

Novel New Zealand marine bioactive natural products for the control of Psa biovar 3



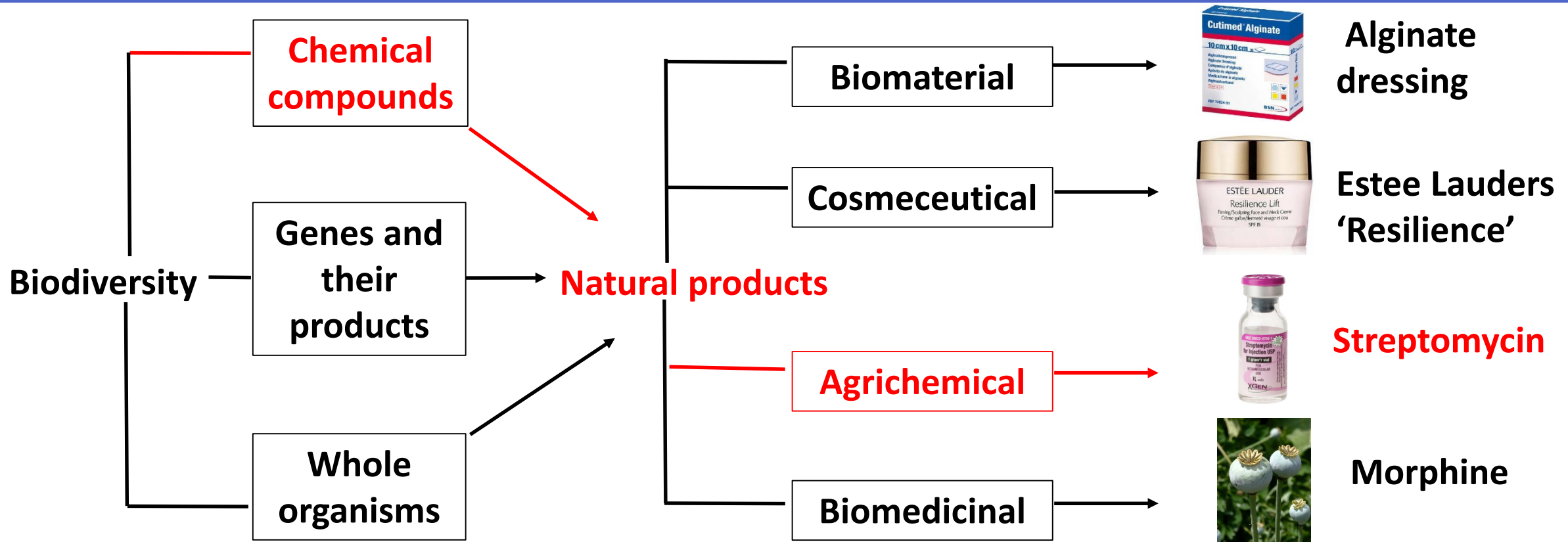
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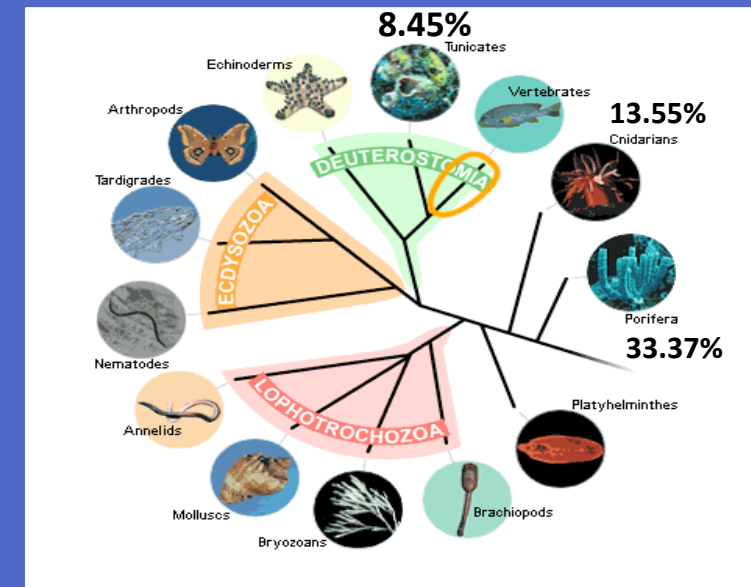
BIODISCOVERY:

“ The examination of biological resources for characteristics which may have wider application and/ or commercial value ”.



NATURAL PRODUCT DISCOVERY

- Secondary metabolites produced by living organisms
 - e.g. Poison Dart Frog
- Features are of high relevance to drug discovery
 - Chemically and structurally diverse
 - Functionally relevant modes of biological activity
- Marine environment is an important natural product resource
- Decline in commercial interest
 - Ecologically guided discovery suggested to increase success rate



MARINE NATURAL PRODUCT POTENTIAL

- Research explores potential novel New Zealand marine bioactive natural products for the control of Psa biovar 3
- Literature provides insight for the selection of organisms
 1. Marine organisms with anti- *Pseudomonas* bioactivity
 2. Marine organisms with quorum sensing inhibition activity
- ‘Ecologically guided’ biodiscovery will increase the success rate of ‘hit’ organisms with target biological activity



METHODOLOGY

- **Field collections**
 - 19 marine macroalgae specimens comprising 16 species
 - 11 targeted and 10 randomly selected for screening
 - Collected in both summer and winter
- **Preliminary screening**
 - Small scale extractions of crude compounds (2 x summer, 1 x winter)
 - *In vitro* bioassay for anti-Psa activity
 - LCMS for preliminary compound information



METHODOLOGY

- **Secondary screening**
 - Selection and large scale extraction of 'hit' candidates
 - Fractionation
 - *In vitro* bioassay of fractions for anti-Psa activity
 - LCMS analysis of fractions
- **Elicitor screening**
 - Pilot experiment to determine concentration and quantity required for *in vivo* bioassay



PRELIMINARY SCREENING RESULTS

Table 2.4. Summary of biological activity of all crude, small scale macroalgae extracts when screened against Psa biovar 3.

Season of collection	Summer								Winter				KEY	
	2 hour				24 hour				2 hour		24 hour		-	No inhibition
	A		B		A		B		A		A		+/-	Decrease of incidence (>log cfu/mL)
Replicate	1	2	1	2	1	2	1	2	1	2	1	2	+	Full inhibition
AB1	-	-	-	-	-	-	-	-	-	-	-	-	-	
AB2	-	-	-	-	-	-	-	-	-	-	-	-	-	
AB3	-	-	+	+	+	+	+	+	+/-	+/-	+	+		
AB4	-	-	-	-	-	-	-	-	-	-	-	-	-	
AB5	-	-	-	-	-	-	-	-	-	-	-	-	-	
AB6	-	-	-	-	+	+	+	+	N/A					
AB7	-	-	-	-	-	+	-	-	-	-	+	+		
AB8	-	-	-	-	-	+/-	-	-	N/A					
AB9	-	-	-	-	+	+	+	+	-	-	+/-	+/-		
AB10	-	-	-	-	-	-	-	-	-	-	-	-	-	
AB11	-	-	-	-	-	-	+	+	-	-	+	-		
AB12	-	-	-	-	-	-	-	-	-	-	-	-	-	
AB13	-	-	-	-	+/-	+/-	-	-	+/-	+/-	+	+		
AB14	+	+	+	+	+	+	+	+	+	+	+	+		
AB15	-	-	-	-	+/-	+/-	-	-	-	-	-	-		
AB16	-	-	-	-	-	-	-	-	-	-	+/-	+		
AB17	-	-	-	-	-	-	-	-	N/A					
AB18	N/A								-	-	-	-		
AB19	N/A								-	-	-	-		

- 5 specimens (4 sp.) consistently inhibited/ decreased the incidence of Psa biovar 3
- 26 % 'hit' success rate
 - 10 % randomly selected
 - 16 % targeted
- Supports hypothesis

SECONDARY SCREENING RESULTS

Table 3.5. Biological activity of fractions ABS3.1-14 when screened against Psa biovar 3.

Fraction	2 hour		24 hour	
	1	2	1	2
3.1	-	-	-	-
3.2	-	-	-	-
3.3	+/-	+/-	+/-	+
3.4	+/-	+/-	+/-	+/-
3.5	+/-	+/-	+/-	+
3.6	-	-	-	-
3.7	-	-	-	-
3.8	-	-	-	-
3.9	-	-	-	-
3.10	+/-	+/-	+/-	+/-
3.11	-	-	-	-
3.12	-	-	-	-
3.13	-	-	-	-
3.14	-	-	-	-

KEY	
-	No inhibition
+/-	Decrease of incidence (>log cfu/mL)
+	Full inhibition

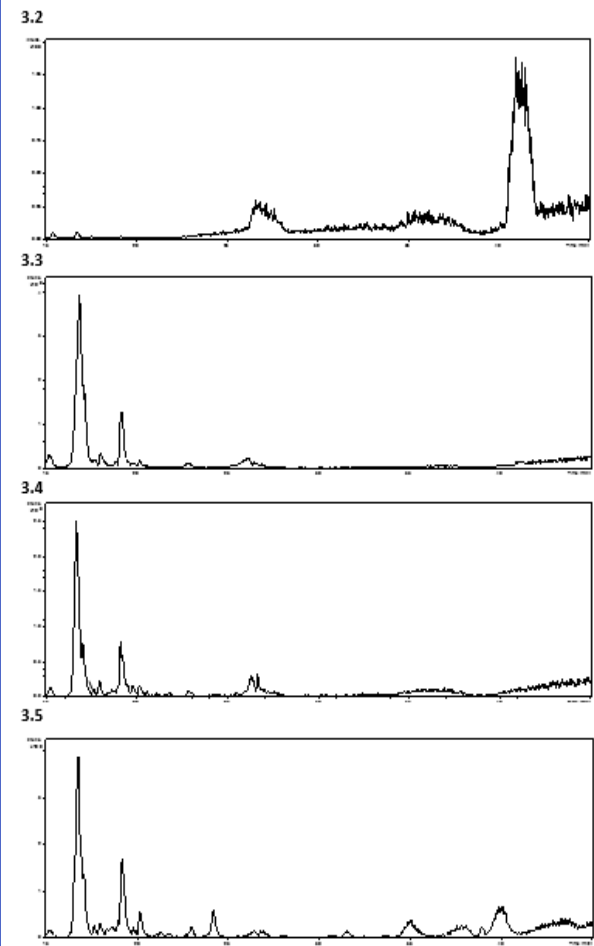


Table 3.10. Ions of interest in biologically active fractions of AB3 and adjacent fractions.

Ion (m/z)	Present in	Size
A	3.3	Small
	3.4	Small
	3.5	Small
	3.10	Trace
B	3.3	Small
	3.4	Small
	3.5	Small
	3.10	Trace
C	3.2	Small
	3.3	Small
	3.4	Small
	3.5	Small
	3.6	Trace
	3.9	Small
	3.10	Small
D	3.11	Trace
	3.11	Large

→ 'Hit' candidate AB3

- Of highest priority

- 4 ions of interest

- Representative of potentially novel and/ or bioactive compounds

CONCLUSIONS

- High success rate of 'hit' macroalgae candidates (26 percent)
- Ecologically guided approach fast tracked the preliminary screening process
- Four potential structurally novel compounds with patentability and commercial marketability
- Research is a small (but important) part of a bigger picture



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