Supplementary Materials

Inhibition of aminoglycoside 6'-*N*-acetyltransferase type Ib [AAC(6′)-Ib]: structure-activity relationship of substituted pyrrolidine pentamine derivatives as inhibitors

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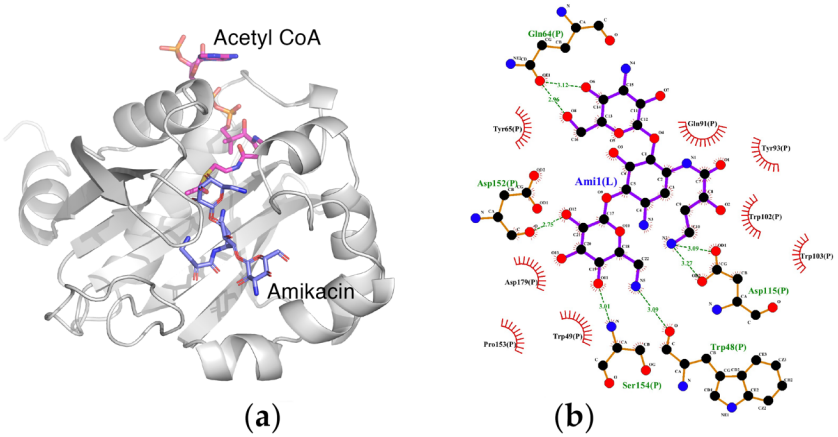

Figure S1. (a) The complex of amikacin and AAC(6′)-Ib obtained from molecular docking. The bound acetyl CoA is also shown. **(b)** Amikacin has hydrogen bonds with side chain of the charged residues Glu64, Asp115, and Asp52 as well as hydrogen bonds with the backbone of resides Ser154 and Trp48.

	Amk (µg/mL)					
2637-001 (µM)	0	8	16	24	32	64
24.0	10.8%	84.8%	88.2%	89.7%	88.5%	88.3%
16.0	4.3%	78.7%	85.1%	87.9%	88.9%	88.9%
8.0	8.6%	50.2%	74.5%	84.2%	87.4%	87.0%
4.0	6.7%	33.2%	63.2%	77.2%	85.0%	85.9%
0.0	0.0%	8.9%	29.4%	27.4%	52.8%	89.4%

	Amk (µg/mL)					
2637.020 (µM)	0	8	16	24	32	64
24.0	6.3%	86.6%	87.2%	77.4%	89.7%	91.8%
16.0	6.3%	82.6%	88.0%	88.1%	87.8%	90.9%
8.0	10.2%	43.9%	79.4%	87.2%	88.8%	88.5%
4.0	8.2%	34.5%	58.0%	85.3%	79.8%	90.9%
0.0	0.0%	8.0%	23.7%	41.4%	75.4%	91.5%

	Amk (µg/mL)					
2637.004 (µM)	0	8	16	24	32	64
24.0	5.0%	88.4%	89.6%	90.5%	90.7%	90.7%
16.0	3.5%	25.5%	85.4%	88.4%	85.3%	86.9%
8.0	5.3%	14.7%	47.1%	52.7%	77.1%	87.8%
4.0	6.0%	13.7%	40.9%	45.6%	55.8%	86.3%
0.0	0.0%	6.8%	22.0%	20.4%	27.7%	88.2%

	Amk (µg/mL)					
2637.019 (µM)	0	8	16	24	32	64
24.0	90.8%	91.2%	90.8%	91.0%	91.1%	91.3%
16.0	19.1%	91.3%	90.5%	89.8%	90.6%	91.0%
8.0	5.9%	26.1%	87.8%	81.7%	89.1%	90.3%
4.0	8.0%	16.1%	30.2%	36.0%	26.1%	90.5%
0.0	0.0%	7.2%	16.2%	26.6%	23.8%	90.7%

	Amk (µg/mL)					
2637.007 (µM)	0	8	16	24	32	64
24.0	1.6%	63.7%	67.8%	79.0%	77.6%	82.2%
16.0	1.3%	61.0%	72.6%	78.3%	78.8%	81.1%
8.0	2.2%	51.4%	70.5%	79.3%	75.7%	82.3%
4.0	3.6%	39.4%	61.9%	78.1%	52.5%	88.7%
0.0	0.0%	6.9%	16.0%	26.4%	42.6%	89.1%

	Amk (µg/mL)					
2637.010 (µM)	0	8	16	24	32	64
24.0	4.6%	71.8%	78.8%	81.4%	81.1%	87.2%
16.0	4.5%	68.8%	80.0%	78.7%	81.6%	86.2%
8.0	4.8%	60.5%	71.8%	79.8%	84.4%	87.9%
4.0	4.3%	50.7%	69.6%	78.7%	83.6%	87.6%
0.0	0.0%	4.6%	25.5%	20.3%	65.5%	89.1%

	Amk (µg/mL)					
2637.012 (µM)	0	8	16	24	32	64
24.0	-0.7%	89.5%	89.4%	87.6%	85.1%	91.5%
16.0	0.5%	33.5%	79.2%	83.3%	85.9%	87.9%
8.0	2.7%	15.6%	44.0%	54.0%	70.2%	88.3%
4.0	4.8%	12.2%	33.4%	57.9%	54.4%	85.7%
0.0	0.0%	8.9%	16.8%	21.8%	52.1%	86.0%

	Amk (µg/mL)					
2637.011 (µM)	0	8	16	24	32	64
24.0	2.5%	86.1%	83.6%	80.8%	83.1%	82.0%
16.0	1.8%	77.6%	85.4%	86.2%	86.7%	88.6%
8.0	4.7%	36.7%	70.4%	80.6%	84.8%	87.0%
4.0	4.8%	27.5%	46.5%	69.3%	82.1%	86.2%
0.0	0.0%	3.7%	31.3%	54.5%	76.2%	87.1%

	Amk (µg/mL)					
2637.013 (µM)	0	8	16	24	32	64
24.0	2.4%	81.2%	83.7%	88.3%	83.3%	90.0%
16.0	3.9%	74.3%	84.1%	87.5%	86.2%	86.0%
8.0	5.0%	48.2%	76.1%	85.2%	78.4%	88.4%
4.0	4.9%	25.2%	55.9%	77.5%	58.4%	87.5%
0.0	0.0%	5.6%	33.1%	31.2%	57.2%	89.0%

	Amk (µg/mL)					
2637.014 (µM)	0	8	16	24	32	64
24.0	3.9%	61.1%	73.1%	75.2%	77.7%	78.0%
16.0	3.3%	57.0%	65.2%	64.1%	57.8%	87.5%
8.0	2.9%	41.4%	43.6%	52.8%	54.3%	84.3%
4.0	3.6%	22.2%	32.8%	59.7%	42.1%	89.4%
0.0	0.0%	6.4%	8.7%	16.3%	27.1%	90.5%

Adjusted values (antimicrobial activity of compounds removed)

	Amk (µg/mL)					
2637-001 (µM)	0	8	16	24	32	64
24.0	0.0%	83.0%	86.8%	88.4%	87.1%	86.9%
16.0	0.0%	77.7%	84.5%	87.3%	88.4%	88.4%
8.0	0.0%	45.6%	72.1%	82.8%	86.2%	85.8%
4.0	0.0%	28.4%	60.6%	75.5%	84.0%	84.9%
0.0	0.0%	8.9%	29.4%	27.4%	52.8%	89.4%

	Amk (µg/mL)					
2637.020 (µM)	0	8	16	24	32	64
24.0	0.0%	85.7%	86.3%	75.9%	88.9%	91.2%
16.0	0.0%	81.5%	87.2%	87.3%	86.9%	90.3%
8.0	0.0%	37.5%	77.0%	85.7%	87.5%	87.2%
4.0	0.0%	28.7%	54.3%	84.0%	78.0%	90.1%
0.0	0.0%	8.0%	23.7%	41.4%	75.4%	91.5%

	Amk (µg/mL)					
2637.004 (µM)	0	8	16	24	32	64
24.0	0.0%	87.8%	89.1%	90.0%	90.2%	90.2%
16.0	0.0%	22.9%	84.9%	88.0%	84.8%	86.4%
8.0	0.0%	9.9%	44.1%	50.0%	75.8%	87.2%
4.0	0.0%	8.3%	37.2%	42.2%	53.0%	85.4%
0.0	0.0%	6.8%	22.0%	20.4%	27.7%	88.2%

	Amk (µg/mL)					
2637.019 (µM)	0	8	16	24	32	64
24.0	0.0%	4.9%	0.7%	2.4%	3.9%	5.5%
16.0	0.0%	89.2%	88.3%	87.4%	88.4%	88.9%
8.0	0.0%	21.5%	87.0%	80.6%	88.4%	89.7%
4.0	0.0%	8.8%	24.1%	30.5%	19.7%	89.7%
0.0	0.0%	7.2%	16.2%	26.6%	23.8%	90.7%

	Amk (µg/mL)					
2637.007 (µM)	0	8	16	24	32	64
24.0	0.0%	63.2%	67.3%	78.6%	77.3%	81.9%
16.0	0.0%	60.5%	72.3%	78.0%	78.5%	80.8%
8.0	0.0%	50.3%	69.8%	78.8%	75.2%	81.9%
4.0	0.0%	37.1%	60.5%	77.3%	50.7%	88.3%
0.0	0.0%	6.9%	16.0%	26.4%	42.6%	89.1%

	Amk (µg/mL)					
2637.010 (µM)	0	8	16	24	32	64
24.0	0.0%	70.4%	77.8%	80.5%	80.2%	86.6%
16.0	0.0%	67.3%	79.1%	77.7%	80.7%	85.5%
8.0	0.0%	58.5%	70.4%	78.8%	83.7%	87.3%
4.0	0.0%	48.5%	68.2%	77.8%	82.9%	87.1%
0.0	0.0%	4.6%	25.5%	20.3%	65.5%	89.1%

	Amk (µg/mL)					
2637.012 (µM)	0	8	16	24	32	64
24.0	0.0%	89.6%	89.5%	87.7%	85.2%	91.6%
16.0	0.0%	33.2%	79.0%	83.2%	85.8%	87.9%
8.0	0.0%	13.3%	42.4%	52.7%	69.4%	88.0%
4.0	0.0%	7.8%	30.0%	55.7%	52.1%	85.0%
0.0	0.0%	8.9%	16.8%	21.8%	52.1%	86.0%

	Amk (µg/mL)					
2637.011 (µM)	0	8	16	24	32	64
24.0	0.0%	85.7%	83.2%	80.3%	82.6%	81.5%
16.0	0.0%	77.2%	85.2%	85.9%	86.4%	88.4%
8.0	0.0%	33.5%	68.9%	79.6%	84.0%	86.4%
4.0	0.0%	23.9%	43.8%	67.8%	81.2%	85.5%
0.0	0.0%	3.7%	31.3%	54.5%	76.2%	87.1%

	Amk (µg/mL)					
2637.013 (µM)	0	8	16	24	32	64
24.0	0.0%	80.7%	83.3%	88.0%	82.9%	89.7%
16.0	0.0%	73.2%	83.5%	87.0%	85.7%	85.4%
8.0	0.0%	45.5%	74.8%	84.4%	77.3%	87.8%
4.0	0.0%	21.3%	53.6%	76.3%	56.3%	86.9%
0.0	0.0%	5.6%	33.1%	31.2%	57.2%	89.0%

	Amk (µg/mL)					
2637.014 (µM)	0	8	16	24	32	64
24.0	0.0%	59.5%	72.0%	74.2%	76.7%	77.1%
16.0	0.0%	55.5%	64.0%	62.9%	56.3%	87.1%
8.0	0.0%	39.7%	42.0%	51.4%	52.9%	83.8%
4.0	0.0%	19.3%	30.3%	58.2%	39.9%	89.0%
0.0	0.0%	6.4%	8.7%	16.3%	27.1%	90.5%

Figure S2. Checkerboard assays. The left column shows the measured values (medians %). The right column shows the adjusted values after removing any antimicrobial activity exerted by the testing compounds. Adjustment was carried out as described in Materials and Methods.