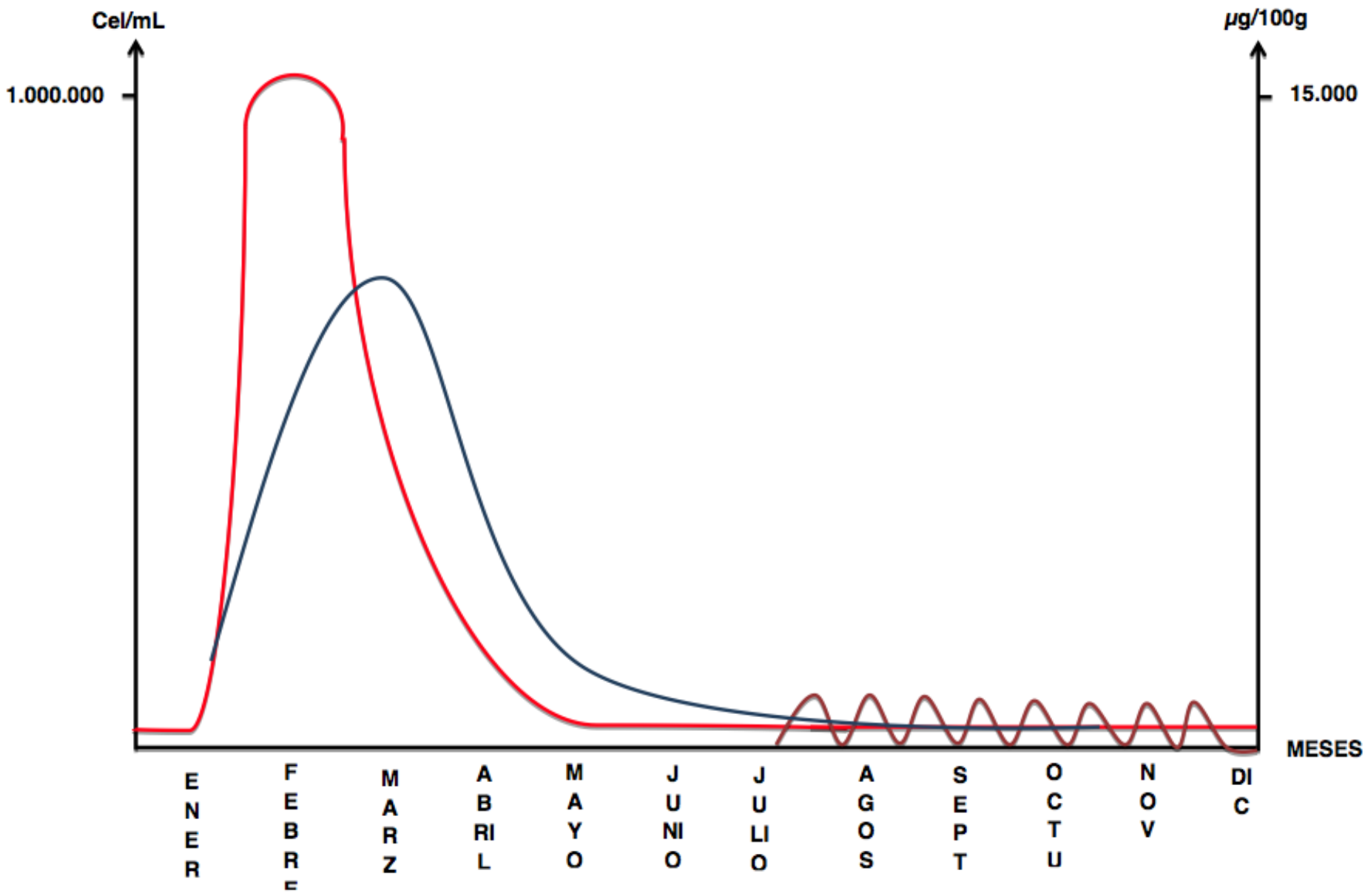


García et al., 2006; Doucet et al., 2007; García et al., 2015



Comparison of lipophilic toxin profiles of bivalve species: A) Blue mussels (*Mytilus chilensis*); B) Ribbed mussels (*Aulacomya ater*); C) Razor Clam (*Tagelus dombeii*) and D) carnivorous gastropods Loco (*Concholepas concholepas*) from the South Pacific Ocean. García et al., 2017





PROPUESTAS

- Establecer el recuento celular para fijar decisiones ante el FAN.
- Actualizar la normativa sanitaria nacional, que establezca límites y análisis para las toxinas lipofílicas.
- Establecer un método analítico para el grupo de Saxitoxina, que permita identificar los perfiles tóxicos en los distintos organismos hidrobiológicos durante el desarrollo y termino de un FAN.

AGRADECIMIENTOS



FONDECYT
Fondo Nacional de Desarrollo
Científico y Tecnológico



Capitanía de Puerto de Puerto Aguirre