Supporting Information For:

Antibacterial Properties and Computational Insights of Potent Novel Linezolid-Based Oxazolidinones

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Keywords: Oxazolidinone, Linezolid, antibacterial, molecular modeling, molecular dynamics, ADME properties

Contents:

Table S1. Physicochemical properties of compounds **2**, **3a-j**, **4a-j** and linezolid (control).

Molecule	#Heavy atoms	#Aromatic heavy atoms	Fraction Csp3	#Rotatable bonds	#H-bond acceptors	#H-bond donors	MR	TPSA
2	38	11	0.46	10	9	1	143.52	150.38
3a	35	11	0.4	8	10	1	131.55	166.6
3b	41	17	0.31	9	10	1	155.36	166.6
3c	43	17	0.3	10	11	1	160.58	183.67
3d	44	17	0.31	10	13	1	155.39	166.6
3e	42	17	0.31	10	11	1	156.88	175.83
3f	41	17	0.28	9	10	1	155.4	166.6
3g	41	17	0.28	9	11	1	150.35	166.6
3h	42	17	0.28	9	12	1	150.31	166.6
3i	42	17	0.28	9	12	1	150.31	166.6
3j	44	21	0.25	9	11	1	165.69	179.49
4a	37	18	0.24	8	4	1	152.46	87.18
4b	32	15	0.3	6	5	1	127.24	100.32
4c	29	12	0.37	6	6	1	113.06	112.96
4d	34	15	0.33	6	4	1	142.83	115.42
4e	37	17	0.26	8	5	1	149.89	100.32
4f	36	6	0.62	9	6	1	149.63	119.96
4g	43	6	0.66	12	8	1	174.6	124.2
4h	36	12	0.46	9	8	1	138.02	117.2
4i	40	15	0.41	9	6	2	159.26	107.21
4j	37	12	0.44	9	7	1	145.24	104.31
Linezolid	24	6	0.5	5	5	1	91.06	71.11

Table S2. Lipophilicity and water solubility of compounds **2**, **3a-j**, **4a-j** and linezolid (control).

Molecule	iLOGP	XLOGP3	WLOGP	MLOGP	Silicos-IT Log P	Consensus Log P	ESOL Log S	ESOL Solubility (mg/ml)	ESOL Solubility (mol/l)
2	3.53	2.94	2.42	1.67	-0.48	2.02	-4.55	1.49E-02	2.79E-05
3a	2.45	1.34	1.52	0.34	-1.99	0.73	-3.56	1.41E-01	2.75E-04
3b	3.4	3.27	3.26	1.39	-0.46	2.17	-5.26	3.26E-03	5.55E-06
3c	2.74	2.58	3.15	0.78	-0.5	1.75	-4.91	7.49E-03	1.22E-05
3d	3.08	3.78	5.12	1.69	0.12	2.76	-5.82	9.60E-04	1.50E-06
3e	3.2	2.87	2.96	0.92	-0.91	1.81	-5.03	5.64E-03	9.34E-06
3f	3.34	3.53	3.61	1.66	-0.34	2.36	-5.55	1.73E-03	2.84E-06
3g	2.77	3	3.51	1.56	-0.56	2.06	-5.11	4.59E-03	7.76E-06
3h	2.83	3.1	4.07	1.93	-0.13	2.36	-5.28	3.22E-03	5.28E-06
3i	3.04	3.1	4.07	1.93	-0.13	2.4	-5.28	3.22E-03	5.28E-06
3j	2.81	3.17	3.5	1.14	-0.57	2.01	-5.47	2.12E-03	3.40E-06
4a	4.18	5.21	4.61	4.04	4.71	4.55	-6.16	3.55E-04	6.86E-07
4b	3.22	3.55	3.54	2.71	3.23	3.25	-4.85	6.41E-03	1.41E-05
4c	2.53	1.34	1.58	0.93	1.73	1.62	-3.18	2.74E-01	6.57E-04
4d	4.2	5.49	4.97	4.2	5.64	4.9	-6.45	1.83E-04	3.52E-07
4e	4.32	4.96	5	3.35	5.02	4.53	-6.14	3.95E-04	7.29E-07
4f	3.46	2.16	1.86	2.39	1.17	2.21	-3.98	5.53E-02	1.06E-04
4g	5.33	2.39	1.99	2.26	0.66	2.53	-4.42	2.32E-02	3.82E-05
4h	3.27	1.57	1.71	0.85	1.13	1.71	-3.59	1.30E-01	2.60E-04
4i	4.02	4.21	3.71	2.73	3.33	3.6	-5.6	1.40E-03	2.54E-06
4j	3.25	3.27	2.96	2.29	2.35	2.82	-4.86	7.43E-03	1.39E-05
Linezolid	2.58	0.69	0.78	0.99	1.25	1.26	-2.22	2.03E+00	6.01E-03

Table S3. Some other water solubility parameters of compounds **2**, **3a-j**, **4a-j** and linezolid (control).

Molecule	ESOL Class	Ali Log S	Ali Solubility (mg/ml)	Ali Solubility (mol/l)	Ali Class	Silicos-IT LogSw	Silicos-IT Solubility (mg/ml)	Silicos-IT Solubility (mol/l)	Silicos-IT class
2	Moderately soluble	-5.76	9.27E-04	1.74E-06	Moderately soluble	-4.22	3.21E-02	6.01E-05	Moderately soluble
3a	Soluble	-4.44	1.86E-02	3.63E-05	Moderately soluble	-3.66	1.12E-01	2.18E-04	Soluble
3b	Moderately soluble	-6.44	2.12E-04	3.61E-07	Poorly soluble	-6.08	4.85E-04	8.26E-07	Poorly soluble
3c	Moderately soluble	-6.09	5.06E-04	8.21E-07	Poorly soluble	-5.99	6.24E-04	1.01E-06	Moderately soluble
3d	Moderately soluble	-6.97	6.84E-05	1.07E-07	Poorly soluble	-6.51	1.99E-04	3.10E-07	Poorly soluble
3e	Moderately soluble	-6.22	3.62E-04	6.00E-07	Poorly soluble	-5.8	9.52E-04	1.58E-06	Moderately soluble
3f	Moderately soluble	-6.71	1.18E-04	1.94E-07	Poorly soluble	-6.29	3.15E-04	5.19E-07	Poorly soluble
3g	Moderately soluble	-6.16	4.07E-04	6.87E-07	Poorly soluble	-5.97	6.34E-04	1.07E-06	Moderately soluble
3h	Moderately soluble	-6.27	3.30E-04	5.41E-07	Poorly soluble	-6.22	3.63E-04	5.96E-07	Poorly soluble
3i	Moderately soluble	-6.27	3.30E-04	5.41E-07	Poorly soluble	-6.22	3.63E-04	5.96E-07	Poorly soluble
3j	Moderately soluble	-6.61	1.53E-04	2.45E-07	Poorly soluble	-6.95	7.02E-05	1.12E-07	Poorly soluble
4a	Poorly soluble	-6.79	8.43E-05	1.63E-07	Poorly soluble	-8.13	3.85E-06	7.45E-09	Poorly soluble
4b	Moderately soluble	-5.34	2.07E-03	4.55E-06	Moderately soluble	-6.48	1.51E-04	3.32E-07	Poorly soluble
4c	Soluble	-3.31	2.03E-01	4.85E-04	Soluble	-4.88	5.48E-03	1.31E-05	Moderately soluble
4d	Poorly soluble	-7.67	1.11E-05	2.13E-08	Poorly soluble	-7.47	1.77E-05	3.41E-08	Poorly soluble
4e	Poorly soluble	-6.8	8.49E-05	1.57E-07	Poorly soluble	-7.93	6.38E-06	1.18E-08	Poorly soluble
4f	Soluble	-4.31	2.55E-02	4.88E-05	Moderately soluble	-3.68	1.10E-01	2.09E-04	Soluble
4g	Moderately soluble	-4.64	1.39E-02	2.29E-05	Moderately soluble	-3.7	1.21E-01	2.00E-04	Soluble
4h	Soluble	-3.64	1.14E-01	2.28E-04	Soluble	-4.92	5.99E-03	1.20E-05	Moderately soluble
4i	Moderately soluble	-6.17	3.72E-04	6.74E-07	Poorly soluble	-6.88	7.29E-05	1.32E-07	Poorly soluble
4j	Moderately soluble	-5.13	3.91E-03	7.33E-06	Moderately soluble	-5.87	7.19E-04	1.35E-06	Moderately soluble
Linezolid	Soluble	-1.76	5.86E+00	1.74E-02	Very soluble	-3.19	2.18E-01	6.47E-04	Soluble

Table S4. Pharmacokinetics parameters of compounds **2**, **3a-j**, **4a-j** and linezolid (control).

Molecule	GI absorption	BBB permeant	Pgp substrate	CYP1A2 inhibitor	CYP2C19 inhibitor	CYP2C9 inhibitor	CYP2D6 inhibitor	CYP3A4 inhibitor	log Kp (cm/s)
2	Low	No	Yes	No	Yes	Yes	No	Yes	-7.47
3a	Low	No	Yes	No	Yes	Yes	No	Yes	-8.47
3b	Low	No	Yes	No	No	Yes	No	Yes	-7.56
3c	Low	No	Yes	No	No	Yes	No	Yes	-8.22
3d	Low	No	Yes	No	No	Yes	No	Yes	-7.53
3e	Low	No	Yes	No	No	Yes	No	Yes	-7.94
3f	Low	No	Yes	No	No	Yes	No	Yes	-7.5
3g	Low	No	Yes	No	No	Yes	No	Yes	-7.78
3h	Low	No	Yes	No	No	Yes	No	Yes	-7.82
3i	Low	No	Yes	No	No	Yes	No	Yes	-7.82
3j	Low	No	Yes	No	No	Yes	No	Yes	-7.86
4a	High	No	Yes	No	Yes	Yes	Yes	Yes	-5.76
4b	High	No	Yes	Yes	Yes	Yes	Yes	Yes	-6.56
4c	High	No	Yes	No	Yes	No	Yes	Yes	-7.9
4d	Low	No	Yes	Yes	Yes	Yes	Yes	Yes	-5.57
4e	High	No	Yes	No	Yes	Yes	Yes	Yes	-6.08
4f	High	No	Yes	No	Yes	No	Yes	Yes	-7.96
4g	High	No	Yes	No	Yes	Yes	Yes	Yes	-8.3
4h	High	No	Yes	No	Yes	Yes	No	Yes	-8.24
4i	High	No	Yes	No	Yes	Yes	Yes	Yes	-6.68
4j	High	No	Yes	No	Yes	Yes	Yes	Yes	-7.24
Linezolid	High	No	Yes	No	No	No	No	No	-7.87

Table S5. Drug likeness and medicinal chemistry of compounds **2**, **3a-j**, **4a-j** and linezolid (control).

Molecule	Lipinski #violations	Ghose #violations	Veber #violations	Egan #violations	Muegge #violations	Bioavailability Score	PAINS #alerts	Brenk #alerts	Leadlikeness #violations	Synthetic accesibility
2	2	2	1	1	1	0.17	1	3	2	4.57
3a	2	2	1	1	1	0.17	1	2	2	4.22
3b	2	2	1	1	1	0.17	1	2	2	4.63
3c	2	2	1	1	3	0.17	1	2	2	4.69
3d	2	2	1	1	3	0.17	1	2	3	4.63
3e	2	2	1	1	3	0.17	1	2	2	4.63
3f	2	2	1	1	2	0.17	1	2	3	4.51
3g	2	2	1	1	2	0.17	1	2	2	4.53
3h	2	2	1	1	3	0.17	1	2	2	4.56
3i	2	2	1	1	3	0.17	1	2	2	4.54

3j	2	2	1	1	3	0.17	1	2	2	4.72
4a	1	2	0	0	1	0.55	1	2	3	4.31
4b	0	0	0	0	0	0.55	1	0	2	3.99
4c	0	0	0	0	0	0.55	1	0	1	3.59
4d	2	2	0	0	1	0.17	1	0	2	4.1
4e	1	2	0	0	0	0.55	1	1	3	4.52
4f	1	2	0	0	0	0.55	1	1	2	4.58
4g	2	3	1	0	1	0.17	1	1	2	5.19
4h	2	2	0	0	0	0.17	1	1	2	4.22
4i	1	3	0	0	0	0.55	1	1	3	4.46
4j	1	2	0	0	0	0.55	1	2	2	4.19
Linezolid	0	0	0	0	0	0.55	1	0	0	3.32

Table S6. Toxicity of compounds **2**, **3a-j**, **4a-j** and linezolid (control).

Molecule	hERG Blockers	Human Hepatotoxicity	Drug induced liver injury	Ames Toxicity	Rat Oral Acute Toxicity	FDA Maximum Daily Dose	Skin Sensitization	Carcinogencity	Eye Corrosion	Eye Irritation	Respiratory Toxicity
2	0.43	0.993	0.982	0.995	0.493	0.249	0.457	0.975	0.003	0.008	0.029
3a	0.719	0.993	0.985	0.998	0.371	0.44	0.331	0.968	0.003	0.007	0.187
3b	0.817	0.992	0.99	0.998	0.282	0.208	0.18	0.963	0.003	0.007	0.146
3c	0.85	0.993	0.992	0.998	0.287	0.216	0.153	0.966	0.003	0.007	0.094
3d	0.757	0.994	0.988	0.993	0.363	0.88	0.181	0.949	0.003	0.006	0.341
3e	0.855	0.994	0.99	0.998	0.264	0.189	0.157	0.961	0.003	0.007	0.155
3f	0.844	0.991	0.99	0.998	0.36	0.175	0.176	0.962	0.003	0.007	0.145
3g	0.806	0.996	0.99	0.998	0.26	0.233	0.148	0.965	0.003	0.007	0.205
3h	0.64	0.995	0.988	0.997	0.145	0.44	0.166	0.968	0.003	0.007	0.263
3i	0.69	0.998	0.989	0.998	0.154	0.394	0.152	0.969	0.003	0.006	0.318
3j	0.741	0.992	0.991	0.998	0.321	0.236	0.172	0.956	0.003	0.007	0.15
4a	0.409	0.98	0.986	0.619	0.05	0.962	0.281	0.517	0.003	0.009	0.327
4b	0.299	0.982	0.969	0.938	0.676	0.758	0.411	0.911	0.003	0.01	0.197
4c	0.568	0.984	0.985	0.819	0.055	0.8	0.468	0.575	0.003	0.01	0.072
4d	0.138	0.99	0.974	0.93	0.053	0.907	0.814	0.942	0.003	0.011	0.27
4e	0.458	0.972	0.979	0.943	0.202	0.527	0.664	0.901	0.003	0.011	0.347
4f	0.135	0.992	0.959	0.66	0.219	0.307	0.304	0.937	0.003	0.007	0.016
4g	0.084	0.997	0.939	0.348	0.287	0.177	0.234	0.956	0.003	0.005	0.004
4h	0.476	0.993	0.983	0.249	0.077	0.365	0.586	0.759	0.003	0.007	0.035
4i	0.505	0.993	0.946	0.692	0.529	0.841	0.194	0.894	0.003	0.008	0.06
4j	0.427	0.995	0.97	0.754	0.327	0.503	0.209	0.916	0.003	0.007	0.039
Linezolid	0.029	0.971	0.918	0.676	0.042	0.373	0.577	0.725	0.003	0.011	0.046