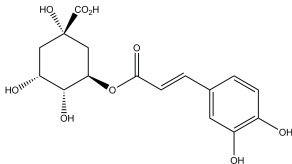
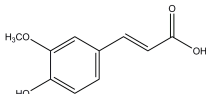
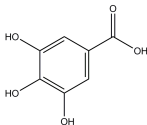
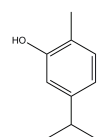
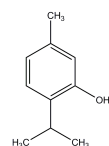
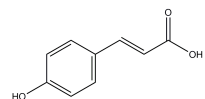
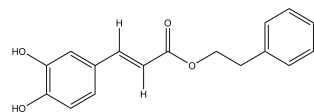
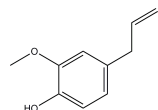


Table 1. Known antibacterial mechanisms of action of plant phenolic compounds

Structure	Phenolic	Organisms	Mechanisms	Methods	References
	chlorogenic acid	<i>Streptococcus pneumoniae</i> , <i>Staphylococcus aureus</i> , <i>Bacillus subtilis</i> , <i>Escherichia coli</i> , <i>Shigella dysenteriae</i> , <i>Salmonella Typhimurium</i>	cell membrane disruption	efflux of cell components, uptake of hydrophobic antibiotics, intracellular pH, membrane potential, microscopy	Lou et al. 2011, Li et al. 2013
	ferulic acid	<i>Pseudomonas aeruginosa</i> , <i>Escherichia coli</i> , <i>Staphylococcus aureus</i> , <i>Listeria monocytogenes</i> , <i>Cronobacter sakazakii</i>	cell membrane disruption	efflux of cellular components, uptake of hydrophobic dyes, intracellular pH and ATP concentration, membrane potential, surface zeta potential, membrane hydrophobicity using contact angles, microscopy	Borges et al. 2013, Shi et al. 2016
	gallic acid	<i>Pseudomonas aeruginosa</i> , <i>Escherichia coli</i> , <i>Staphylococcus aureus</i> , <i>Listeria monocytogenes</i> , <i>Salmonella Typhimurium</i>	cell membrane disruption (Mg ²⁺ chelation)	efflux of cellular components, uptake of hydrophobic dyes, intracellular pH and ATP concentration, membrane potential, surface zeta potential, membrane hydrophobicity using contact angles, exogenous magnesium added to membrane integrity assay	Borges et al. 2013, Nohynek et al. 2006



caffeic acid phenethyl ester	<i>Escherichia coli</i> , <i>Staphylococcus aureus</i>	cell membrane disruption)	efflux of cellular components, uptake of hydrophobic dye	Meyuhas et al. 2015
p-coumaric acid	<i>Streptococcus pneumoniae</i> , <i>Staphylococcus aureus</i> , <i>Bacillus subtilis</i> , <i>Escherichia coli</i> , <i>Shigella dysenteriae</i> , <i>Salmonella Typhimurium</i>	cell membrane disruption (outer membrane), DNA intercalation	efflux of cellular components, uptake of hydrophobic antibiotics, competitive binding of DNA with ethidium bromide	Lou et al. 2012
thymol	<i>Escherichia coli</i> , <i>Salmonella Typhimurium</i> , <i>Pseudomonas fluorescens</i> , <i>Staphylococcus aureus</i> , <i>Brochotrix thermosphacta</i> , <i>Salmonella Thompson</i>	cell membrane disruption (reduced unsaturated fatty acids), energy generation	efflux of cellular components, uptake of hydrophobic dyes, membrane polarization, intracellular pH, microscopy, HRGC	Xu et al. 2008, Lambert et al. 2001, Di Pasqua et al. 2007, Walsh et al. 2003, Helander et al. 1998, Di Pasqua et al. 2010
carvacrol	<i>Escherichia coli</i> , <i>Salmonella Typhimurium</i> , <i>Pseudomonas fluorescens</i> , <i>Staphylococcus aureus</i> , <i>Brochotrix thermosphacta</i> , <i>Bacillus cereus</i> , <i>Lactobacillus plantarum</i> , <i>Listeria innocua</i>	cell membrane disruption (reduced unsaturated fatty acids)	efflux of cellular components, uptake of hydrophobic dyes, membrane polarization, intracellular pH, membrane potential, microscopy, HRGC	Xu et al. 2008, Lambert et al. 2001, Di Pasqua et al. 2007, Fitzgerald et al. 2004, Ultee et al. 1999, Helander et al. 1998, Gill and Holley 2006



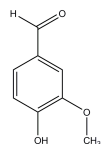
eugenol

Salmonella Typhi, *Escherichia coli*, *Salmonella Typhimurium*, *Pseudomonas fluorescens*, *Staphylococcus aureus*, *Listeria monocytogenes*, *Lactobacillus sakei*

cell membrane disruption (energy generation, reduced unsaturated fatty acids)

efflux of cellular components, uptake of hydrophobic dyes, intracellular pH, microscopy, HRGC

Devi et al 2010, Gill and Holley 2004, Walsh et al. 2003, Gill and Holley 2006, Di Pasqua et al. 2007



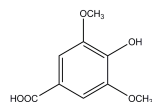
vanillin

Escherichia coli, *Lactobacillus plantarum*, *Listeria innocua*

cell membrane disruption

efflux of cellular components, membrane polarization, respiration

Fitzgerald et al. 2004



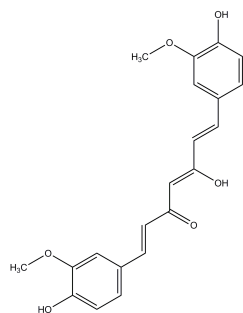
syringic acid

Cronobacter sakazakii

cell membrane disruption

uptake of hydrophobic dyes, membrane potential, microscopy

Shi et al. 2016



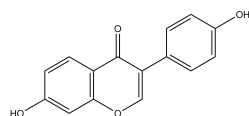
curcumin

Escherichia coli, *Salmonella Typhimurium*, *Photobacterium leiognathi*, *Bacillus subtilis*, *Staphylococcus aureus*, *Enterococcus faecalis*, *Pseudomonas aeruginosa*

cell membrane disruption, cell elongation (inhibited FtsZ protofilament assembly, FtsZ binding)

efflux of cellular components, uptake of hydrophobic dyes, membrane potential, microscopy, GTPase activity assay for FtsZ

Tyagi et al. 2015, Rai et al. 2008, Yun and Lee 2016



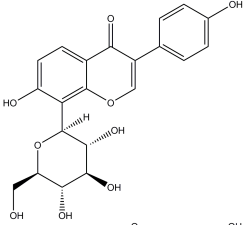
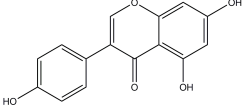
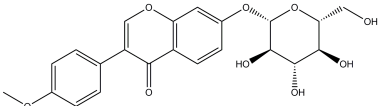
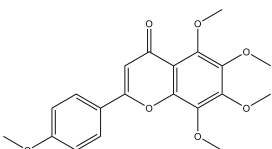
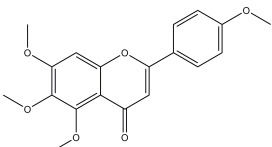
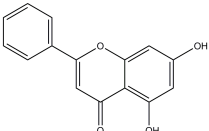
daidzein

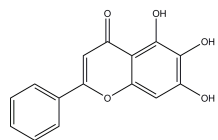
model membrane, *Escherichia coli*

cell membrane disruption

interaction of molecules with large unilamellar vesicles (fluorescence monitoring)

Wu, He et al. 2013

	puerarin	model membrane, <i>Escherichia coli</i>	cell membrane disruption	interaction of molecules with large unilamellar vesicles (fluorescence monitoring)	Wu, He et al. 2013
	genistein	model membrane, <i>Escherichia coli</i>	cell membrane disruption	interaction of molecules with large unilamellar vesicles (fluorescence monitoring)	Wu, He et al. 2013
	ononin	model membrane, <i>Escherichia coli</i>	cell membrane disruption	interaction of molecules with large unilamellar vesicles (fluorescence monitoring)	Wu, He et al. 2013
	tangeritin	model membrane, <i>Escherichia coli</i> , <i>Pseudomonas fluorescens</i> , <i>Pseudomonas aeruginosa</i>	cell membrane disruption, DNA gyrase inhibition, reduced protein synthesis, inhibition of succinate dehydrogenase and malate dehydrogenase	efflux of cellular components, microscopy, DNA-gyrase supercoiling inhibition assay, interaction of molecules with large unilamellar vesicles (fluorescence monitoring)	Wu, He et al. 2013, Wu, Zang et al. 2013, Yao et al. 2011
	5,6,7,4'-tetramethoxyflavone	model membrane, <i>Escherichia coli</i>	cell membrane disruption, DNA gyrase inhibition	DNA-gyrase supercoiling inhibition assay, interaction of molecules with large unilamellar vesicles (fluorescence monitoring)	Wu, He et al. 2013, Wu, Zang et al. 2013
	chrysin	model membrane, <i>Escherichia coli</i>	cell membrane disruption, DNA gyrase inhibition	DNA-gyrase supercoiling inhibition assay, interaction of molecules with large unilamellar vesicles (fluorescence monitoring)	Wu, He et al. 2013, Wu, Zang et al. 2013



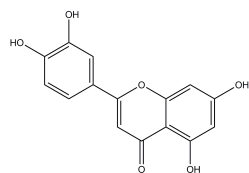
baicalein

model membrane,
Escherichia coli

cell membrane
disruption, DNA
gyrase inhibition,
Type III secretion
inactivation

DNA-gyrase supercoil-
ing inhibition assay,
Type III secretion
assay by monitor-
ing fluorescence of
Glu-CyFur dye, inter-
action of molecules
with large unilamellar
vesicles (fluorescence
monitoring)

Wu, He et al.
2013, Wu, Zang
et al. 2013, Tsou
et al. 2016



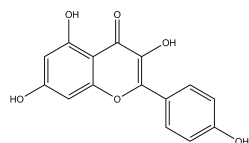
luteolin

model membrane,
Escherichia coli

cell membrane
disruption, DNA
gyrase inhibition,
Type III secretion
inactivation, he-
licase inhibition
(RepA)

DNA-gyrase supercoil-
ing inhibition assay,
Type III secretion
assay by monitoring fluores-
cence of Glu-CyFur
dye, ATPase activity
assay with RepA, in-
teraction of molecules
with large unilamellar
vesicles (fluorescence
monitoring)

Wu, He et al.
2013, Wu, Zang
et al. 2013, Xu et
al. 2001



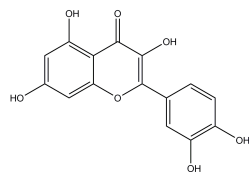
kaempferol

model membrane,
Escherichia coli

cell membrane
disruption, DNA
gyrase inhibition,
Type III secretion
inactivation

DNA-gyrase supercoil-
ing inhibition assay,
Type III secretion
assay by monitor-
ing fluorescence of
Glu-CyFur dye, inter-
action of molecules
with large unilamellar
vesicles (fluorescence
monitoring)

Wu, He et al.
2013, Wu, Zang
et al. 2013



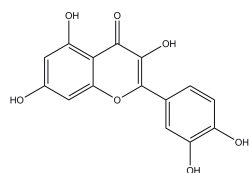
quercetin

model membrane, *Escherichia coli*, *Helicobacter pylori*

cell membrane disruption (membrane rigidification), DNA intercalation, DNA gyrase inhibition, Type III secretion inactivation, dehydratase inhibition (HpFabZ), protein kinase inhibition

DNA-gyrase supercoiling inhibition assay, type III secretion assay by monitoring fluorescence of Glu-CyFur dye, interaction of molecules with large unilamellar vesicles (fluorescence monitoring), kinase enzyme inhibition assays

Wu, He et al. 2013, Wu, Zang et al. 2013, Plaper et al. 2003, Tsou et al. 2016, Zhang et al. 2008, Shakya et al. 2011



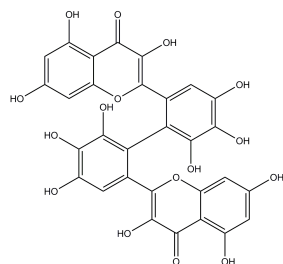
myricetin

model membrane, *Escherichia coli*, *Salmonella Typhimurium*

DNA gyrase inhibition, Type III secretion inactivation-ab, helicase inhibition (RepA)

DNA-gyrase supercoiling inhibition assay, Type III secretion assay by monitoring fluorescence of Glu-CyFur dye, ATPase activity assay with RepA, interaction of molecules with large unilamellar vesicles (fluorescence monitoring)

Wu, Zang et al. 2013, Tsou et al. 2016 Xu et al. 2001



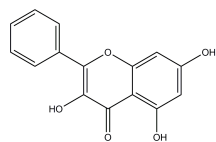
dimyricetin (oxidation product of myricetin)

Escherichia coli

helicase inhibition (RepA)

ATPase activity assay with RepA, interaction of molecules with large unilamellar vesicles (fluorescence monitoring)

Xu et al. 2001



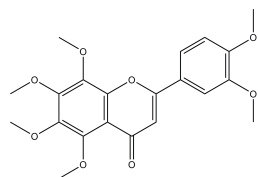
galangin

Escherichia coli

cell membrane disruption, DNA gyrase inhibition

efflux of potassium ions, DNA-gyrase supercoiling inhibition assay

Cushnie and Lamb 2004, Wu, Zang et al. 2013



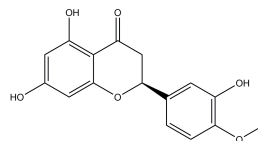
nobiletin

Pseudomonas fluorescens, *Pseudomonas aeruginosa*, *Escherichia coli*

cell membrane disruption, DNA gyrase inhibition, reduced protein synthesis, inhibition of succinate dehydrogenase and malate dehydrogenase

efflux of cellular components, microscopy, DNA-gyrase supercoiling inhibition assay

Yao et al. 2011, Wu, Zang et al. 2013



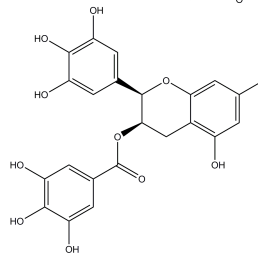
hesperetin

Helicobacter pylori

cell membrane disruption, urease inhibition

urease activity assay, microscopy

Moon et al. 2013



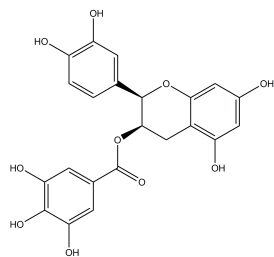
epigallocatechin gallate

model membranes, *MRSA*, *Bacillus subtilis*, *Escherichia coli*

cell membrane disruption (aggregation and inhibition of cell surface proteins, porin inhibition)

microscopy, purified cell wall components, phosphorus content, exogenous peptidoglycan added to activity assay, glass adherence, penicillin binding protein abundance/expression, Triton-X-autolysis assay, lysostaphin activity assay, collection of bacteriolytic enzymes and lipotechoic acid, mass spectrometry proteomics, interaction of molecules with multilamellar vesicles

Hashimoto et al. 1999, Kumazawa et al. 2004, Stapleton et al. 2007, Nakayama 2013, Nakayama 2015



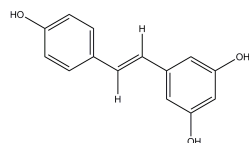
epicatechin
gallate

model membranes,
Staphylococcus
aureus

cell mem-
brane disruption
(increased mem-
brane autolysins,
lipoteichoic acid
release)

purified cell wall com-
ponents, phosphorus
content, exogenous
peptidoglycan added
to activity assay, glass
adherence, penicillin
binding protein abun-
dance/expression,
Triton-X-autolysis
assay, lysostaphin
activity assay, collec-
tion of bacteriolytic
enzymes and lipote-
choic acid, interaction
of molecules with
multilamellar vesicles

Hashimoto et al.
1999, Stapleton
et al. 2007



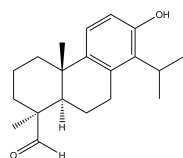
resveratrol

Escherichia coli

cell elongation
(suppressed FtsZ
expression),
DNA fragmen-
tation, increased
SOS response

Z-ring inhibition as-
say, western blot,
microscopy

Hwang et al.
2015



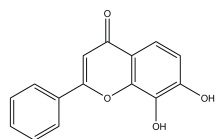
totaral

Staphylococcus
aureus

reduced ex-
pression of
enterotoxins,
multi-drug efflux
pump inhibitor

ethidium bromide accu-
mulation/efflux assays,
quantitative real time
PCR

Shi et al. 2015,
Smith et al. 2007



7,8-dihydroxy-
flavone

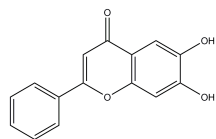
Salmonella
phimurium

Ty-

Type III secretion
inactivation

Type III secretion as-
say by monitoring fluo-
rescence of Glu-CyFur
dye

Tsou et al. 2016



6,7-dihydroxy-
flavone

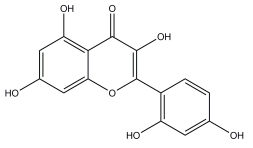
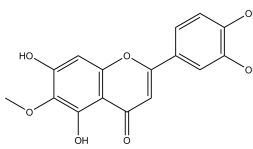
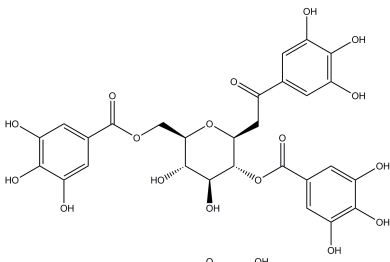
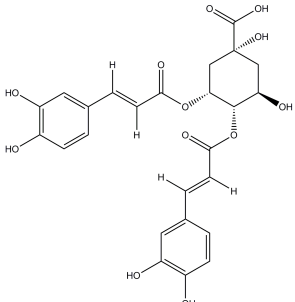
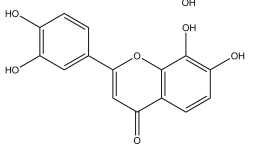
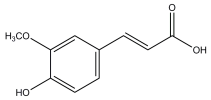
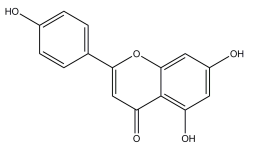
Salmonella
phimurium

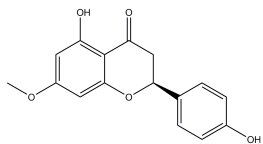
Ty-

Type III secretion
inactivation

Type III secretion as-
say by monitoring fluo-
rescence of Glu-CyFur
dye

Tsou et al. 2016

	morin	<i>Salmonella phimurium</i>	Ty-	Type III secretion inactivation, helicase inhibitor (RepA)	Type III secretion assay by monitoring fluorescence of Glu-CyFur dye, ATPase activity assay with RepA	Tsou et al. 2016, Xu et al. 2001
	eupafolin	<i>Salmonella phimurium</i>	Ty-	Type III secretion inactivation	Type III secretion assay by monitoring fluorescence of Glu-CyFur dye	Tsou et al. 2016
	1,2,6-tri-O-galloyl- β -D-glucopyranose	<i>Escherichia coli</i>		multi-drug efflux pump inhibition	ethidium bromide accumulation/efflux assays	Bag and Chattopadhyay 2014
	4,5-O-dicaffeoylquinic acid		no activity observed in tested range of mechanism study	multi-drug efflux pump inhibition	berberine accumulation/efflux assays	Fiamegos et al. 2011
	3',4',7,8-tetrahydroxyflavone	- RecA purified from <i>Esherichia coli</i>		helicase inhibition (RepA)	ATPase activity assay with RepA	Xu et al. 2001
	ellagic acid	<i>Salmonella phimurium</i>	Ty-	DNA gyrase inhibition, not cell membrane	DNA-gyrase supercoiling inhibition assay, DNA-gyrase "cleavable complex" assay	Ohemeng et al. 1993, Nohynek et al. 2006
	apigenin	<i>Helicobacter pylori</i>		dehydratase inhibition (HpFabZ), protein kinase inhibition	HpFabZ enzyme inhibition assay, interaction of molecules with large unilamellar vesicles (fluorescence monitoring), kinase enzyme inhibition assays	Zhang et al. 2008, Shakya et al. 2011



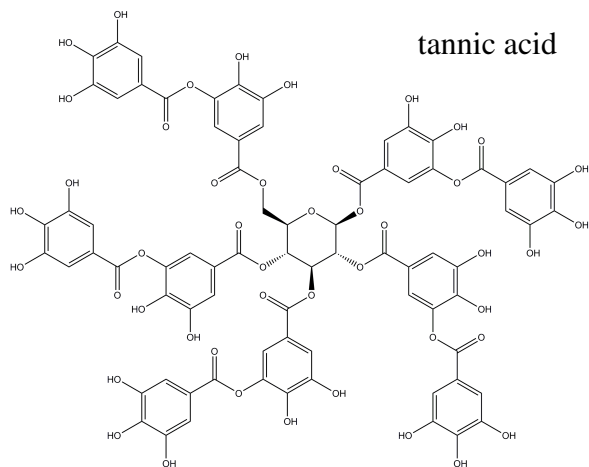
S-sakuranetin

Helicobacter pylori

dehydratase inhibition (HpFabZ)

HpFabZ enzyme inhibition assay, interaction of molecules with large unilamellar vesicles (fluorescence monitoring)

Zhang et al. 2008



tannic acid

Escherichia coli

binds iron

iron binding assay, addition of exogenous iron

Chung et al. 1998

MRSA: methicillin resistant *Staphylococcus aureus*
HRGC: high resolution gas chromatography