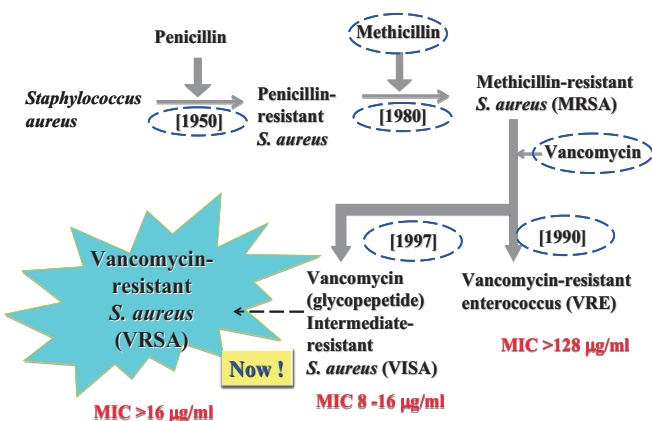


# Synthesis and Evaluation of Flavonol Derivatives as Novel Anti-VRE Agent

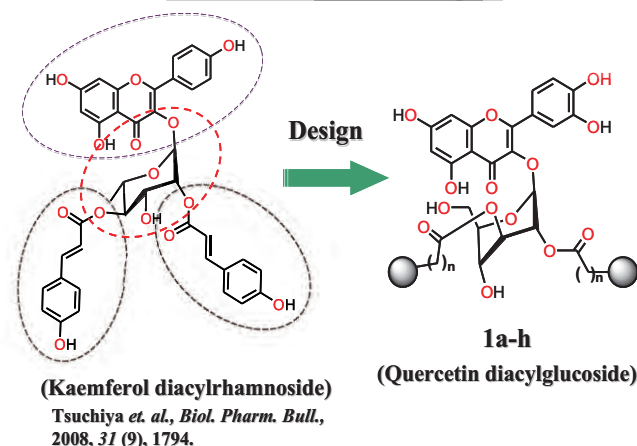
Center for Faculty Development , Okayama University

Kenji Sasaki

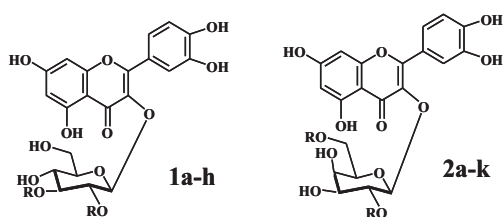
## Evolution of Antibacterial Resistance



## Structure-Based Design

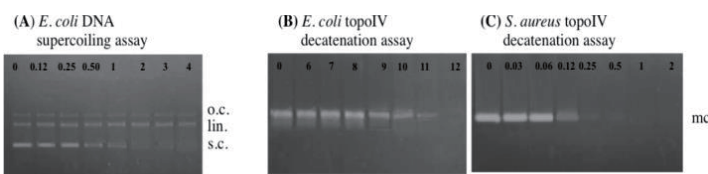


## Antibacterial Activity Against Drug Resistance Bacterial Strains



Compounds	R	MIC ( $\mu\text{g/mL}$ )			
		VRE		MRSA	
		FN-1	NCTC 12201	OM481	OM584
1a	COC <sub>2</sub> H <sub>4</sub> C <sub>6</sub> H <sub>4</sub> ((4-OCH <sub>2</sub> Ph)	8	8	4	4
1b	COC <sub>2</sub> H <sub>4</sub> C <sub>6</sub> H <sub>4</sub> (4-OEt)	8	8	4	8
1c	COC <sub>2</sub> H <sub>4</sub> C <sub>6</sub> H <sub>4</sub> (4-Me)	2	4	2	2
1d	COC <sub>2</sub> H <sub>4</sub> C <sub>6</sub> H <sub>4</sub> (4-F)	1	1	2	2
1e	COC <sub>6</sub> H <sub>4</sub> (4-OEt)	16	16	32	32
1f	COC <sub>6</sub> H <sub>4</sub> ((4- <sup>n</sup> Pr)	8	8	32	32
1g	COC <sub>6</sub> H <sub>4</sub> (4-F)	8	8	16	16
1h	COCH <sub>2</sub> C <sub>6</sub> H <sub>4</sub> (4-F)	8	8	8	8
2a	COC <sub>6</sub> H <sub>4</sub> ((4-OEt)	8	8	4	4
2b	COC <sub>6</sub> H <sub>4</sub> ((4- <sup>n</sup> Pr)	8	4	4	8
2c	COC <sub>6</sub> H <sub>4</sub> ((4-F)	4	4	2	2
2d	COCH <sub>2</sub> C <sub>6</sub> H <sub>4</sub> (4-Me)	8	4	2	2
2e	COCH <sub>2</sub> C <sub>6</sub> H <sub>4</sub> (4-F)	0.5	0.5	1	1
2f	COC <sub>2</sub> H <sub>4</sub> C <sub>6</sub> H <sub>4</sub> (4-OH)	4	4	1	1
2g	COC <sub>2</sub> H <sub>4</sub> C <sub>6</sub> H <sub>4</sub> (4-OEt)	2	2	1	1
2h	COC <sub>2</sub> H <sub>4</sub> C <sub>6</sub> H <sub>4</sub> (4-Me)	0.5	0.5	0.25	0.25
2i	COC <sub>2</sub> H <sub>4</sub> C <sub>6</sub> H <sub>4</sub> (4-F)	0.25	0.25	0.13	0.13
2j	COC <sub>3</sub> H <sub>6</sub> C <sub>6</sub> H <sub>4</sub> (4-F)	8	8	2	2
2k	COC <sub>4</sub> H <sub>8</sub> C <sub>6</sub> H <sub>4</sub> (4-F)	16	16	4	4
Quercetin		>128	>128	>128	>128
Vancomycin		>128	>128	>128	>128

## DNA Gyrase and Topo IV Activity Assays of Compound 1d



(A) DNA supercoiling assay by gyrase from *E. coli* strains JMtacA and JMtacB.

(B) decatenation assay by topoIV from *E. coli* ParC and ParE subunits.

(C) decatenation assay by topoIV from *S. aureus*. Gels were run in the absence of ethidium bromide or chloroquine. o.c., open-circular DNA; lin., linear DNA; s.c., supercoiled DNA; and mc, decatenated mini circles.

## High Molecular Mass and Bulky Side Chain of Compound 1a-h Accumulate in Gram-Positive Organism

