Control de biofilms

IIBCE

Pablo Zunino

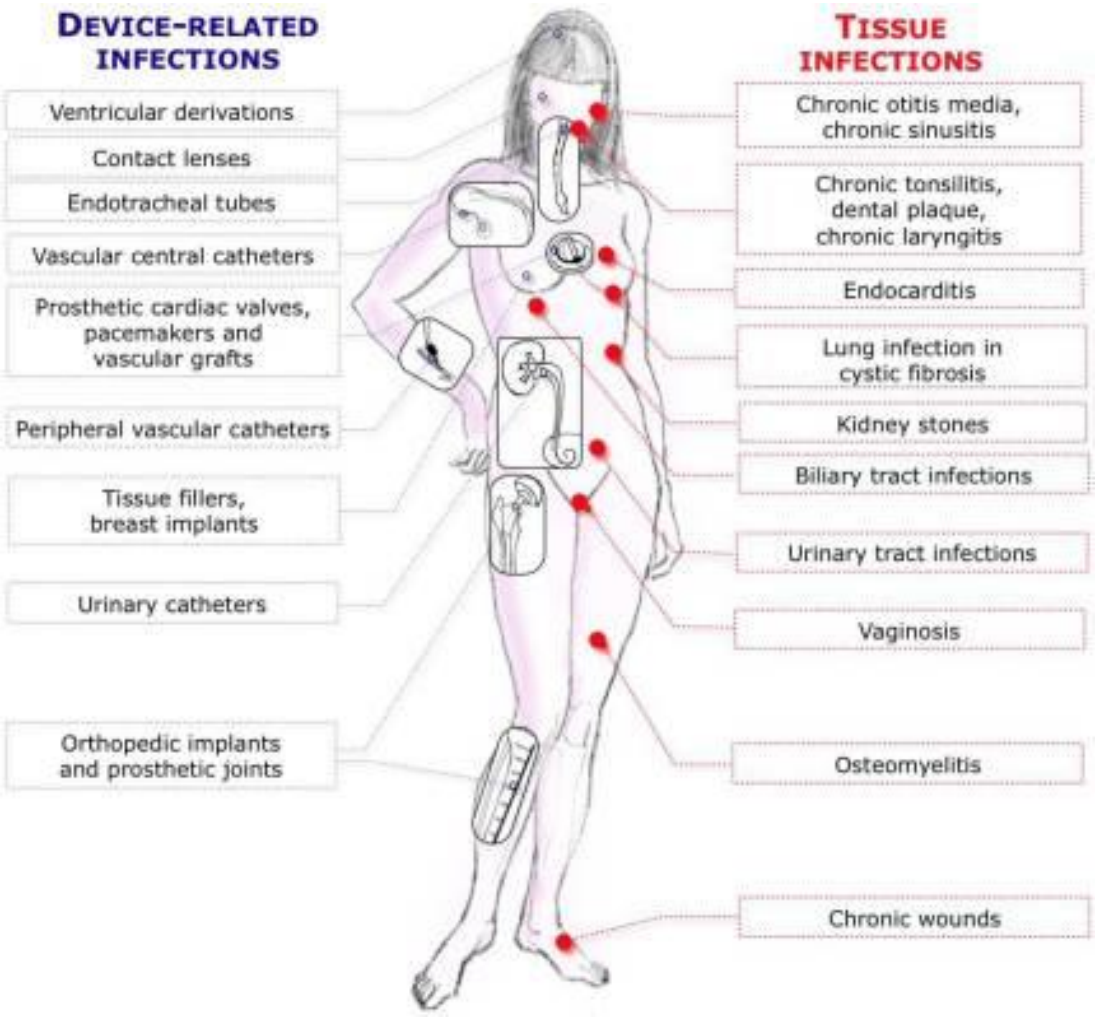
Departamento de Microbiología, IIBCE

Impacto de los biofilms bacterianos en la salud

Los porcentajes de infecciones bacterianas que involucran biofilms se estiman entre un 65% (CDC) y un 80% (NIH) (Jamal et al., 2018):

Ej. endocarditis, fibrosis quística, periodontitis, rinosinusitis, osteomielitis, heridas, meningitis, infecciones urinarias, infecciones asociadas a prótesis y otros implantes, etc.

Infecciones asociadas a biofilms

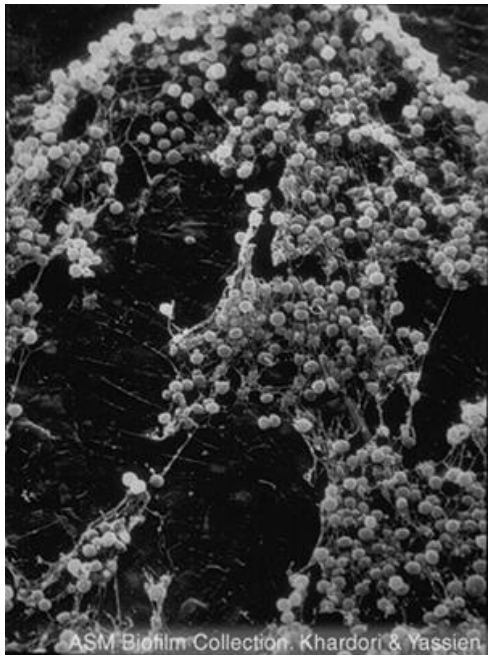


Lebeaux et al., 2013

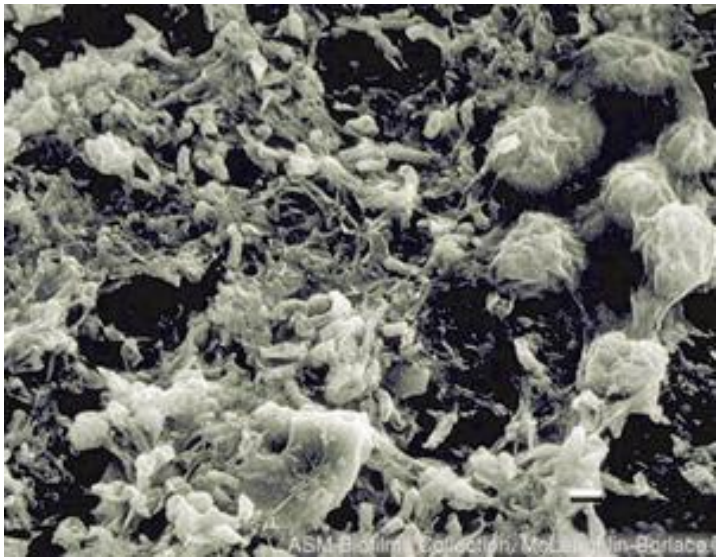
Biofilms en implantes

Representan 50 al 70 % de infecciones nosocomiales

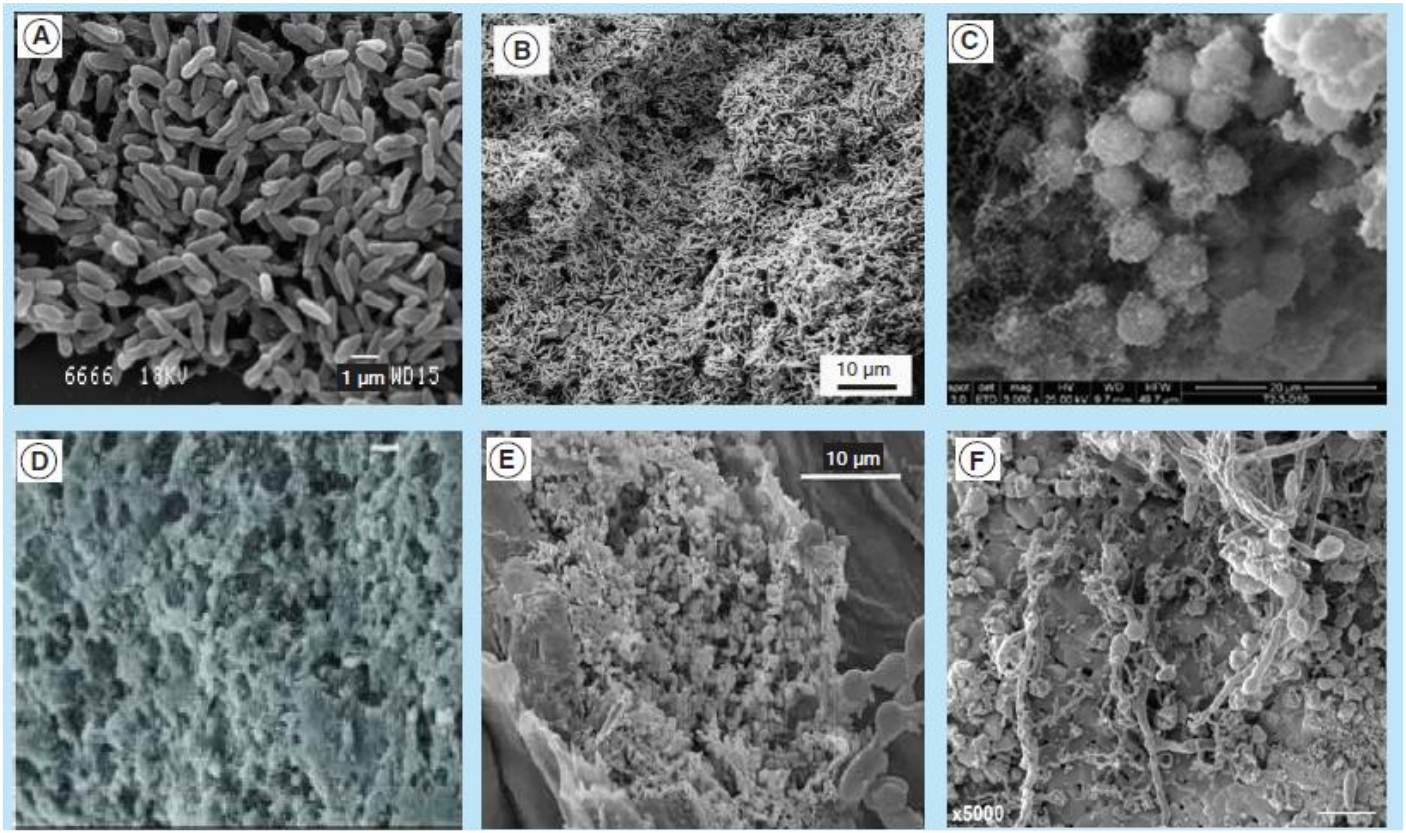
Causan infecciones y pueden interferir con la función del implante; remoción y recambio, serias consecuencias médicas y pérdidas económicas



Catéter vascular (MEB)



Lente de contacto (MEB)



Rabin et al. 2021

A) *Pseudomonas aeruginosa* adherida a superficies de vidrio

B) *Escherichia coli* en superficie del óxido de titanio

C) *Staphylococcus aureus* asociado a catéter intravenoso *in vivo*

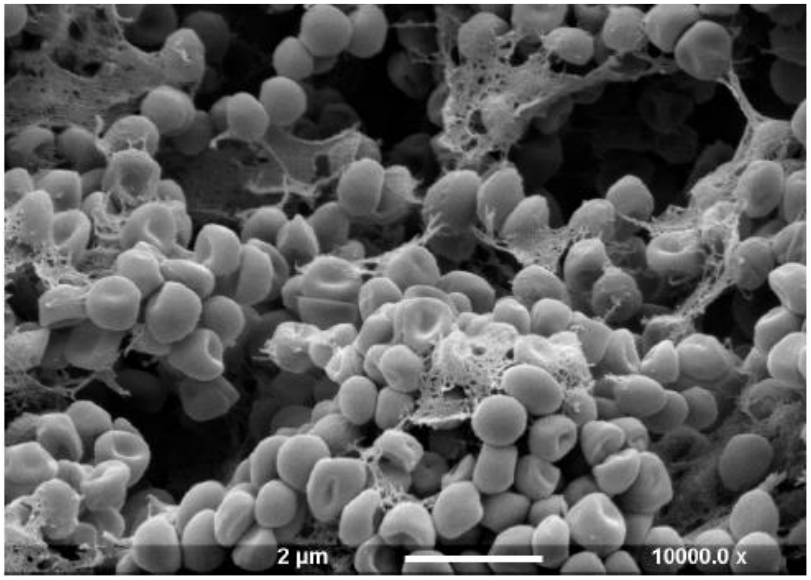
D) *Staphylococcus epidermidis* en un catéter de teflón

E) *Salmonella enterica* serovar Poona sobre tejidos vegetales

F) *Streptococcus mutans y Candida albicans en* discos de hidroxiapatita

El mercado global de los implantes médicos se estimó en unos U$S 79.1 mil millones en 2014, se prevén 133 mil millones en 2022

El aumento en el uso de dispositivos basados en biomateriales se asocia con el envejecimiento de la población, la creciente prevalencia de enfermedades y modificación de estilos de vida (sedentarismo, consumo de alimentos poco saludables, aumento de accidentes traumáticos, aumento de la demanda de injertos y órganos de donantes, etc.)



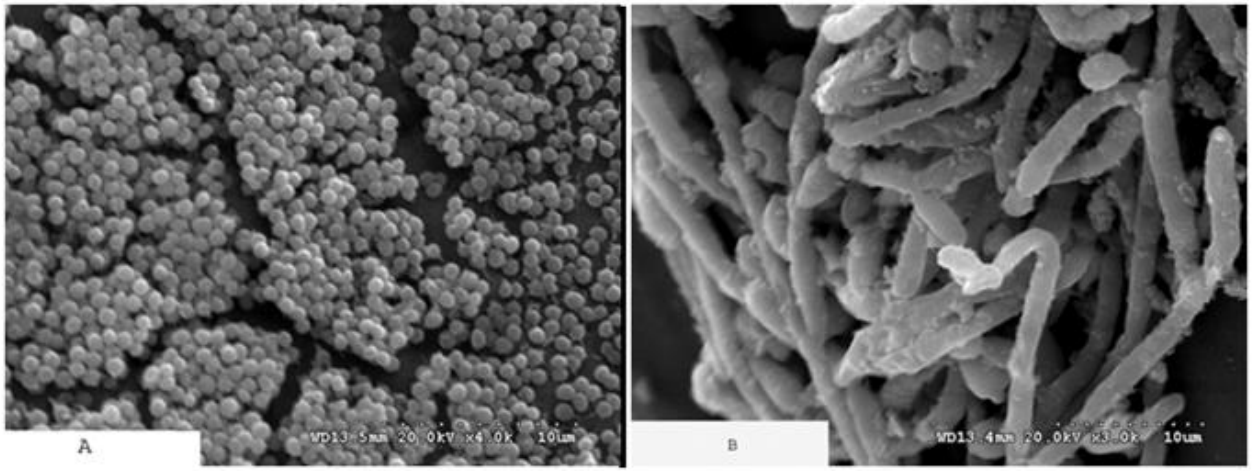
Biofilm de *S. epidermidis* en implante óseo (Rabin et al. 2021)

Cada año alrededor de 250.000 a 500.000 infecciones primarias de la corriente sanguínea ocurren entre los 150 millones de dispositivos intravasculares implantados (USA)

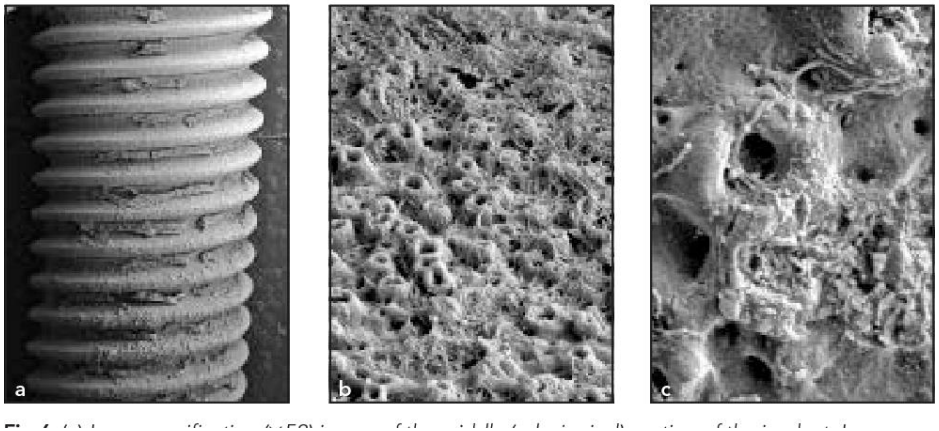
Costo: 670 a 2.680 millones de dólares anuales (prepandemia!!)

Bajo inóculo para la infección a partir de implantes (Nowakowska et al., 2014)

Necesidad de estrategias de prevención y eliminación!!



S. epidermidis y *C. albicans* formando biofilms en catéteres vasculares (El-Azizi, 2015)



Biofilms polimicrobianos en la superficie rugosa de implante dental (Simion et al., 2016)

Medical Devices Bureau (Canadá) reconoce 4 clases de dispositivos médicos de acuerdo al riesgo

- **Clase I:** bajo riesgo para los pacientes y no requiere una licencia o requiere norma normativa más baja (instrumentos quirúrgicos, material dental, etc.)

- **Clase II:** exigir la declaración del fabricante de seguridad y efectividad del dispositivo (lentes de contacto, máquinas de ultrasonido, catéteres médicos, etc.)

- **Clase III:** presenta un mayor riesgo potencial para el paciente (implantes ortopédicos como cemento óseo, implantes de cadera, máquinas de hemodiálisis, etc.)

- **Clase IV:** presenta el mayor riesgo potencial y sujeto a una revisión en profundidad y aprobación reglamentaria previa a la comercialización (implantes cardiovasculares, marcapasos, dispositivos de asistencia ventricular, etc.)

Infecciones urinarias asociadas a catéteres (ITU-C)

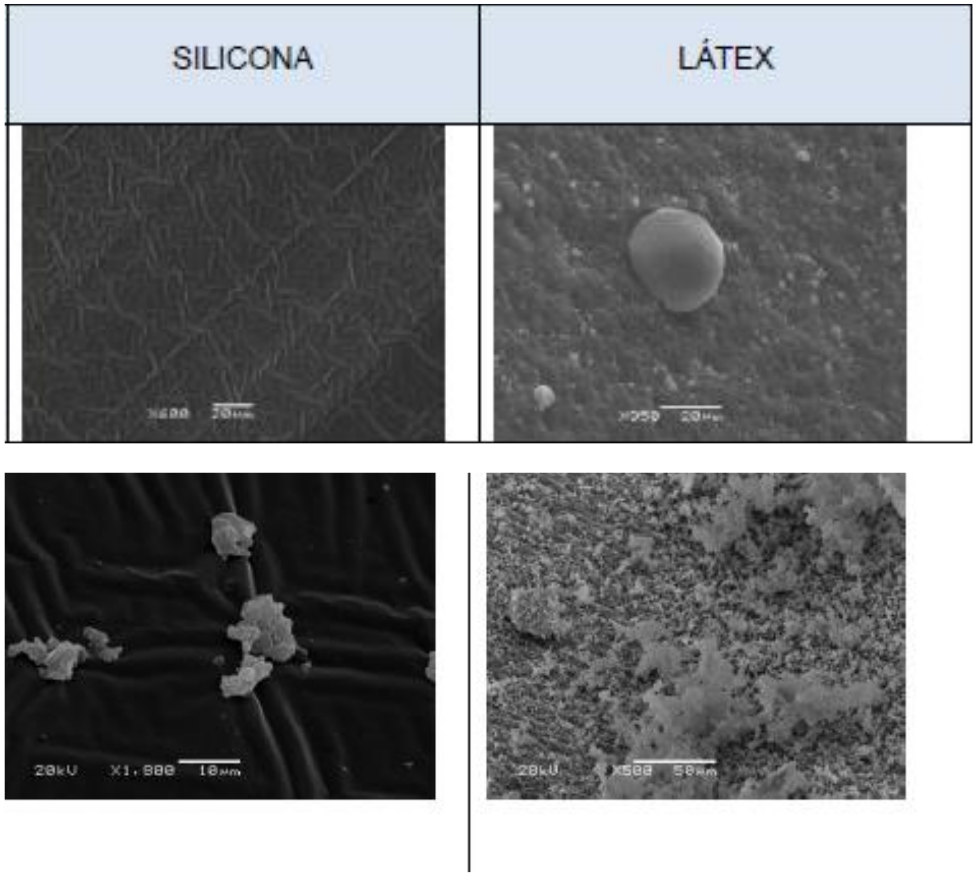
- Vinculadas a la formación de biofilms en la superficie de los catéteres
- Infecciones nosocomiales más comunes
- Costos (USA): U$S 450 millones/año

Incidencia:

Pacientes cateterizados hasta 7 días
→ 10 al 50 % desarrollan ITU-C

Pacientes cateterizados por más de 28 días
→ 100 % desarrollan ITU-C

ITU-C Biofilms de P. *mirabilis* sobre secciones de catéteres (SEM)



Secciones de catéteres

Biofilms de *P. mirabilis*

Departamento de Microbiología, IIBCE; en colaboración con el Servicio de Microscopía de la Fac. de Ciencias

Magnitud del problema de los biofilms asociados a implantes médicos

Device	Estimated no. inserted in the United States per year	Rate of infection, %	Attributable mortality[a]
Bladder catheters[b]	>30,000,000	10–30	Low
Central venous catheters[b,c]	5,000,000	3–8	Moderate
Fracture fixation devices[b]	2,000,000	5–10	Low
Dental implants[d]	1,000,000	5–10	Low
Joint prostheses[b]	600,000	1–3	Low
Vascular grafts[b]	450,000	1–5	Moderate
Cardiac pacemakers[b,d]	300,000	1–7	Moderate
Mammary implants, in pairs[e]	130,000	1–2	Low
Mechanical heart valves[d]	85,000	1–3	High
Penile implants[b,d]	15,000	1–3	Low
Heart assist devices[d]	700	25–50	High

[a] Semiquantitative scale for attributable mortality: low, <5%; moderate, 5%–25%; high, >25%.
[b] Numbers estimated by analysis of market reports.
[c] Numbers estimated by review of the medical literature.
[d] Numbers estimated by personal communication with personnel from device manufacturing companies.
[e] Numbers estimated by review of data provided by medical associations.

Table 2. Device-related factors that may favor bacterial adherence.

Type of device material
Polyvinyl chloride favors bacterial adherence more than does teflon
Polyethylene favors bacterial adherence more than does polyurethane
Latex favors bacterial adherence more than does silicone
Silicone favors bacterial adherence more than does polytetrafluoroethylene
Stainless steel favors bacterial adherence more than does titanium
Source of device material: synthetic favors bacterial adherence more than does biomaterial
Surface of device
Irregular favors bacterial adherence more than does regular
Textured favors bacterial adherence more than does smooth
Hydrophobic favors bacterial adherence more than does hydrophilic
Shape of device: polymeric tubing favors bacterial adherence more than does wire mesh

Darouiche, 2001

Relación virulencia/biofilms en catéteres

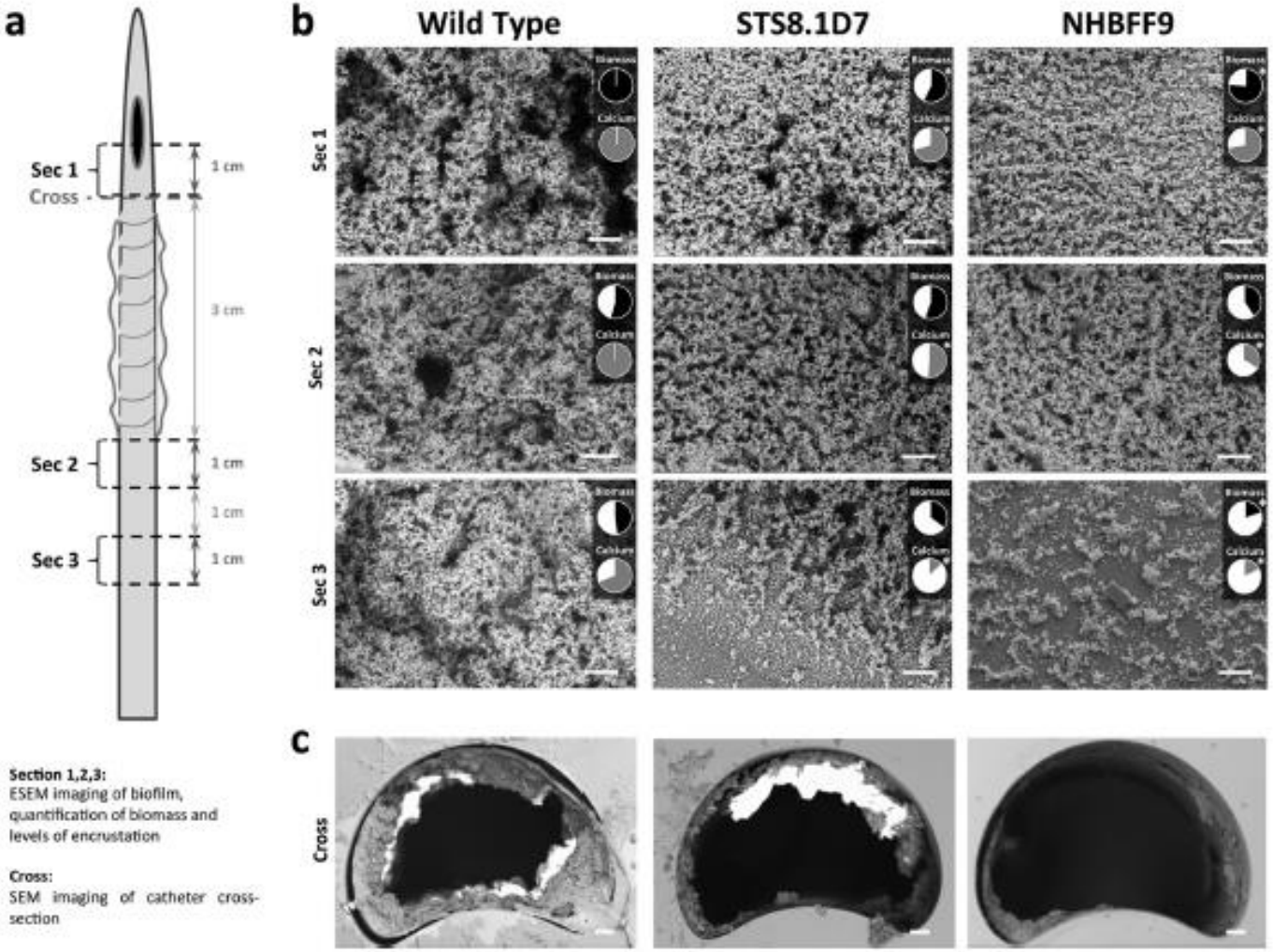
P. mirabilis y biofilms

TABLE 1 Characterization of biofilm formation mutants

Phenotype and strain	*P. mirabilis* HI4320 locus[a]	Disrupted gene	Putative function/product of disrupted gene[b]	Urease production (mean ± SD)[c]	Motility (% of wild type)	
					Swimming	Swarming
Wild type (B4)				5.7 ± 0.4	100	100
Biofilm enhanced						
NHBFG8	PMI3402		Unknown function; putative MuA-like DNA-binding protein (Pfam 02316) (40/40)	5.9 ± 0.3	0	0
NHBFH4	PMI0262[d]	*mrpI*	Fimbrial recombinase (40/40)[d]	4.3 ± 0.1	36.96	0
NHBFE8	PMI2210		Fimbrial subunit (38/40)	5.3 ± 0.4	70.65	111.34
NHBFH5	PMI2359	*glnE*	Glutamate-ammonia-ligase adenylyltransferase (38/40)	4.8 ± 0.4	51.09	0
NHBFA5	PMI1729	*rsbA*	Regulator of swarming behavior; sensor kinase of two-component system (40/40)	5.5 ± 0.1	116.3	32.99
NHBFF9	PMI0829	*bcr*	Bicyclomycin resistance gene (sulfonamide resistance protein, MFS transporter) (40/40)	4.7 ± 0.3	22.82	3.1
Biofilm deficient						
NHSH1	PMI1608		Unknown function; putative transmembrane protein (Pfam 02659) (39/40)	5.6 ± 0.3	27.17	0
ABBF1.1C8	PMI2867	*gltS*	Sodium/glutamate symport carrier protein (20/20)	5.4 ± 0.5	18.48	0
NHSE5	PMI1551		Unknown function; putative lipoprotein (COG3016, DUF399) (40/40)	5.2 ± 0.5	23.91	0
DLD1A6	PMI2861		Unknown function; putative membrane protein (COG2860, Pfam 03458) (40/40)	5.7 ± 0.7	35.86	84.54
DLD1D11	PMI0696[d]	*lrp*	Leucine-responsive regulator (40/40)[d]	5.2 ± 0.2	77.17	34.02
STS8.1D7	PMI1479[e]	*nirB*	Nitrite reductase (30/30)[e]	4.4 ± 0.1	100	77.32

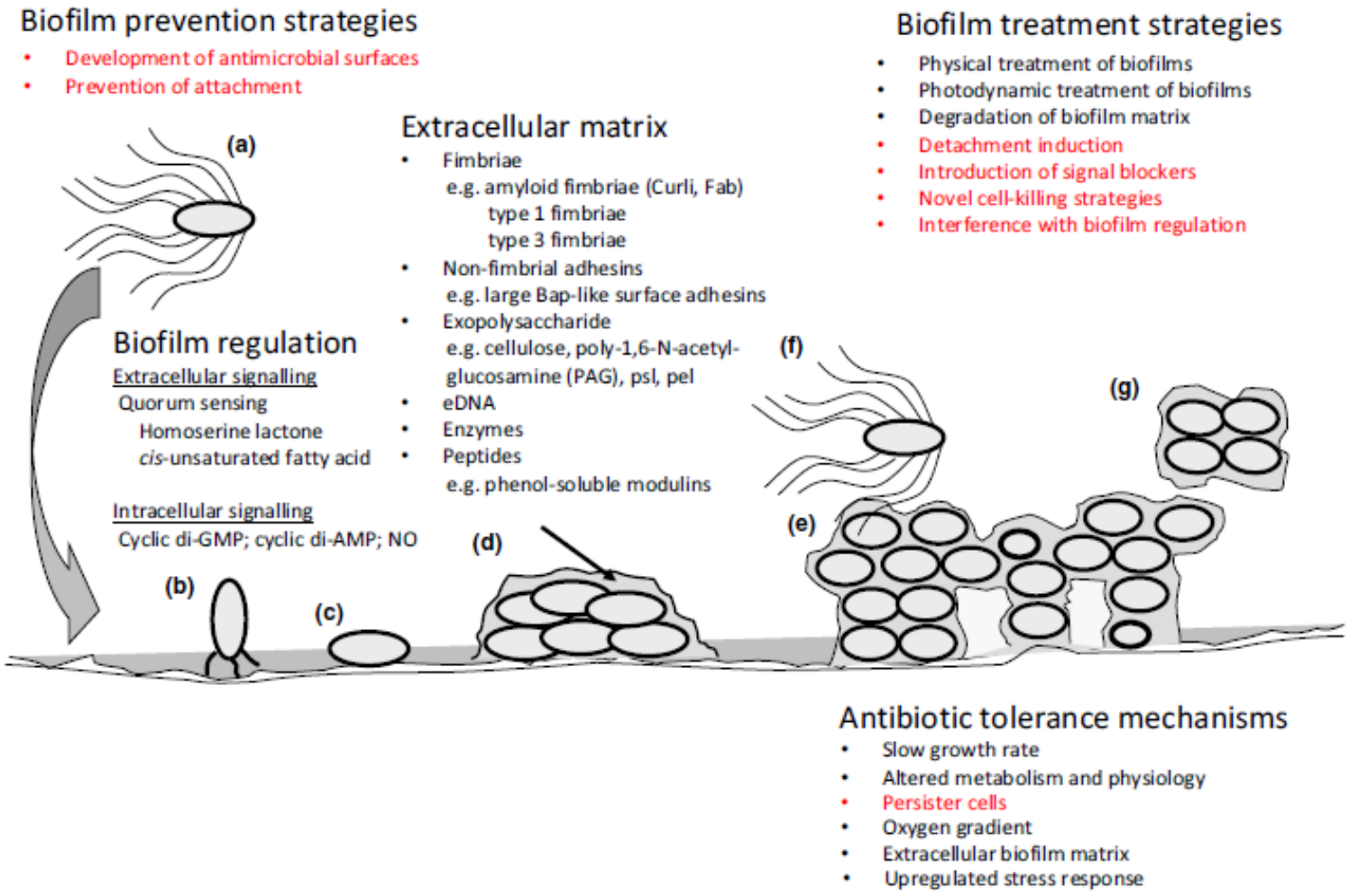
Holling et al., 2014

Mutantes *nirB* y transportador MFS



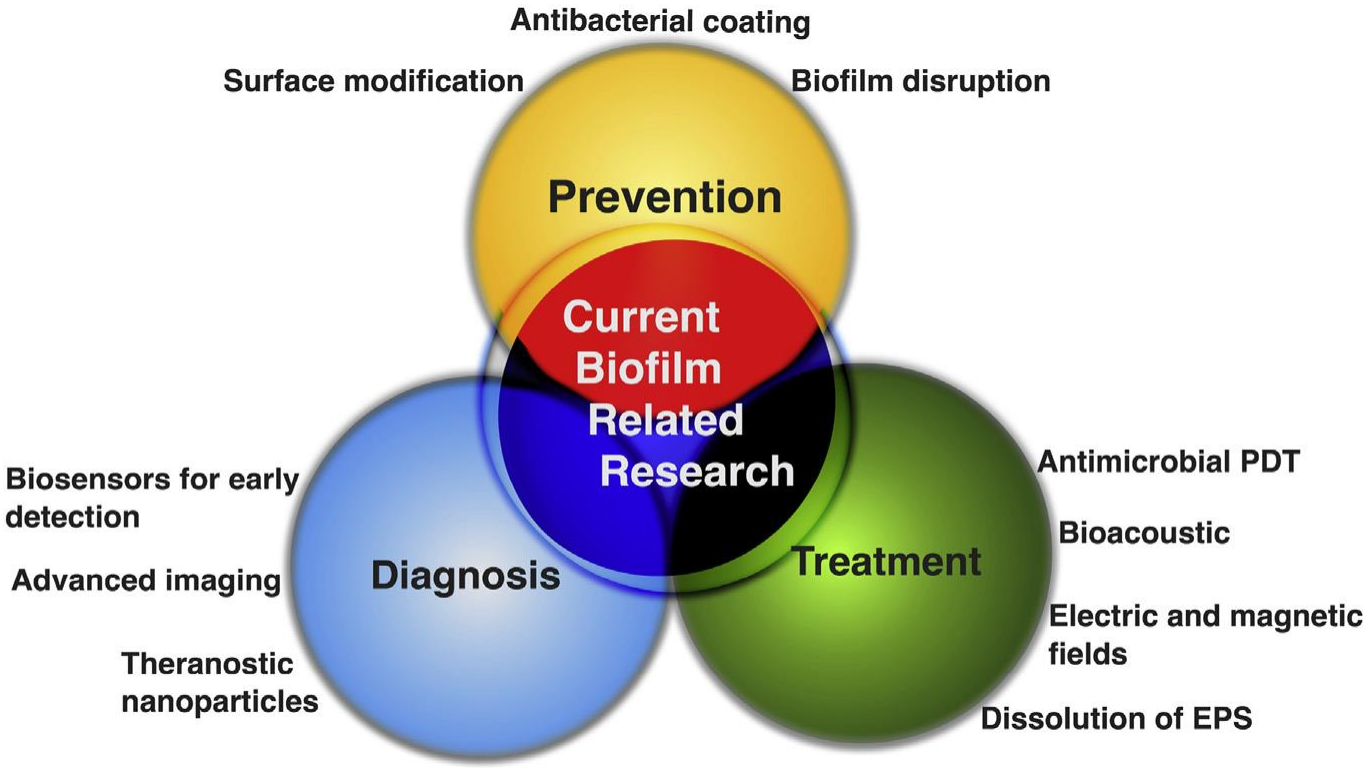
Holling et al., 2014

Biofilms: mecanismos y estrategias de prevención



Romling et al., 2014

Estrategias de prevención, tratamiento y diagnóstico



Khatoon et al., 2018

Estrategias

- Métodos físicos:

- Métodos eléctricos y electromagnéticos (electroporación/ combinaciones, campos eléctricos…)

- Campos magnéticos

- Ultrasonido (combinaciones…)

- Fotocatálisis

- Interferencia con mecanismos de adhesión

- Disrupción

- Interferencia con mecanismos de regulación (ej. QS)

Quorum sensing

Principal mecanismo de regulación (no el único!)

Autoinductores (Bacterias Gram – y Gram +)

Modulación adhesión/dispersión:

La mayoría de las especies aumentan los comportamientos asociados a la formación de biofilms a altas concentraciones celulares.

Mutantes afectadas en el QS forman biofilms débiles – función en la produción de matriz extracelular

Comunicación entre microorganismos: QS en bacterias Gram positivas y Gram negativas

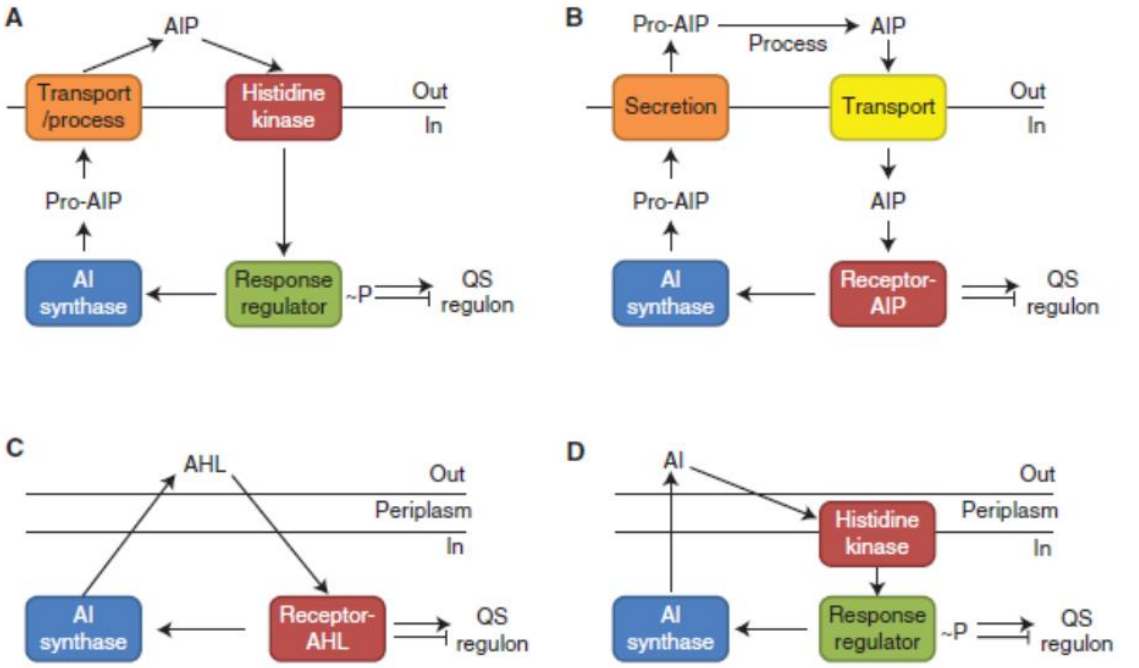
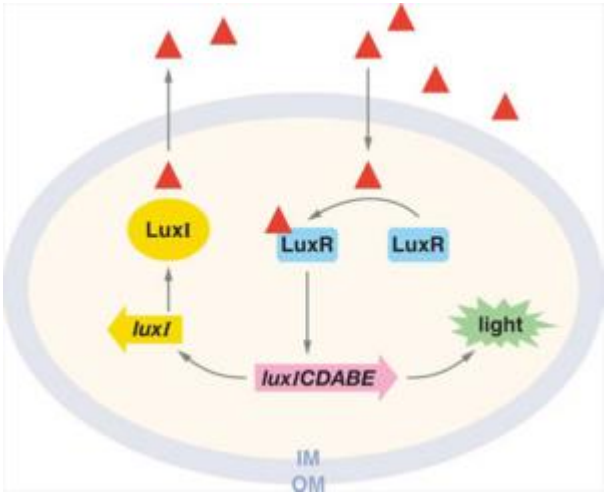


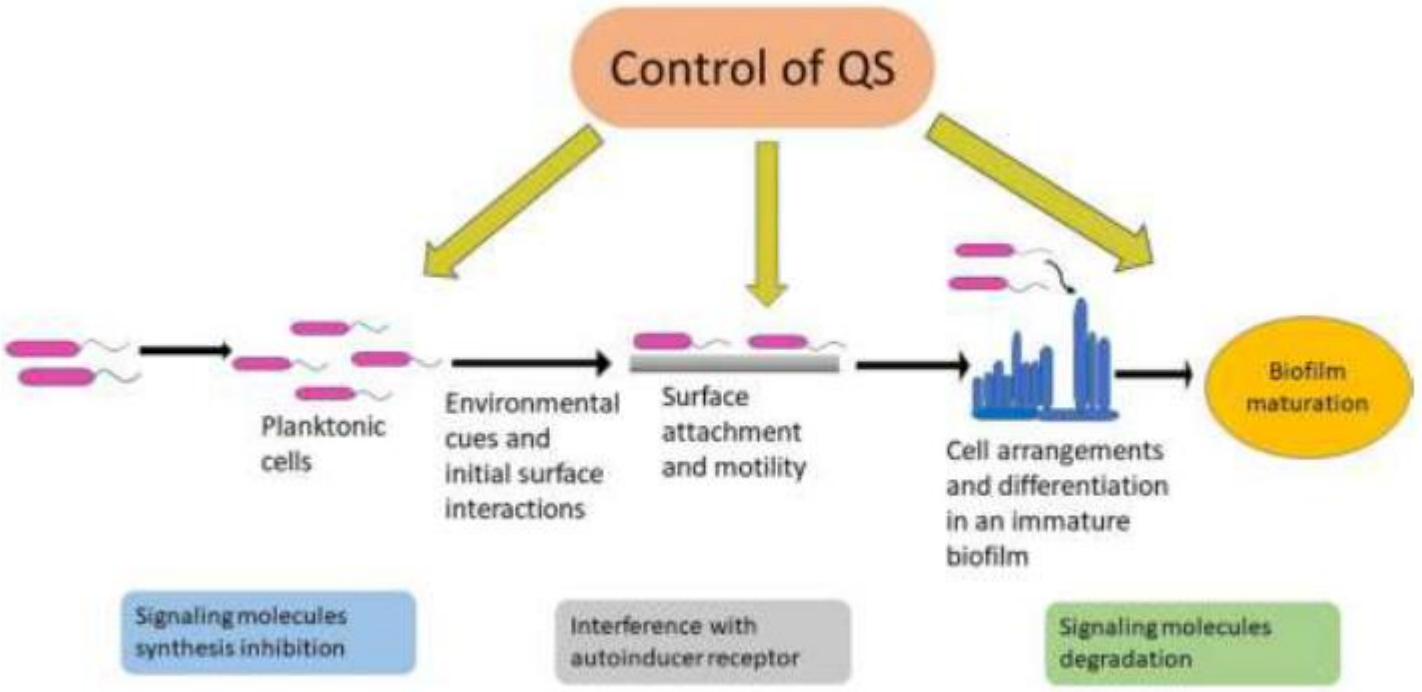
Figure 1. Canonical bacterial quorum-sensing (QS) circuits. Autoinducing peptide (AIP) QS in Gram-positive bacteria by (*A*) two-component signaling, or (*B*) an AIP-binding transcription factor. Small molecule QS in Gram-negative bacteria by (*C*) a LuxI/LuxR-type system, or (*D*) two-component signaling.



Vibrio fischeri

Mecanismos generales de QS

Pasos involucrados en la formación de biofilms y control del QS para la inhibición de la colonización de las superficies



Munir et al. 2020

Mecanismos de interferencia con el QS (*Quorum quenching*)

- Inhibidores con efecto en la vía de síntesis de los AI
- Degradación enzimática de los AI
- Análogos de AHL y compuestos con afinidad por receptores
- Análogos de AIP y compuestos con afinidad por receptores
- Acción a nivel de la cascada de transducción de señales

Bacha et al. BMC Microbiology (2016) 16:139
DOI 10.1186/s12866-016-0765-9

BMC Microbiology

RESEARCH ARTICLE Open Access

Antimicrobial and anti-Quorum Sensing activities of selected medicinal plants of Ethiopia: Implication for development of potent antimicrobial agents

Ketema Bacha[1*], Yinebeb Tariku[2], Fisseha Gebreyesus[3], Shibru Zerihun[4], Ali Mohammed[5], Nancy Weiland-Bräuer[6], Ruth A. Schmitz[6] and Mulugeta Mulat[1,7]

Table 1 Summary of traditional medicinal plants and their extracts evaluated for antimicrobial and Quorum Quenching (anti-Quorum Sensing) activities

Sample No	Code	Scientific name of plant with brief description	Type of Extract
1	ACFA1	*Aframomum corrorima* mature semi-ripe fruit acetone extract	Oleo resin
2	ACFA2	*Aframomum corrorima* mature unripe fruit acetone extract	Oleo resin
3	ACFA3	*Aframomum corrorima* mature ripe fruit acetone extract	Oleo resin
4	ACFO	*Aframomum corrorima* mature unripe fruit oil	Essential oil
5	ACHO	*Aframomum corrorima* mature ripe fruit husk oil	Essential oil
6	ASRM	*Albizia schimperiana* root methanol extract	Crude extract
7	CLRA1	*Curcuma longa* finger rhizome acetone extract	Oleo resin
8	CLRO1	*Curcuma longa* finger rhizome oil	Essential oil
9	CLRO2	*Curcuma longa* main rhizome oil	Essential oil
10	CLRA2	*Curcuma longa* main rhizome acetone extract	Oleo resin
11	EBBP	*Erythrina brucei* stem bark petroleum ether extract	Crude extract
12	JSSP	*Justica schimperiana* seed petroleum ether extract	Crude extract
13	NSSO	*Nigella sativa* seed oil	Essential oil
14	NSSP	*Nigella sativa* seed petroleum ether extract	Crude extract
15	OSLC	*Ocimum sauve* leaf chloroform extract	Crude extract
16	VALC	*Vernonia amygdalina* leaf chloroform extract	Crude extract
17	VALM	*Vernonia amygdalina* leaf methanol extract	Crude extract
18	VALP	*Vernonia amygdalina* leaf petroleum ether extract	Crude extract

Table 4 Quorum Quenching activities of selected medicinal plants of Ethiopia

Extracts	AHL-QQ activity in *E. coli* based reporter strain AI1-QQ.1	Antimicrobial activity against *E. coli* K12 DSM 498
ACFA1	-	-
ACFA2	-	-
ACFA3	-	-
ACFO	-	+++
ACHO	-	+
ASRM	+	+
CLRA1	-	-
CLRA2	-	-
CLRO1	-	-
CLRO2	-	++
EBBP	-	-
JSSP	+	-
NSSO	-	+
NSSP	-	-
OSLC	-	-
VALC	-	-
VALM	-	-
VALP	-	-

Bacha et al., 2016

Uso de cepa de *E. coli* reportera

Contents lists available at ScienceDirect

International Journal of Antimicrobial Agents

journal homepage: http://www.elsevier.com/locate/ijantimicag

Short communication

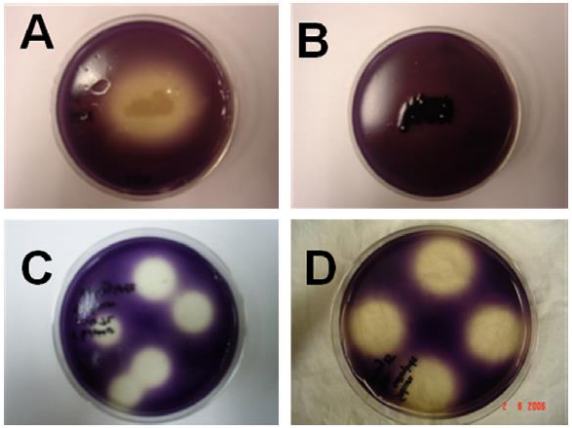
Use of quorum sensing antagonists to deter the formation of crystalline *Proteus mirabilis* biofilms

Steven M. Jones*, Tammy T. Dang, Robert Martinuzzi

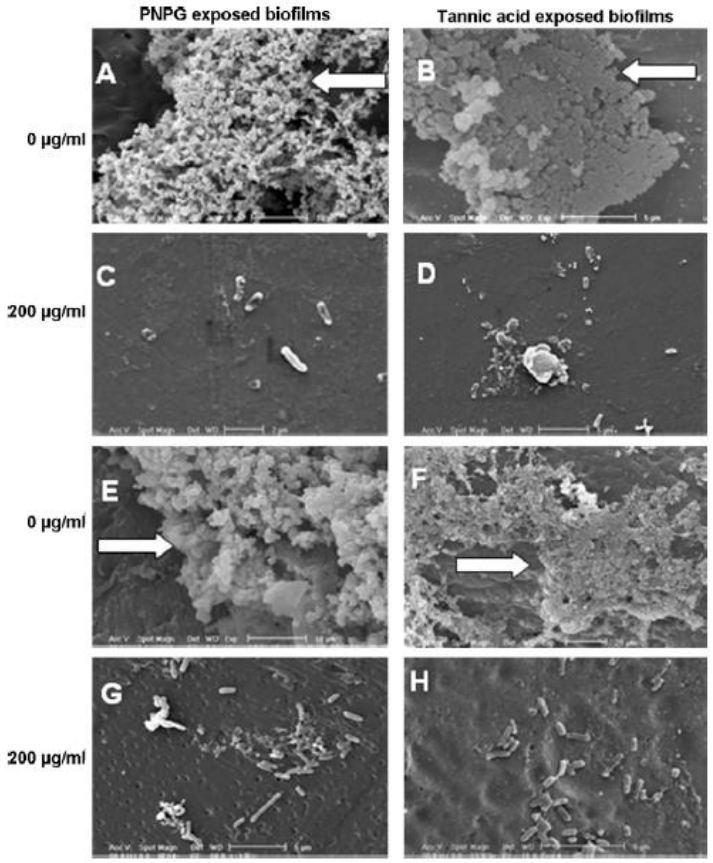
Evaluación del efecto antibiofilm de inhibidores del QS:

- p-nitrofenilglicerol
- taninos

Evaluación: efecto sobre la producción de pigmentos de *Chromobacterium violaceum*



Efecto preventivo y de disrupción del biofilm formado



Micrografías electrónicas de barrido: (A, B) biofilms de *Proteus mirabilis* sin tratar y biofilms (C, D) cultivadas en presencia de 200 g / ml de p-nitrofenil glicerol (PNPG) o ácido tánico durante un período de 24 h; (E, F) biofilms de *P. mirabilis* de 24 h sin tratar y (G, H) biofilms de 24 h expuestos a 200 g / ml de PNPG o ácido tánico durante 24 h. Las flechas representan la presencia de material cristalino en biofilms de *P. mirabilis* sin tratar.

Nuevas tecnologías de superficies

Materiales comúnmente empleados (ej. implantes ortopédicos): cerámica, cromo-cobalto, polietileno, polimetilmetacrilato, aleaciones de titanio, etc.

Estrategias:

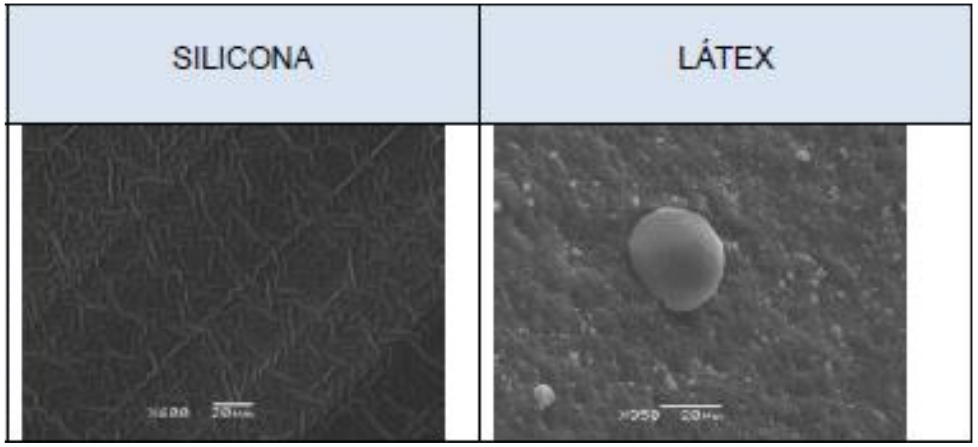
- **Modificaciones pasivas de las superficies**

Reducción de la adhesión bacteriana mediante la alteración de la química de la superficie del implante y / o modificación de la estructura de la superficie, sin liberación local o captura superficial de agentes bactericidas

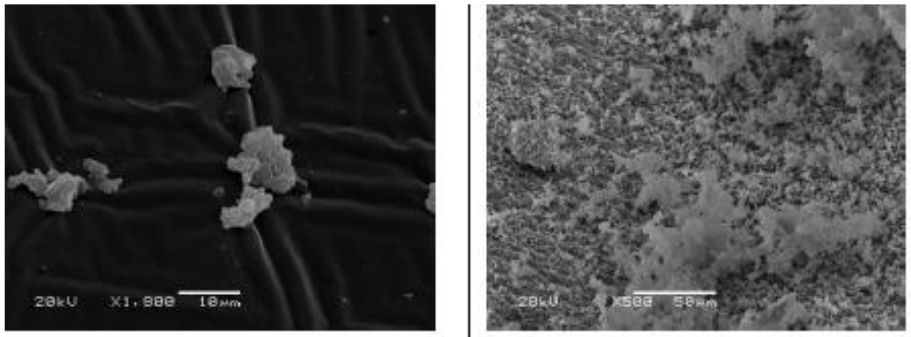
Ej. Metales
Cerámicas
Nanopatrones
Biosurfactantes (ej. lipopéptido producido por *B. subtilis* ATCC 19659)

Superficies - Materiales

ITU-C Biofilms de P. *mirabilis* sobre secciones de catéteres (SEM)



Secciones de catéteres



Biofilms de *P. mirabilis*

Departamento de Microbiología, IIBCE; en colaboración con el Servicio de Microscopía de la Fac. de Ciencias

- **Modificaciones activas de las superficies**

Recubrimientos que se caracterizan farmacológicamente como agentes bactericidas activos

Ej. Moléculas inorgánicas (ej. Ag, actividad antimicrobiana, Cu, Zn)
Ingredientes no metálicos (por ejemplo, yodo, selenio),
Antibióticos (ej. vancomicina, gentamicina)
Péptidos antimicrobianos (12 a 50 aa)
Aceites esenciales
Esfingosina (aminoalcohol)
Nanocoatings (nanopartículas, sales de plata, ZnO, etc.)

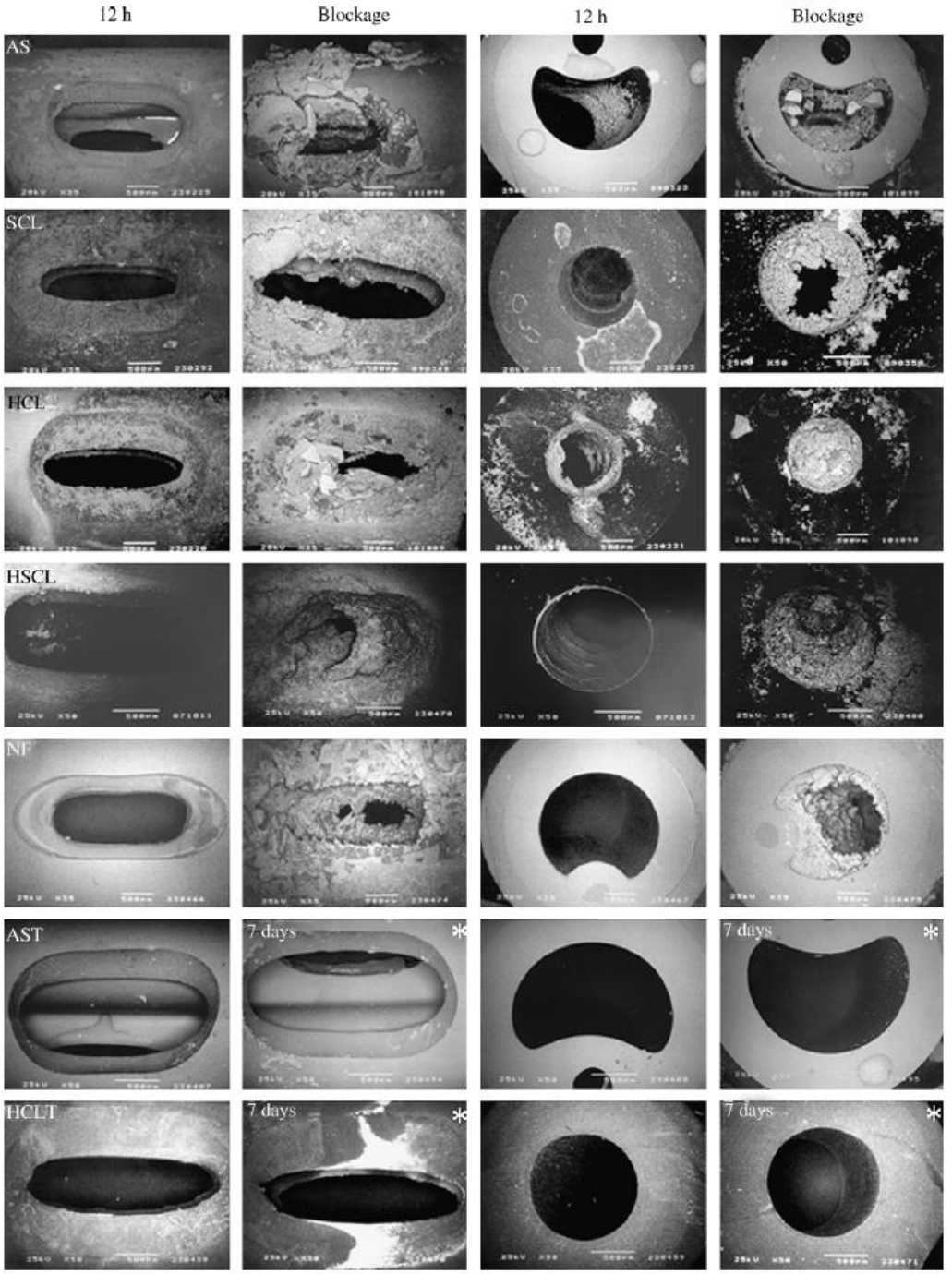
- **Coberturas**

Ej. Albúmina
Elastina
Heparina

Modificado de Rodríguez-Merchán et al. 2021

Estrategias de prevención de biofilms cristalinos de *P. mirabilis* en la luz de catéteres urinarios

AS - silicona
SCL - látex cubierto de silicona
HCL - látex cubierto de hidrogel
HSCL - látex cubierto de hidrogel/oro
NF - silicona nitrofurazona
AST - silicona/triclosan
HCLT - látex cubierto de hidrogel/triclosan



Stickler y Morgan, 2008

Research Article

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Nanomedicine

Magnesium-doped zinc oxide nanoparticles alter biofilm formation of *Proteus mirabilis*

Victoria Iribarnegaray[1], Nicolas Navarro[2,3], Luciana Robino[4], Pablo Zunino[1], Javier Morales[†,2,3] & Paola Scavone*[,†,1]

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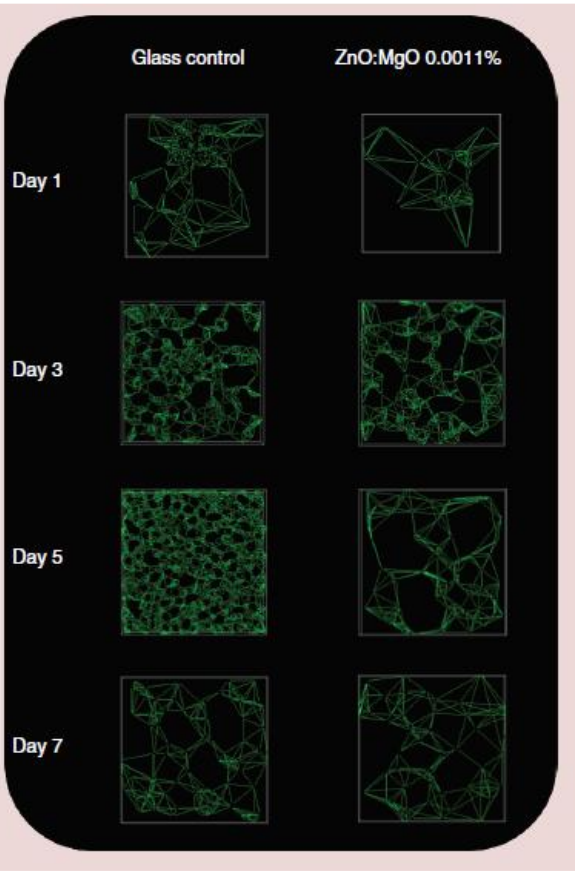
[†]Authors share senior authorship



Estrategias de prevención

- Antimicrobianos (Aslam, 2008)
- Inhibidores del *quorum sensing* (taninos, p-nitrophenyl glycerol - PNPG -, etc.; Jones *et al*., 2009)
- Jugos y extractos vegetales (arándano, Martino et al., 2005; *Ibicella lutea*, Sosa y Zunino, 2009; cinamaldehído, Amalaradjou et al., 2010)
- EDTA (Percival *et al*., 2009)
- Bacteriófagos líticos (Carson *et al*, 2010)
- Interferencia con los mecanismos de captación de Fe (Hancock et al., 2010)
- Uso de bacterias probióticas (ej. *Lactobacillus acidophilus* - Hawthorn & Reid, 1990)
- Impregnación con antisépticos (Hachem et al., 2007)
- Muchos otros…

Ejemplos particulares: catéteres vasculares

Table 1 Summary of the methods that have been attempted or proposed for preventing artificial surface fouling from infectious or thrombotic causes

Infection prevention methods
Antibiotic infusion
Minocycline (16-18)
Rifampin (16-18)
Catheter materials
Polytetrafluoroethylene (21)
Polyurethane (21)
Antiseptic coating
Chlorhexidine (19,20)
Sulfadiazine (19,20)
Other
Silver (11)
Heparin (16)
Thrombosis prevention methods
Hydrophilic polymers
Polyethylene glycol (49)
Zwitterionic materials
Phosphorylcholines (51,52)
Other coatings
Pyrolytic carbon (55-57)
Albumin (62)
Heparin (65)
Direct thrombin inhibitors (71-73)
Sirolimus (74)
SLIPs (77-81)
Micropatterning
Lotus leaf conical cells (85)
Shark skin microgrooves (86)

“Molécula pequeña”

Compuesto orgánico de bajo peso molecular (no más de 800 Da), lo que le posibilita la rápida difusión a través de la membrana celular

Acciones biológicas diversas

“Pequeñas moléculas”

Table 1. Small molecules that can inhibit biofilm formation.

Agent	Mechanism	Effect	Reference
Anti-virulence compounds	Inhibition of gene expression of virulence factors	Inhibition of biofilm formation by *S. aureus*	[23]
Anti-biofilm compounds	Unknown	Inhibition of biofilm formation by *S. epidermidis*	[25]
ABC-1	Inhibition of c-di-GMP-inducible transcription	Inhibition of biofilm formation by multiple Gram-negative and Gram-positive bacterial pathogens	[26]
Aryl rhodanines	Unknown	Inhibition of biofilm formation by *S. aureus* and *S. epidermidis*	[29]
Cis-2-decenoic acid	Unknown	Dispersion of biofilms by *E. coli*, *K. pneumoniae*, *P. mirabilis*, *S. pyogenes*, *B. subtilis*, *S. aureus*, and *C. albicans*	[30]
D-amino acids	Unknown	Inhibition of biofilm formation by *S. aureus* and *P. aeruginosa*	[31]
N-acetylcysteine	Interference with exopolysaccharide formation in biofilms	Inhibition of biofilm formation by *S. epidermidis*	[32]
Chelators	Interference with metal ion’s function in biofilm formation	Inhibition of biofilm formation by *S. aureus*	[33]

Chen et al., 2013

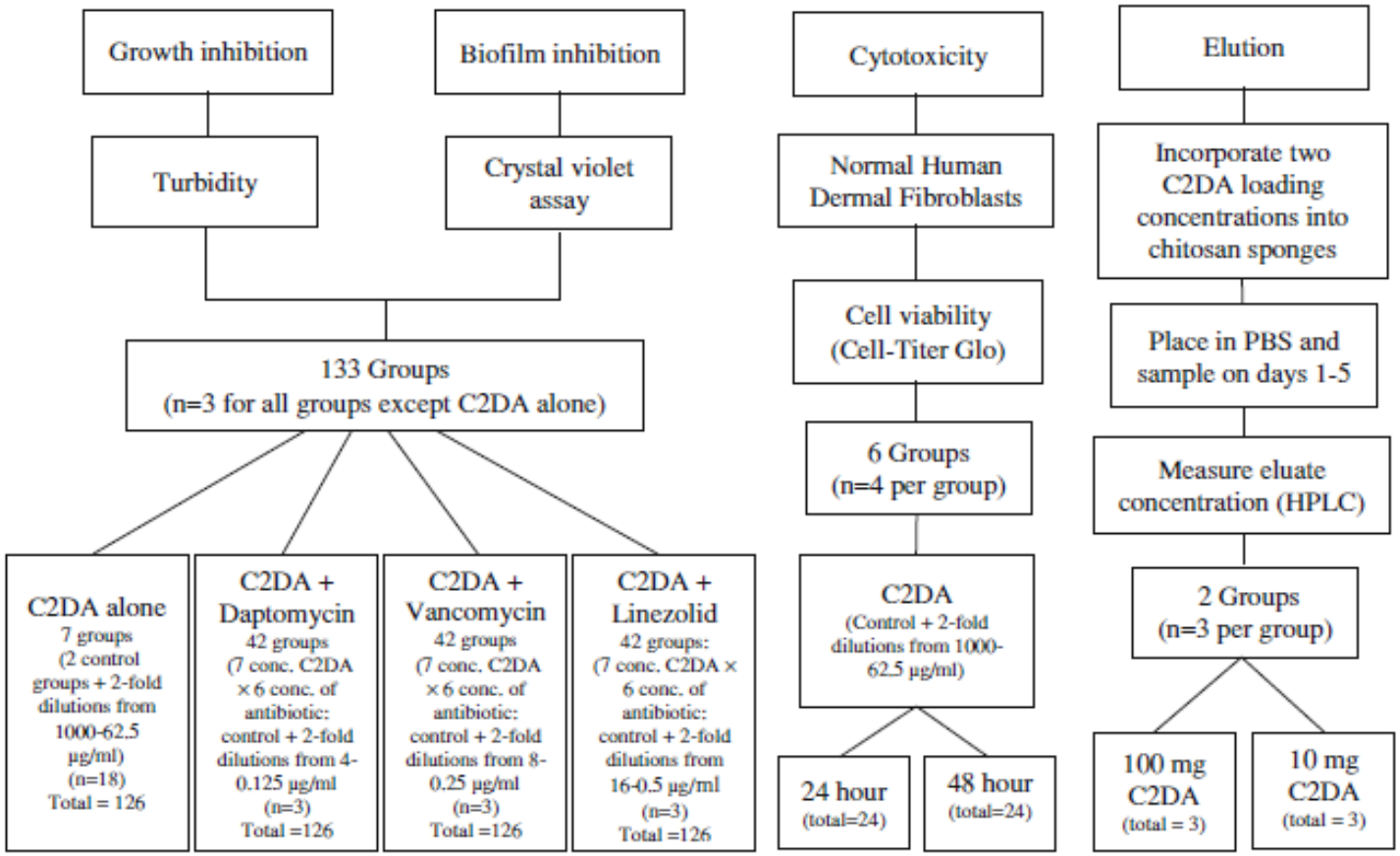
Clin Orthop Relat Res (2012) 470:2663–2670
DOI 10.1007/s11999-012-2388-2

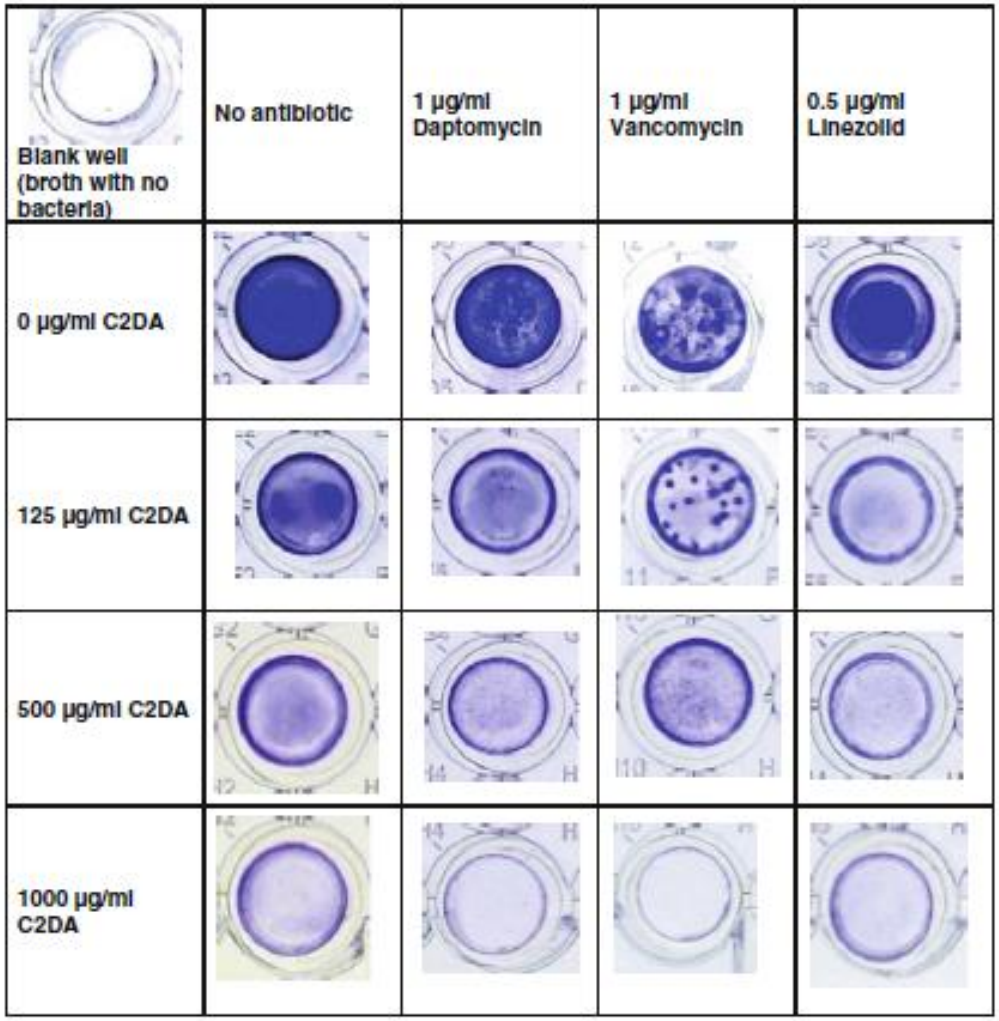
Clinical Orthopaedics and Related Research®
A Publication of The Association of Bone and Joint Surgeons®

SYMPOSIUM: 2011 MUSCULOSKELETAL INFECTION SOCIETY

Cis-2-decenoic Acid Inhibits S. aureus Growth and Biofilm In Vitro: A Pilot Study

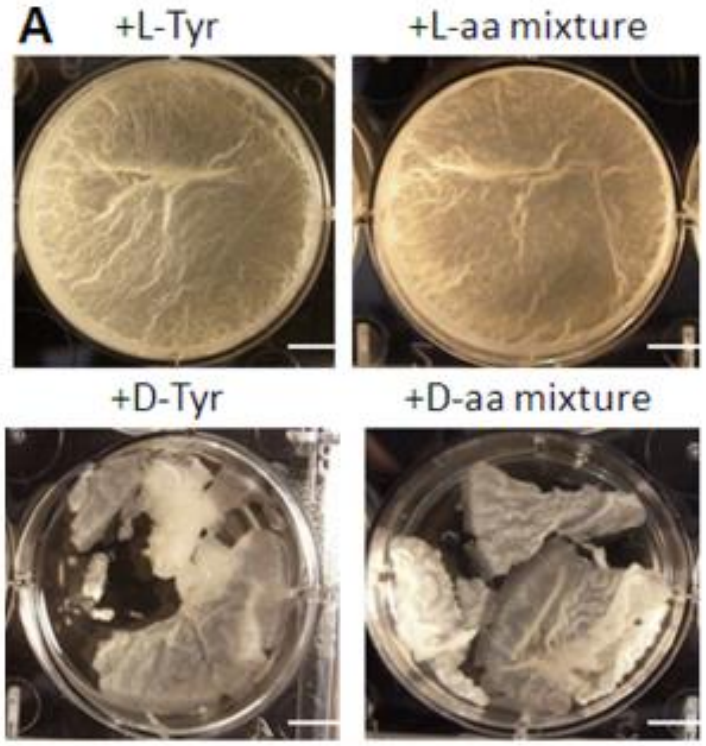
Jessica Amber Jennings PhD, Harry S. Courtney PhD, Warren O. Haggard PhD





Tinción con CV de biofilms sometidos a distintas concentraciones de C2DA y antibióticos

Disrupción: D-aminoácidos



Science. 2010 April 30; 328(5978): 627–629. doi:10.1126/science.1188628.

D-Amino Acids Trigger Biofilm Disassembly

Ilana Kolodkin-Gal[1], Diego Romero[2], Shugeng Cao[3], Jon Clardy[3], Roberto Kolter[2], and Richard Losick[1,*]

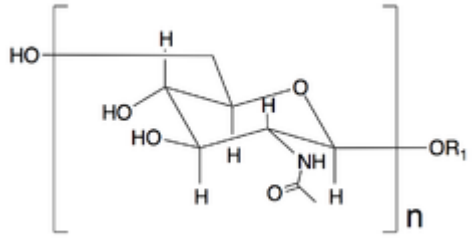
D-aa: racemasas

D-leucina, D-metionina, D-tirosina, D-triptofano: disrupción de fibras amiloides que intervienen en la cohesión del biofilm (*B. subtilis*, *S. aureus, P. aeruginosa*)

Interferencia con la estructura normal de la capa de peptidoglicanos

Enzimas (matriz)

- Dispersina B (DspB; glycoside hydrolase *Actinobacillus actinomycetemcomitans,* 40 kDa)

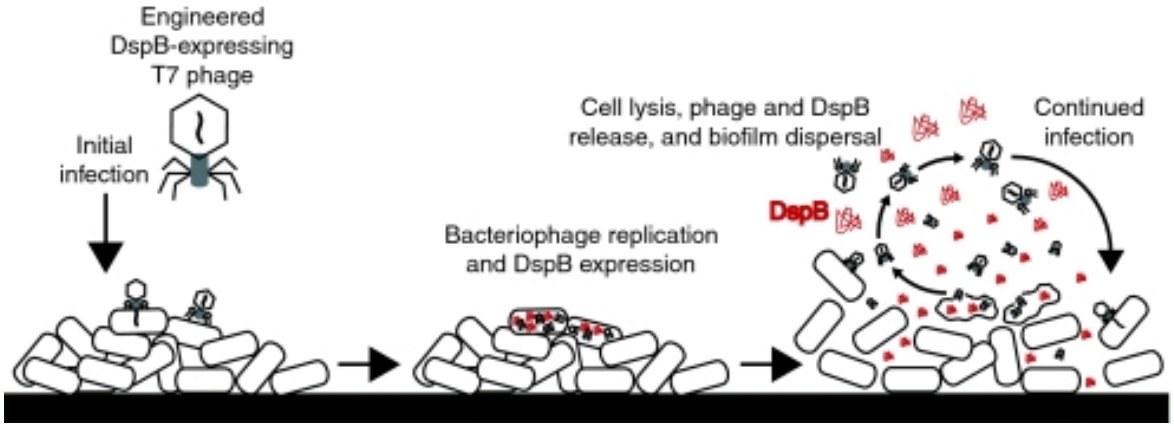


- DNase I

- Proteasas: Proteinasa K, tripsina

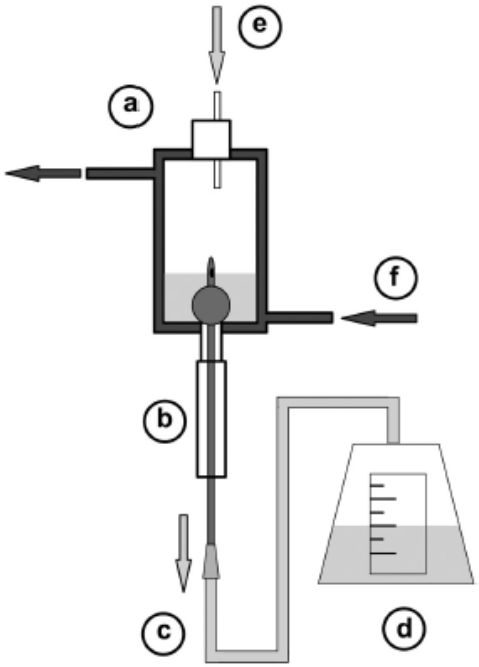
Terapia fágica

- Fagos salvajes
- Fagos modificados

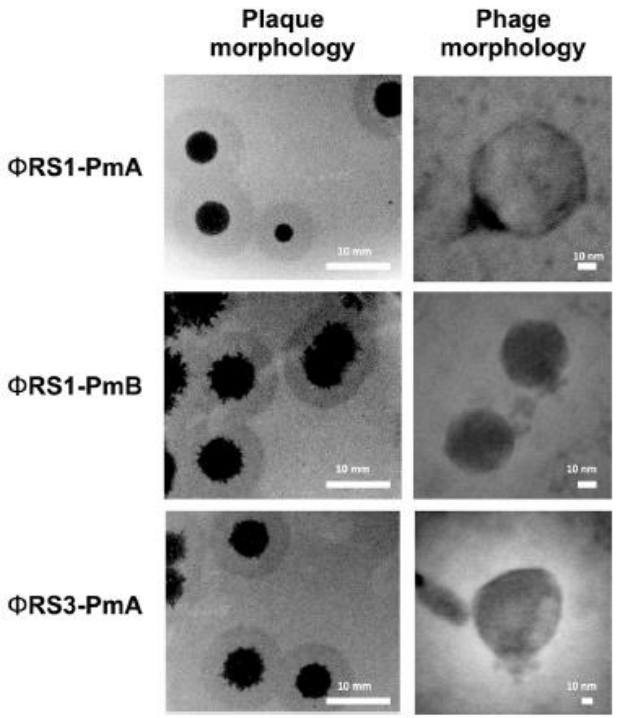


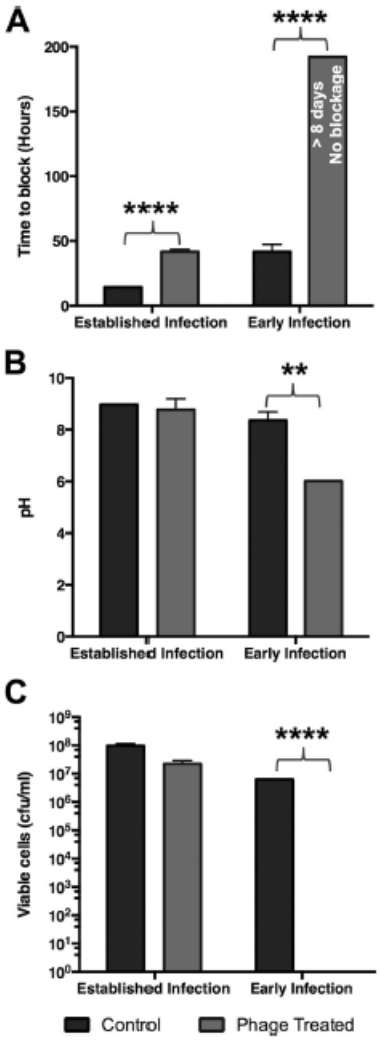
Fagos y biofilms de *P. mirabilis*

Nzakizwanayo *et a*l., 2016



Modelo de vejiga *in vitro*

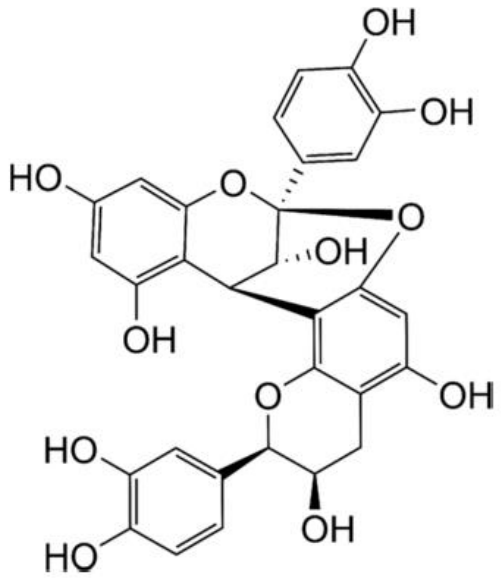




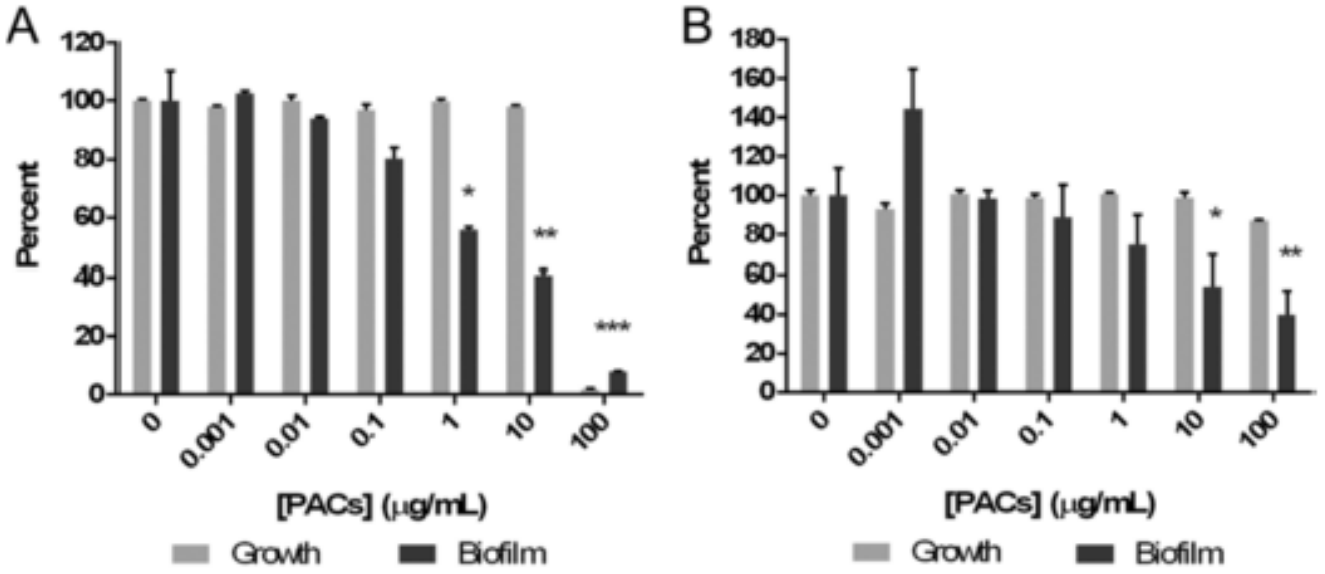
Productos naturales

Arándanos

(*Vaccinium macrocarpon*)



Proantocianidina de arándano



Efecto de proantocianidina de *V. macrocarpum* sobre *P. aeruginosa*

Original Article

Effect of *Ibicella lutea* on uropathogenic *Proteus mirabilis* growth, virulence, and biofilm formation

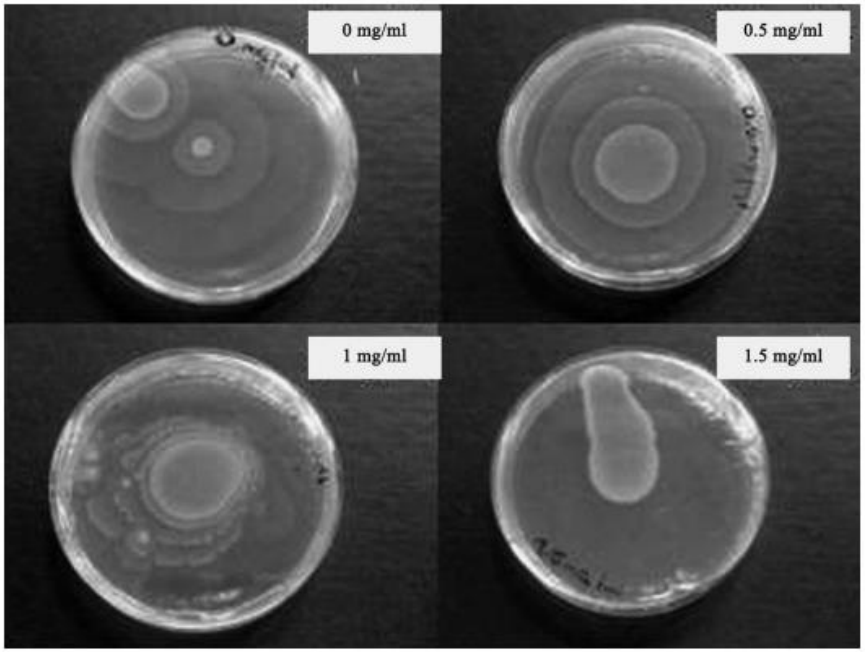
Vanessa Sosa and Pablo Zunino

J Infect Dev Ctries 2009; 3(10):762-770.

Table 2. Effect of *I. lutea* extract on biofilm formation by Pr2921 in polystyrene and glass and on auto-aggregation.

Concentration of *I. lutea*	Biofilm quantification		Auto-aggregation
	Polystyrene	Glass	
0 mg ml^{-1}	1.529 ± 0.600	0.623 ± 0.294	8.95 ± 6.34
1 mg ml^{-1}	0.236 ± 0.020*	0.007 ± 0.003*	7.31 ± 2.90
2 mg ml^{-1}	0.450 ± 0.163*	0.045 ± 0.035*	11.96 ± 2.59

Results are presented as the means ± standard deviations of three independent assays. The *I. lutea* extract inhibited biofilm formation but not affected the auto-aggregation.
*significantly different from control at $P < 0.05$ assessed by Mann-Whitney non-parametric analysis.
No significant differences between the two concentrations of extract *I. lutea* were observed.



Prevención de biofilms en la industria de alimentos

Methodology	Examples	Mechanism of action	Reference
Chemical treatments	Sanitizers (NaOCl, peracetic acid, NaOH, H_2O_2)	Cell structures oxidation	Rosenberg et al., 2008; Bayoumi et al., 2012; Schmidt, 2012; Bang et al., 2014; Nam et al., 2014; Ban and Kang, 2016; Techaruvichit et al., 2016; Yang et al., 2016; Møretrø et al., 2017
Enzymatic disruption	Cellulases	Extracellular matrix disruption	Wang et al., 2012; Coughlan et al., 2016; Stiefel et al., 2016
	Proteases		Oulahal-Lagsir et al., 2003; Chaignon et al., 2007; Boels, 2011; Huang et al., 2014; Coughlan et al., 2016; Stiefel et al., 2016
	Glycosidases		Boels, 2011; Huang et al., 2014; Coughlan et al., 2016
	DNAses		Coughlan et al., 2016
Steel coatings	Nanoparticles (Ag^{2+}, Fe_3O_4, TiO_2, ZnO, CuO, MgO	Alteration of bacterial membrane	Alexander, 2009; Beyth et al., 2015; Rai et al., 2015
	Repelling surfaces (monolayers, hydrogels, modified topography)	Inhibition of bacterial binding	Campoccia et al., 2013; Jindal et al., 2016; Swartjes and Veeregowda, 2016
	Functionalized surfaces (with lisozyme or nisin)	Bactericidal	Sandreschi et al., 2016; Gu et al., 2017
Biosurfactants	Lichenysin	Inhibition of bacterial adhesion	Coronel-León et al., 2016
	Surfactin		Zhang et al., 2017; Zhao et al., 2017
Bacteriophages	P100	Cell lysis	Fister et al., 2016; Iacumin et al., 2016
Bacteriocins	Nisin	Cell membrane alteration	Strempel et al., 2015
QS inhibition	Binding of inhibitors to QS receptors (lactic acid)	Downregulation of adhesion and virulence mechanisms	Rasmussen et al., 2005; Brackman and Coenye, 2015; Coughlan et al., 2015; Amrutha et al., 2017
	Eznymatic degradation of QS signals (paroxonases)		Dong et al., 2001; Yang et al., 2005; Uroz et al., 2008; Koh et al., 2013
	sRNA post-transcriptional control		Perez-Martinez and Haas, 2011
	Inhibition of QS signals biosynthesis		Adonizio et al., 2008; Chung et al., 2011; Zhu et al., 2015; Al-Shabib et al., 2016
	Furanones	Motility inhibition	Keskinen and Annous, 2011; Vestby et al., 2014
Essential oils	Citral	QS inhibition, motility inhibition	Shi et al., 2017
	Carvacrol	Bactericidal	Friedman, 2014
High hydrostatic pressure	H_2O	Bactericidal (also endospores)	Evelyn and Silva, 2015; Santos et al., 2017
Non-thermal plasma	UV plus O_2, N_2, O_3, H_2O and He	Bactericidal	Scholtz et al., 2015
Photocatalysis		Bactericidal	Chorianopoulos et al., 2011; Priha et al., 2011; Nica et al., 2017; Ishwarya et al., 2018

Galie et al. 2018