



An Australian native plant: A novel broad-spectrum antibiotic for the treatment of biofilms and common-wound colonising bacteria

Dr. Trudi Collet



Antibiotic resistant pathogens (ARPs)

- ❑ **Antimicrobials are central to the global health system**
- ❑ **The recent spread of ARPs has significantly depleted the supply of efficacious antibiotics**
- ❑ **In the USA, MRSA kills more Americans every year (~20,000) than:**
 - emphysema, AIDS, Parkinson's disease and homicide combined
- ❑ **Hospital-acquired infections (HAIs) >2M/yr (at US\$20B in direct costs and \$35B in additional productivity costs), cause more than five times this number of deaths (1 every three seconds)**
- ❑ **For the EU, the WHO reports commensurate numbers of HAIs and costs**
 - while low-income countries experience 3 – 4 times this rate of infections per capita

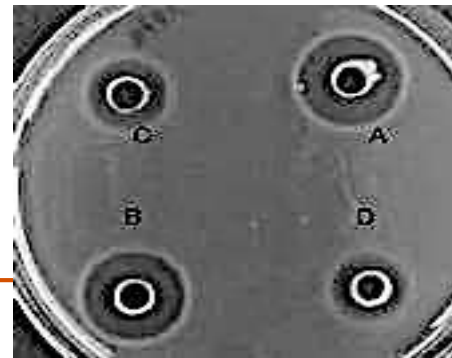


Medicinal plants

- **The history of plant usage for medicinal purposes dates back millennia across a multitude of cultures**
 - medicinal plants continue to play a central role in the healthcare system of a large proportion (~80%) of the world's population
- **Globally, approximately 20,000 plant species are used as ethnomedicines**



Results

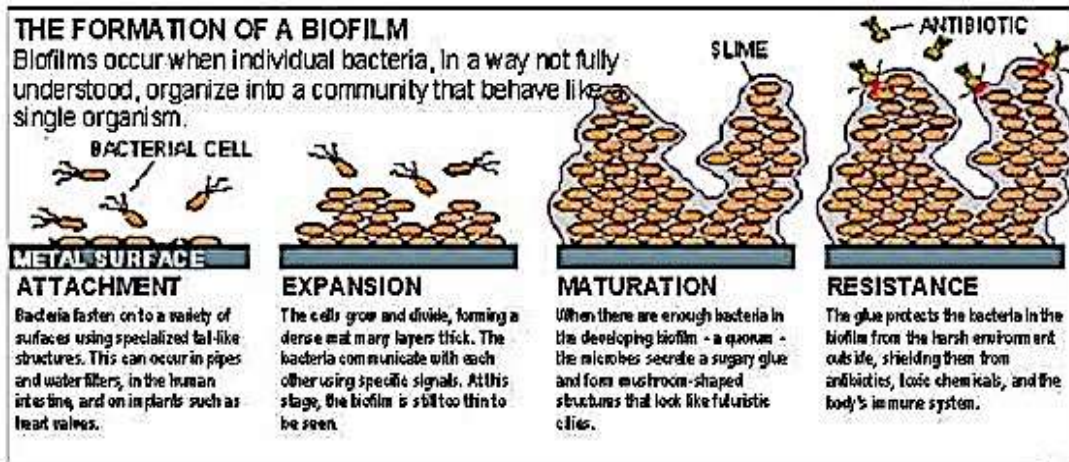


	Bacteria	Controls		Species 8472
		+ve	-ve	
Gram positive	MRSA 1113	7.2±0.8	—	9.0±0.8
	MRSA 1092	9.1±0.7	—	9.0±0.1
	MSSA	17.6±2.1	—	5.0±0.5
	<i>Bacillus cereus</i>	7.3±1.6	—	6.5±0.5
	<i>Streptococcus pyogenes</i>	8.0±0.0	—	9.0±0.3
	<i>Staphylococcus epidermidis</i>	9.0±0.2	—	9.0±0.0
Gram negative	<i>Escherichia coli</i>	4.0±0.0	—	2.0±0.4
	<i>Klebsiella pneumoniae</i>	4.5±0.0	—	0.0±0.0
	<i>Proteus vulgaris</i>	9.0±0.0	—	3.0±0.2
	<i>Proteus mirabilis</i>	9.0±0.2	—	3.0±0.1
	<i>Pseudomonas aeruginosa</i>	5.0±0.0	—	1.0±0.1
VRE	<i>Enterococcus gallinarum</i>	3.0±0.1	—	5.0±0.1
	<i>Enterococcus faecalis</i>	7.0±0.0	—	6.0±0.2
	<i>Enterococcus faecium</i>	6.0±0.0	—	7.0±0.6
	<i>Enterococcus casseliflavus</i>	1.0±0.0	—	6.0±0.4
MDR	<i>Acinetobacter baumannii</i>	6.0±0.3	—	2.0±0.0

Values represent the radius of zone of inhibition (mm). All results are presented as mean ±SEM of triplicate data sets. (VRE = vancomycin-resistant enterococci – Gram +ve; MDR = multi-drug-resistant – Gram –ve; — = zero zone of inhibition).

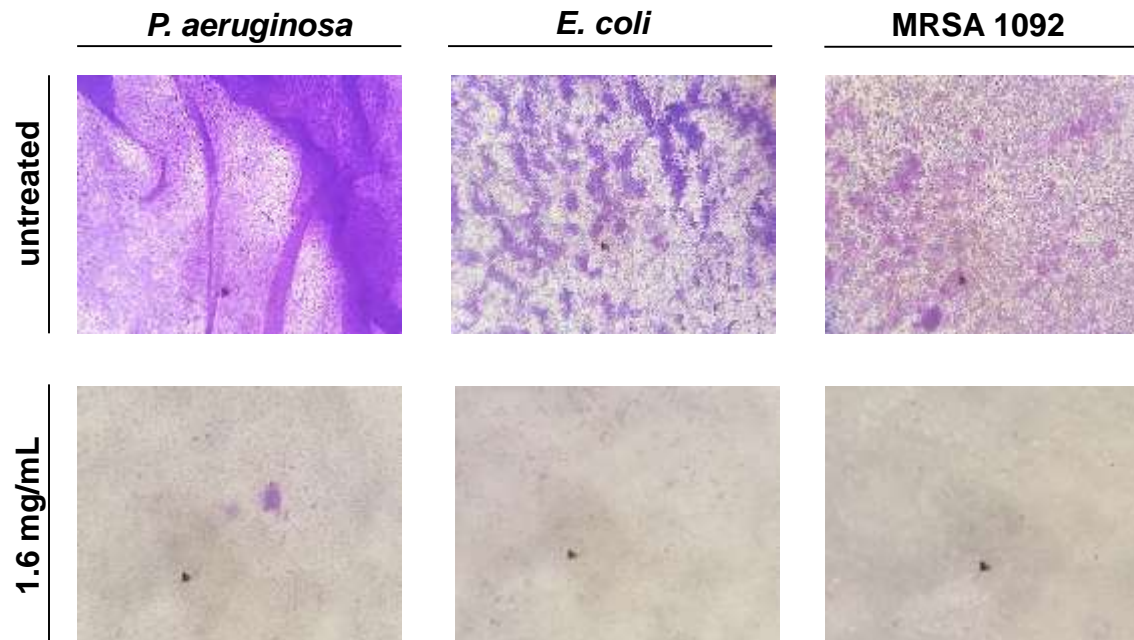
Biofilms

- **Form when bacteria adhere to surfaces in aqueous environments**
 - excrete a slimy glue-like substance that co-anchors them to various materials
- **60% of chronic wounds contain biofilms compared to 6% of acute wounds**



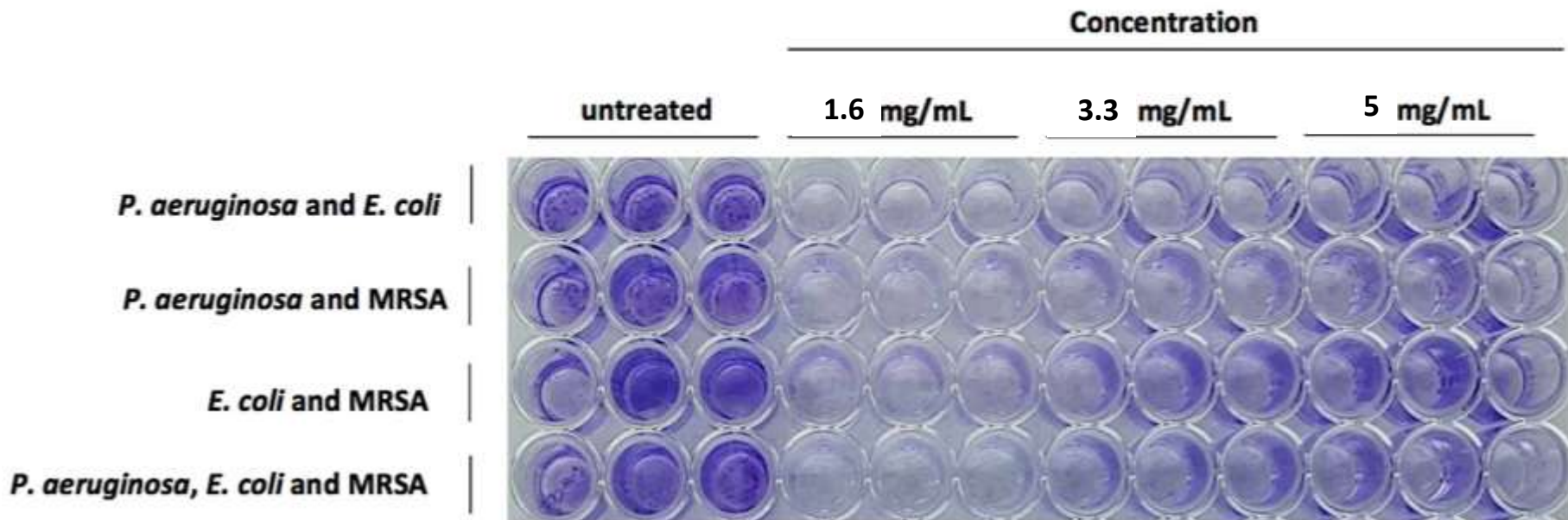
Results

Bacteria	Concentration		
	1.6 (mg/mL)	3.3 (mg/mL)	5 (mg/mL)
<i>P. aeruginosa</i>	87%	78%	69%
<i>E. coli</i>	77%	73%	67%
MRSA 1092	100%	100%	92%



Results

Bacterial combination	Degradation of biofilm (%)		
	mg/mL		
	1.6	3.3	5
<i>P. aeruginosa</i> and <i>E. coli</i>	83	55	41
<i>P. aeruginosa</i> and MRSA	94	86	76
<i>E. coli</i> and MRSA	87	78	68
<i>P. aeruginosa</i> , <i>E. coli</i> and MRSA	93	68	72



Significance

- ❑ **The rate at which resistant organisms are being uncovered exceeds that at which new effective therapeutics are being discovered**
- ❑ **Bactericidal against WHO's top 5 priority pathogens**
 - **ESKAPE bacteria**
- ❑ **Broad spectrum therapy**
 - also highly effective at degrading bacterial biofilms
 - ❑ post-surgical *i.e.* applied directly to the incision to prevent post-op infection
 - ❑ treatment of burns and wounds



Where are we right now and future directions?

- **We have identified the bioactive compounds in question**
 - two new novel class of antibiotics
 - <500 Da
 - synthesisable in the lab

- **ADME testing**

- ***In vivo* testing**
 - animal models

- **Clinical trials**



Acknowledgments

Indigenous Medicines Group

- Dr Peter Katavic
- Dr Satish Dighe
- Dr Raju Tippana
- Dr Marina Mathew
- A/Prof Chris Collet
- O'mezie Ekwudu
- Vajira Agampodi
- Marzieh Negahban
- Mani Manirujjaman
- Suzannah van Akker
- Madusha Perera
- Minna Ahvenainen
- Genevieve Herald
- Rachel Beattie
- Sophie Stewart
- Gabriella Vico
- Brian Ong
- Marianna Yelorm
- Munira Almelhem
- Mackenzie Grice
- Laura Soon
- Phui Qi Ng
- Krystal Fordyce



□ Funding

- HFPA P/L
- Australian Government Commonwealth Innovation Connections Grants (x4)



plant leaves



dried and
ground by
electric grinder



extracted
separately with
different solvents

Extraction of Plant Material



filtered



evaporated in
vacuum
concentrator



resuspended

