

Supplementary

Antibacterial, Antibiofilm, and Antioxidant Activity of 15 different Plant-based Natural compounds in Comparison with Ciprofloxacin and Gentamicin.

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1. Supplementary Materials and methods

1.1. Systematic review for selecting highly effective plant-based natural compounds (PBCs) as antibacterial agents

We conducted a systematic review of available publications to generate a list of potentially highly effective antibacterial plant-based natural compounds (PBCs). The systematic review was performed according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement (PRISMA) guidelines (1). We searched all pieces of literature from January 1, 2000, to September 1, 2021, from Scopus, Embase, Medline (via PubMed), and Web of Science. Search medical subject headings (MeSH) terms used were: “natural compounds”, “natural product”, “herbal extract”, “herbal medicine”, “antibacterial”, “antimicrobial”, “Cannabidiol”, “CBD”, “Cannabis sativa”, “THC”, “tetrahydrocannabinol”, “Cinnamaldehyde”, “Tea Tree Oil”, “Nerolidol”, “Carvacrol”, “*O*-coumaric acid”, “Thymol”, “Thymic acid”, “Canada Balsam”, “resveratrol”, “curcumin” and their synonyms. Moreover, we searched for unpublished and grey literature with Google scholar. We also assessed the references of included identified articles and related reviews to find additional relevant studies. After screening titles and abstracts, the full text of potentially eligible records was examined and retrieved.

Inclusion and exclusion criteria studies had to fulfil the pre-determined criteria to be eligible for inclusion in our systematic review. To facilitate the comparison of our results with those in other publications, studies with minimum inhibitory concentration (MIC) data were included in our systematic review. Studies that reported non-quantitative antibacterial susceptibility with the zone of inhibition diameter or any other method other than MIC, were excluded from this study. The following items were extracted from each article: first author, publication date, bacteria name, MIC, and important relevant comments from each study. Quality assessments of included studies were performed according to the critical appraisal checklist recommended by the Joanna Briggs Institute (2). The checklist is composed of nine questions, the 'Yes' answer to each question received one point. Thus, the final scores for each study could range from 0 to 9.

1.2. Bacterial strains and culture media

Based on the company's instructions, bacterial strains were stored at -70°C in Micro-bank vials (Richmond Hill, Ontario, Canada). Six indicator strains were used for all experiments; including *Pseudomonas aeruginosa* ATCC 27853, *Klebsiella pneumoniae* ATCC 11296, *Staphylococcus aureus* ATCC 25923, *Escherichia coli* ATCC 25922, *Proteus mirabilis* MMX 6442, and *Acinetobacter baumannii* CDC strain AR Bank # 0033 (3). Mueller-Hinton Broth (MHB, BD Bacto, Oxoid, Basingstoke, UK Cat# X243B) was used as the growth medium for susceptibility testing media in this study (4, 5).

1.3. Antibiotics and Plant-based natural compounds (PBCs)

We generated a list of eleven of the most potent antibacterial PBCs by the systematic review of available publications. These eleven PBCs are Cannabidiol (CBD) (SIGMA, MO, USA, LOT#SLCC9048), (-)-11-nor-9-carboxy- Δ^9 -tetrahydrocannabinol (THC) (SIGMA, MO, USA, LOT#FE05081905), Cinnamaldehyde (Fisher Scientific, Ottawa, Canada, LOT #5018R23W, >98%), Tea Tree Oil (Newconatural, Australia, LOT 80038607, >98%), Nerolidol (TCI, Portland, USA LOT #IKUMH-BE, >97%), Carvacrol (TCI, Portland, USA LOT #NDFYD-GT, >98%), *o*-coumaric acid (SIGMA, MO, Germany, LOT#106H0966), Thymol (Fisher Scientific, Ottawa, Canada, LOT #W12E020, >98%), Resveratrol (TCI, Portland, USA LOT #QWDXI-RF, >99%), Curcumin (Alfa Aesar, Ontario, Canada LOT #1022628, >95%), and Canada Balsam (SIGMA, MO, USA, LOT#125H2518). The two most common antibiotics, gentamicin (Amresco, Solon, Ohio, USA LOT #339C337) and ciprofloxacin (6) (SIGMA, MO, Germany, LOT#146C0896) were used as controls to provide a comparison of the antibacterial properties of the PBCs.

1.4. Minimum Inhibitory Concentration (MIC) Assay

All planktonic and biofilm susceptibility testing were carried out using the Calgary biofilm device; commercially available as the MBEC physiology and genetics assay [Innovotech Inc., Edmonton, Alberta, Canada]), as originally developed and described by the Calgary Biofilm Research Group (7). This device is a peg lid fitted into a 96 well microtiter plate. Serial dilutions of each PBC, with a dilution factor of two, were prepared; the first column served as a negative control (Media, 0 mM PBCs and no bacteria) and the last column served as a positive control

(Media and bacteria, 0 mM PBCs with bacteria). Briefly, $-70\text{ }^{\circ}\text{C}$ stored bacteria were sub-cultured two times overnight (O/N) at $37\text{ }^{\circ}\text{C}$ on MHA plates to obtain a pure single colony. $75\text{ }\mu\text{L}$ of 1.0×10^6 CFU/ml inoculum of bacteria were then added to each well and the plate was incubated for 24 hours at $37\text{ }^{\circ}\text{C}$ in a microplate shaker at 150 rpm (5). The well with the highest dilution, but which did not show evidence of bacterial growth, was considered as the minimal inhibitory concentration (MIC). Bacterial growth was determined by reading the optical density at 600 nm (OD600), using a Thermomax microtiter plate reader with Softmax Pro data analysis software (Molecular Devices, Sunnyvale, CA). Due to unclear MIC for some of the PBCs that gave high solution turbidity, colony-forming units (CFU) were obtained for the determination of the exact MIC.

1.5. Minimum Bactericidal Concentration (MBC) Assay

At the end of the MIC determination experiment, $10\text{ }\mu\text{L}$ of each MIC well were transferred in $140\text{ }\mu\text{L}$ of the same fresh media in a new 96 plate and incubated 24 hours at 37°C in a microplate shaker at 150 rpm. MBC was determined by reading the optical density at 600 nm (OD600) of the recovery plates using a Thermomax microtiter plate reader with Softmax Pro data analysis software (Molecular Devices, Sunnyvale, CA).

1.6. Prevention of biofilm

All biofilm experiments were carried out using a Calgary biofilm device. Briefly, $-70\text{ }^{\circ}\text{C}$ stored bacteria were sub-cultured on MHA at $37\text{ }^{\circ}\text{C}$ overnight (O/N) to obtain a pure single colony. $75\text{ }\mu\text{L}$ of the desired concentration of PBCs was added to 96 wells, $75\text{ }\mu\text{L}$ of bacteria (1.0×10^6 CFU/ml) added in each well, finally the polystyrene CBD pegged lid was placed into the 96 wells and incubated 48 hours at 37°C in a microplate shaker incubator at 150 rpm. The CBD lids were removed from the media and the adhered biomass was rinsed two times with distilled water. The extent of the biofilm biomass was determined using a crystal violet assay (8), which allowed the minimum biofilm inhibitory concentration (MBIC) to be determined. The well with the highest dilution of PBCs, but which had no bacterial biofilm and zero OD600 absorption, were considered MBIC. Results from at least three separate biological replicates were reported (4, 9).

1.7. Cannabis sativa oil Extraction

Preliminary results showed promising antibacterial and anti-biofilm features for high purity CBD and THC. Therefore, the whole plant of two different cultivars of *Cannabis sativa* (sample #98 and #112) was extracted with food-grade extra virgin olive oil or canola oil to compare the results with ultra-pure components. In a simple extraction method, ground plant flower heads were added to each oil in the desired concentration and stirred for four hours at 80 °C. The extraction was then used for the same antibacterial and anti-biofilm testing as the pure compounds. The relative concentrations of CBD and THC in the resulting oils were not known or determined and information not provided by the supplier.

Table S1. A systematic review on plant-based natural compounds (PBCs) as an antibacterial agent.

Study ID	Pub	PBCs	Bacteria evaluated	MIC (µg/ml)	Comment/s	Ref	Quality Score	
Esra	2020	<i>Cannabis sativa</i> extracts (Seeds oil)	<i>S. aureus</i>	25	The oil of the seeds of <i>Cannabis sativa</i> exerted pronounced antibacterial activity (21 - 28 mm) against <i>Bacillus subtilis</i> and <i>Staphylococcus aureus</i> , moderate activity (15 mm) against <i>Escherichia coli</i> and high activity (16 mm) against <i>Pseudomonas aeruginosa</i> and inactive against the two fungi tested.	(24)	7	
			<i>E. coli</i>	25				
			<i>P. aeruginosa</i>	50				
		<i>Cannabis sativa</i> extracts (Whole plant oil)	<i>S. aureus</i>	50				The petroleum ether extract of the whole plant exhibited pronounced antibacterial activity (23 - 28 mm) against both <i>Bacillus subtilis</i> and <i>Staphylococcus aureus</i> organisms, high activity (16 mm) against <i>Escherichia coli</i> and inactive against <i>Pseudomonas aeruginosa</i> and both fungi.
			<i>E. coli</i>	25				
			<i>P. aeruginosa</i>	125				
Appendino	2008	Cannabinoids and their analogues	13# Drug-Resistant Strains of <i>S. aureus</i>	4 (1-128)	methylation and acetylation of the phenolic hydroxyls, esterification of the carboxylic group of pre-cannabinoids, and introduction of a second prenyl moiety were all detrimental for antibacterial activity.	(25)	8	
Radwan	2009	9 Cannabinoids isolated from a high-potency variety of <i>Cannabis sativa</i>	MRSA	7-53	Compounds 6 and 7 displayed significant antibacterial and antifungal activities, respectively, while 5 displayed strong antileishmanial activity. Strong antileishmanial activity Significant antibacterial and antifungal activities	(26)	7	
			<i>S. aureus</i>	3-30				
			<i>E. coli</i>	54				
			<i>M. intracellulare</i>	30				
Nissen	2010	freshly extracted essential oils from three legal (THC_b0.2% w/v) hemp varieties (Carmagnola, Fibranova and Futura)	Gram (+), opportunistic and moderate pathogenic bacteria including <i>Clostridium</i> spp. and <i>Enterococcus</i> spp.;	>2-11 (% v/v)	essential oils of industrial hemp can significantly inhibit microbial growth, to an extent depending on variety and sowing time. Resulted in effective control of <i>Enterococcus hirae</i> , <i>Enterococcus faecium</i> and <i>S. salivarius</i> subsp. <i>thermophilus</i> . Futura confirmed the best results even on Gram (-), with MIC values always well below the threshold limit (2.00% v/v). both Carmagnola and Fibranova-II were above the MIC limit only in one case out of seven: <i>Pseudomonas savastanoi</i> and <i>Pectobacterium carotovorum</i> subsp. <i>carotovorum</i> , respectively for the two varieties. alpha-pinene was again the most effective compound for contrasting Gram (-) bacteria	(27)	7	
			Gram (-), phytopathogens bacteria including <i>Pseudomonas</i> spp. and <i>Pectobacterium</i> spp.;	>2-1.05 (% v/v)				
Sarmadyan	2014	hydro-alcoholic extract of cannabis	<i>E. coli</i>	50	The maximum anti-microbial effect of the hydro-alcoholic extract of cannabis was seen for gram-positive cocci, especially <i>S. aureus</i> , whereas nonfermentative gram negatives presented resistance to the extract. This extract had an intermediate effect on Enterobacteriaceae family. Cannabis components extracted through chemical analysis can perhaps be effective in the treatment of nosocomial infections	(28)	6	
			<i>E. coli</i> ESBL +	100				
			<i>S. aureus</i>	25				
			MRSA	50				
			<i>P. aeruginosa</i> ESBL+	>100				
			<i>P. aeruginosa</i>	100				
			<i>K. pneumoniae</i>	100				
<i>A. baumannii</i>	>100							
Thu Vu	2015	Methanol extracts <i>Cannabis sativa</i> (<i>Cannabis sativa</i>)	<i>B. cereus</i>	2000	Gram (-) bacteria were less susceptible to <i>Cannabis sativa</i>	(29)	7	
			<i>S. aureus</i>	2000				
			<i>E. coli</i>	>2000				
			<i>P. aeruginosa</i>	>2000				
Lelario	2018	Hemp-type <i>C. sativa</i> extract	<i>B. cereus</i>	5	Hemp-type <i>C. sativa</i> extract showed antimicrobial activity only against Gram+ bacteria, but the main individual components tested showed always a limited bioactivity	(30)	7	
			<i>B. thuringiensis</i>	5-10				
			<i>B. amyloliquefaciens</i>	5				
			<i>P. orientalis</i>	NI				
			<i>P. orientalis</i>	NI				
Zengin	2018	hemp EO, parts of <i>C. sativa</i>	<i>S. aureus</i> , ATCC and 3 clinical isoaltes	8000	the antibacterial and antibiofilm activities of hemp EO suggested it could be a possible candidate for the treatment of infections related to those abovementioned microorganisms	(31)	8	

Iseppi	2019	17 hemp EOs	<i>S. aureus</i> ATCC and food samples	2-16	Seventeen essential oils from different fibre-type varieties of <i>C. sativa</i> (industrial hemp or hemp) using GC-MS and GC-FID techniques. The results showed good antibacterial activity of six hemp essential oils against the Gram-positive bacteria, thus suggesting that hemp essential oil can inhibit or reduce bacterial proliferation and can be a valid support to reduce microorganism contamination, especially in the food processing field.	(32)	8
		Ciprofloxacin	<i>S. aureus</i> ATCC and food samples	0.5-16			
		17 hemp EOs	<i>S. epidermidis</i> food sample	1-16			
		Ciprofloxacin	<i>S. epidermidis</i> food sample	0.5			
		17 hemp EOs	<i>L. monocytogenes</i> ATCC and food samples	1-16			
		17 hemp EOs	<i>E. faecalis</i> ATCC and food samples	0.5-32			
		Ciprofloxacin	<i>E. faecalis</i> ATCC and food samples	0.5-16			
		17 hemp EOs	<i>E. hirae</i> ATCC and food samples	4-32			
		Ciprofloxacin	<i>E. hirae</i> ATCC and food samples	8			
		17 hemp EOs	<i>E. faecium</i> ATCC	1-16			
		Ciprofloxacin	<i>E. faecium</i> ATCC	4-8			
		17 hemp EOs	<i>B. subtilis</i> ATCC	2-16			
		17 hemp EOs	<i>B. cereus</i> EB 362	2 (1-16)			
		CDB	<i>S. aureus</i> ATCC and food samples	8-32			
		CDB	<i>S. epidermidis</i> food sample	16			
		CDB	<i>L. monocytogenes</i> ATCC and food samples	1-4			
		CDB	<i>E. faecalis</i> ATCC and food samples	1-4			
CDB	<i>E. faecium</i> ATCC	1-4					
CDB	<i>E. hirae</i> ATCC and food samples	2					
CDB	<i>B. subtilis</i> ATCC	8					
CDB	<i>B. cereus</i> EB 362	8					
Palmieri	2021	10# <i>Cannabis sativa</i> essential oils	<i>L. monocytogenes</i> ATCC	>20 (0.625- >20)	except for Futura 75, the effect of time on the antimicrobial activity was variable and requires further investigations; nevertheless, the inhibitory activity of all EOs against <i>Pseudomonas fluorescens</i> P34 was significant.	(33)	8
			<i>S. aureus</i>	>20 (0.15- >20)			
			<i>P. fluorescens</i> P34	1.5 (0.31-2-5)			
			<i>B. thermosphacta</i> B1	2.5 (0.31->20)			
			<i>S. Enteriditis</i> S2	>20 (10- >20)			
			<i>S. Typhimurium</i> S4	>20			
<i>E. faecium</i> ATCC	2.5 (0.625 - >20)						
Claudia	2021	two extracts from a new Chinese accession of <i>Cannabis sativa</i> L. (Δ^9 - tetrahydrocannabinol <0.2%)	<i>S. aureus</i> ATCC	39	two extracts from a new Chinese accession (G-309) of <i>Cannabis sativa</i> L. (Δ^9 - tetrahydrocannabinol <0.2%)	(34)	7
			19# MRSA clinical strains	39			
Blaskovich	2021	CBD	<i>S. aureus</i> , MRSA	1-2	results demonstrate that cannabidiol has excellent activity against biofilms, little propensity to induce resistance, and topical in vivo efficacy. selectively kill a subset of Gram-negative bacteria that includes the 'urgent threat' pathogen <i>N. gonorrhoeae</i> . CBD does not lead to resistance after repeated exposure.	(35)	9
			<i>S. epidermidis</i>	1-2			
			<i>S. pneumoniae</i>	1-4			
			<i>S. pyogenes</i>	1			
			<i>E. faecium</i>	0.5-1			
			<i>E. faecalis</i>	2-4			
			<i>C. difficile</i>	2-4			
			<i>C. acnes</i>	1-2			
			Gram (-) such as the key ESKAPE pathogens <i>E. coli</i> , <i>K. pneumoniae</i> , <i>P. aeruginosa</i> and <i>A. baumannii</i>	>64			
			<i>N. gonorrhoeae</i>	1			
<i>N. meningitidis</i>	0.25						
<i>L. pneumophila</i>	1						
Martinenghi	2020	CBDA	<i>S. aureus</i> ATCC, MRSA	2, 4	Two compounds were extracted by ethanol, purified on a C18 sep-pack column.	(36)	8
		CBDA	<i>S. epidermidis</i>	4			

		CBDA	<i>E. coli</i>	>64	CBD displayed a substantial inhibitory effect on Gram-positive bacteria with minimal inhibitory concentrations ranging from 1 to 2 µg/mL CBDA presented a two-fold lower antimicrobial activity than its decarboxylated form		
		CBDA	<i>P. aeruginosa</i>	>64			
		CBD	<i>S. aureus</i> ATCC, MRSA	1			
		CBD	<i>S. epidermidis</i>	2			
		CBD	<i>E. coli</i>	>64			
		CBD	<i>P. aeruginosa</i>	>64			
Paulo, Valle, Ingmer, and Zetterström, Martínez, Sun, Makobongo	2010, 2016, 2019, 2013, 2020, 2012, 2014	Resveratrol	<i>E. coli</i> EHEC	10	Resveratrol has antibacterial activity against all tested Gram-positive bacteria using both the disk diffusion and broth microdilution methods.	(37)	8,
			<i>B. cereus</i> ATCC	50		(37)	7,
			<i>S. aureus</i> ATCC	100		(37)	8,
			3# MRSA and MSSA	200 (100-200)		(37)	7,
			<i>E. faecalis</i> ATCC	100-1000		(37-39)	7,
			Gram (-) including <i>E. coli</i> , <i>K. pneumoniae</i> , <i>S. typhimurium</i> , and <i>S. aeruginosa</i>	>400		(37, 39, 40)	7,
			<i>E. faecium</i> D344R	128		(41)	8
			<i>M. tuberculosis</i> H37Rv	100		(42)	
			<i>S. pyogenes</i>	>200		(39)	
			<i>B. cereus</i> ATCC, NCTR	50, 1000		(39)	
			<i>S. aureus</i>	100- >1000		(39)	
			<i>M. tuberculosis</i> H37Rv	100		(39)	
			<i>S. pneumoniae</i> HM145	100		(39)	
<i>H. pylori</i>	25-100	(40, 43)					
Lemos, Imelouane, Ahmad, Fournomiti	2017, 2009, 2014, 2015	Thyme Essential oils	<i>S. aureus</i>	20-1000	The period of the harvests affected the chemical composition, antioxidant activity, and antimicrobial activity of thyme essential oils, and these differences can be related to seasonal variations of temperature and humidity. The largest antioxidant and antimicrobial activities were displayed by the essential oil produced in spring (October/2012).	(44-46)	7, 7, 8, 8
			<i>E. coli</i>	500-128000		(44-47)	
			<i>S. typhimurium</i>	500-750		(44)	
			<i>S. epidermidis</i> ATCC	1330		(45)	
			Streptococcus sp	2670		(45)	
			<i>M. catarrhalis</i> ATCC	1000		(46)	
			<i>St. aureus</i> ATCC	500		(46)	
			<i>B. cereus</i> ATCC	500		(46)	
			<i>K. pneumoniae</i>	16000-32000		(47)	
Imelouane, Veldhuizen, Guarda, Javier, Chueca, AL-Ani, Cacciatore, Mariri, Cacciatore	2009, 2006, 2011, 2019, 2016, 2015, 2015, 2015	Carvacrol	<i>S. aureus</i>	250-1700, 250 ppm	CAR interacts with the lipid bilayer of the bacterial cytoplasmic membrane due to its hydrophobic nature and aligns itself between fatty acid chains causing the expansion and destabilization of the membrane structure by increasing its fluidity and permeability for protons and ions. The loss of the ion gradient leads to bacterial cell death	(44, 48-51)	7, 7, 7, 7, 8, 7, 7, 8
			<i>E. coli</i>	250-1200, 250 ppm		(48) (44, 49, 51-54)	
			<i>S. typhimurium</i>	<0.4- 375		(44, 51, 54, 55)	
			<i>K. pneumoniae</i> ATCC,	3-300		(51, 54)	
			<i>S. enteritidis</i>	187		(55)	
			<i>Y. enterocolitica</i> O9	0.75		(51, 54)	
			<i>P. aeruginosa</i>	6-500		(51, 53, 54)	
			Proteus spp	<0.375		(54)	
Yu-Meng Song,	2020	Tea tree oil	<i>S. mutans</i>	0.125%	0.25% (MBC)	(56)	8
			<i>E. coli</i>	2 (2-4)		(57),	
			<i>L. monocytogenes</i>	1 (1-2)		(57),	
Shi	2018		MRSA	0.5-2.5 (%v/v)		(58)	8
Shi	2018		<i>P. aeruginosa</i>	0.25-2 (%v/v)		(58)	
Brun	2019	10 #	<i>S. epidermidis</i>	2000-16000	there may be a role for essential oils, in particular EO, for improved skin antiseptics when combined with chlorhexidine digluconate	(59)	7
Brun	2019	Tea tree oil	<i>S. aureus</i>	0.5-2 (%v/v)		(60)	
Karpanen	2008	Tea tree oil	<i>P. aeruginosa</i>	1-16 (%v/v)			
Low,	2011		<i>S. aureus</i>	250	In cell viability tests, 2 mg/ml of cinnamaldehyde reduced the number of viable cells by 5.74 Log CFU/ml.	(61)	8
			<i>E. coli</i>	250			
			<i>S. epidermidis</i>	250			
			<i>S. pyogenes</i>	500			
			<i>P. aeruginosa</i>	500			
Firmino	2018	Cinnamaldehyde	<i>H. pylori</i>	2		(62)	8
Khan	2005		<i>S. mutans</i>	1000	cinnamaldehyde at sub-MIC level suppressed the microbial activity on <i>S. mutans</i> biofilm by modulating hydrophobicity, aggregation, acid production, acid tolerance, and virulence gene expression.	(63)	7
Zhiya	2019						

Krist	2014	cis-Nerolidol, rans-Nerolidol	<i>E.coli</i> ATCC	0.2		(64)	8		
			<i>P.aeruginosa</i>	0.4					
			<i>S. aureus</i>	0.1					
			<i>S.epidermidis</i>	0.1					
			<i>B.cereus</i> ATCC	0.1					
Khatkar, Jorge, Doria	2017, 2008, 2019	36# p-coumaric acid	<i>S. aureus</i>	1.67->2000		(65, 66)	7,8		
			<i>B. subtilis</i>	2				(65)	7
			<i>E. coli</i>	1.7->300					
Jorge, Doria	2008, 2019	p-coumaric acids	<i>P. aeruginosa</i>	>2000	All the evaluated propolis samples exhibited similar antibacterial activity, but different contents of prenylated p-coumaric acids throughout the year.	(66, 67)	8, 8		
Doria	2019		<i>S. epidermidis</i>	<15->2000				(66)	8
	2019		<i>A. baumannii</i>	250->2000				(66)	8
Mandroli	2013	Curcumin	<i>S. mutans</i>	333.3		(68)	7		
			<i>L. casei</i>	125					
			<i>L. casei</i>	167.67					
			<i>P. gingivalis</i>	125					
			<i>P. intermedia</i>	208.33					
			<i>A.actinomycetemcomitans</i>	> 100					
Izui	2016		<i>F. nucleatum</i>	10	Curcumin possesses antibacterial activity against periodontopathic bacteria and may be a potent agent for preventing periodontal diseases	(69)	8		
			<i>P. gingivalis</i>	15					

Essential oils (EOs), cannabidiol acid (CBDA), cannabidiol (CBD).

Joanna Briggs Institute checklist questions for quality assessment of included studies are as follows.

Q1= Was the sample frame appropriate to address the target population?

Q2= Were study participants sampled in an appropriate way?

Q3= Was the sample size adequate?

Q4= Were the study subjects and the setting described in detail?

Q5= Was the data analysis conducted with sufficient coverage of the identified sample?

Q6= Were valid methods used for the identification of the condition?

Q7= Was the condition measured in a standard, reliable way for all participants?

Q8= Was there appropriate statistical analysis?

Q9= Was the response rate adequate, and if not, was the low response rate managed appropriately?

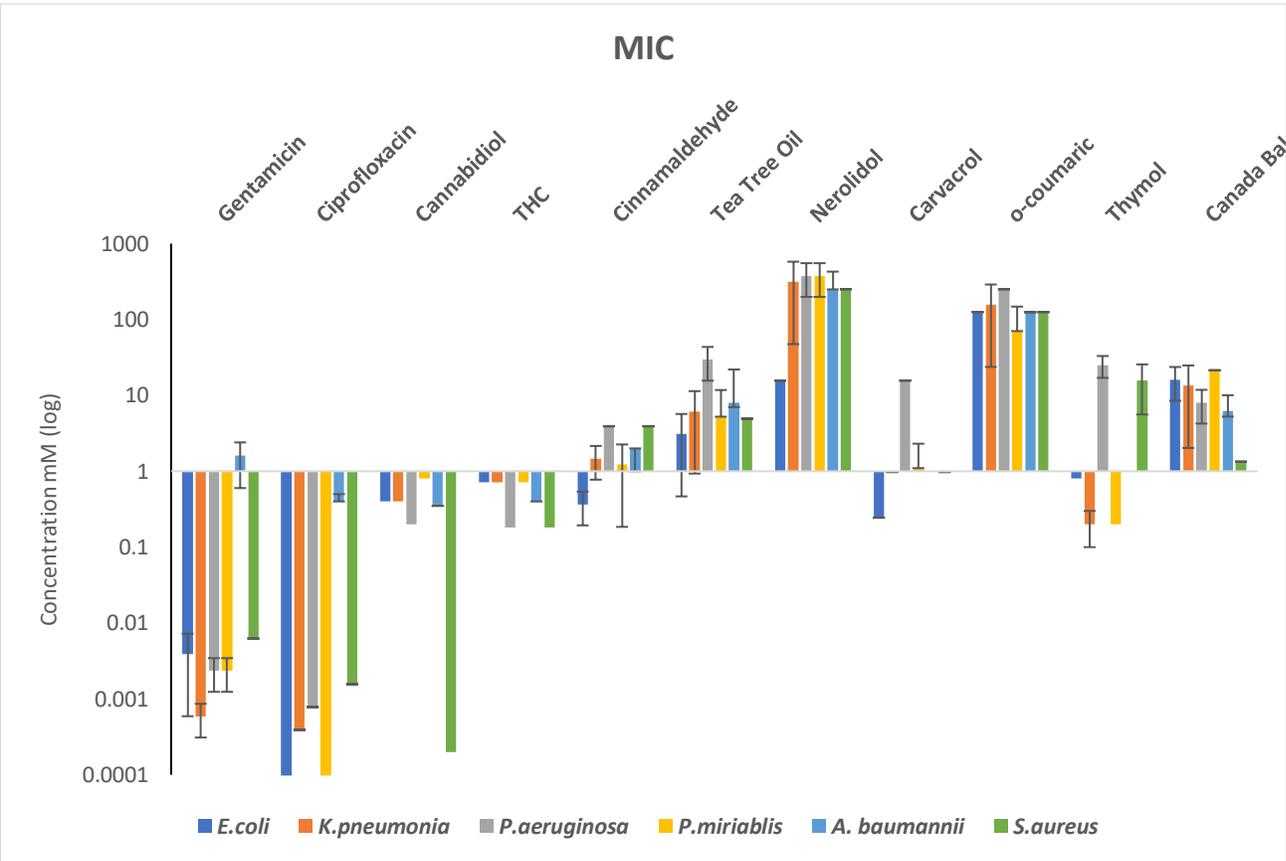


Figure S1. Bacteriostatic potency of natural products in comparison with gentamycin and ciprofloxacin (n=3).

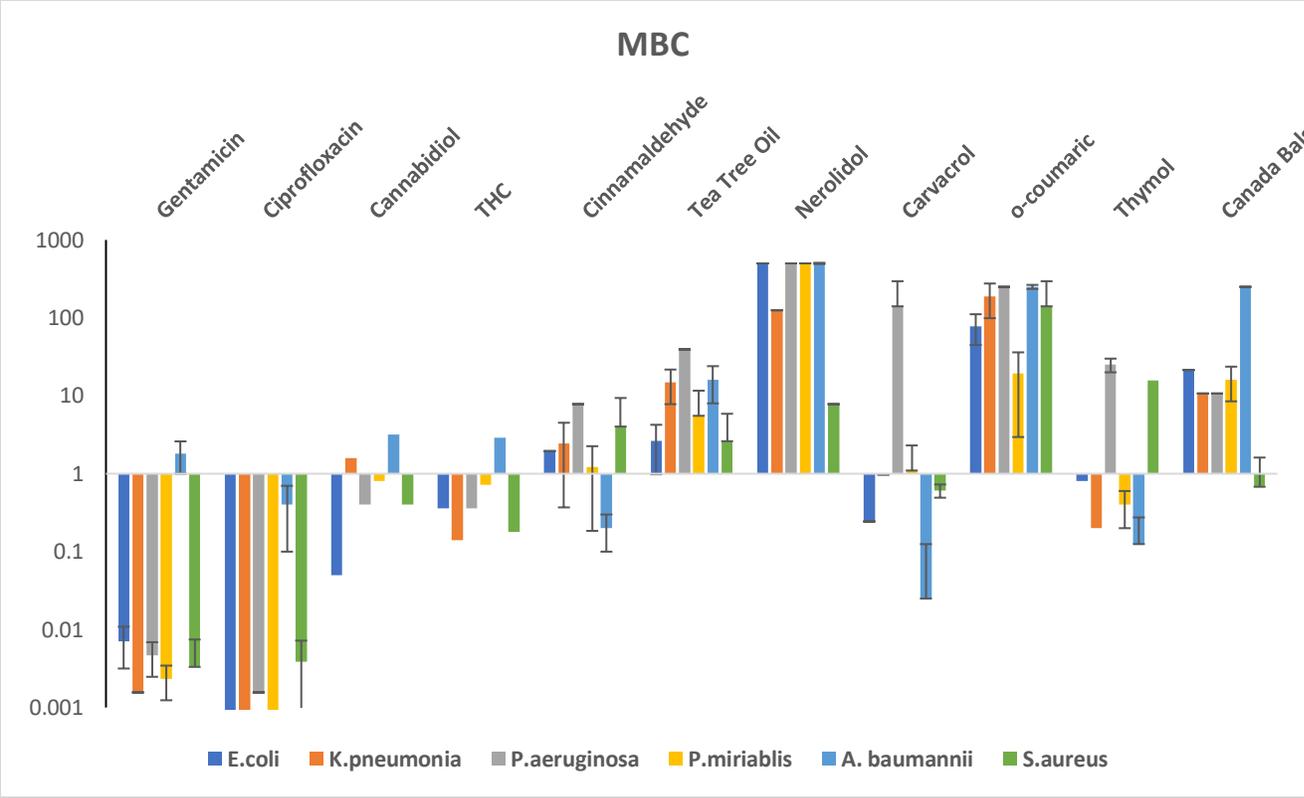


Figure S2. Bactericidal potency of natural products in comparison with gentamycin and ciprofloxacin (n=3).

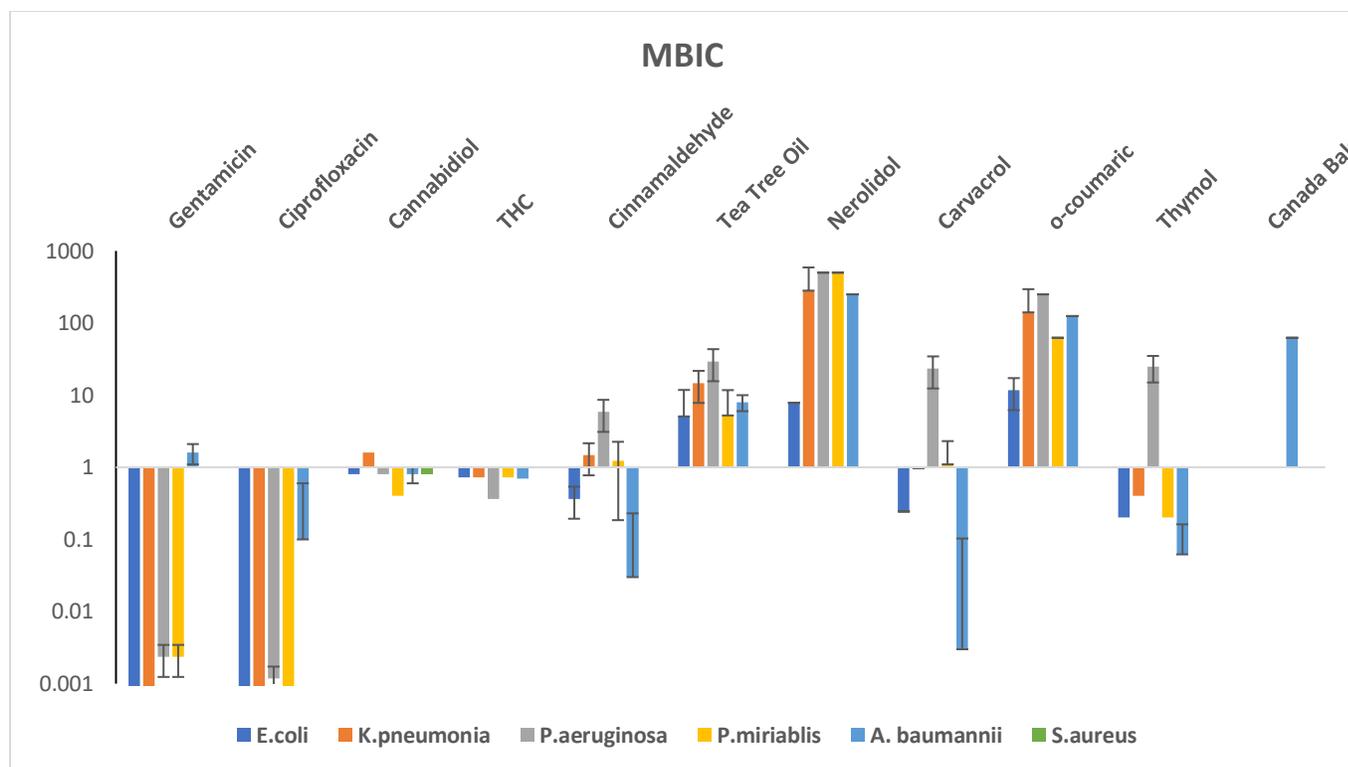


Figure S3. Biofilm inhibition potency of natural products in comparison with gentamycin and ciprofloxacin (n=3).

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