Electronic Supplementary Material (ESI) for RSC Advances.

Appendix A: Supplementary Information

Time-dependent and Pb-dependent antagonism and synergism towards Vibrio qinghaiensis sp.-Q67 within heavy metal mixtures

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Table S1 The model parameters (α and β), some statistics (*RMSE* and *R*), and median effective concentration (EC_{50}) of the three heavy metals in five time points

	Time/h	*F* [a]	α	β	*RMSE*	*R*	EC_{50}	pEC_{50} [b]
Pb	0.25	L	5.46	1.67	0.067	0.9563	6.06E-04	3.22
	2	L	6.36	2.13	0.064	0.9695	1.11E-03	2.96
	4	L	7.44	2.39	0.058	0.9790	8.61E-04	3.07
	8	W	5.44	1.79	0.051	0.9858	5.70E-04	3.24
	12	W	5.55	1.85	0.052	0.9852	6.34E-04	3.19
Cd	0.25	W	16.98	4.65	0.043	0.9935	1.82E-04	3.74
	2	W	16.91	4.67	0.016	0.9990	1.94E-04	3.71
	4	W	11.94	3.22	0.043	0.9922	1.43E-04	3.85
	8	W	11.65	3.05	0.049	0.9954	1.06E-04	3.98
	12	W	15.91	4.08	0.021	0.9938	1.00E-04	4.00
Mn	0.25	L	8.14	3.19	0.086	0.9552	2.81E-03	2.55
	2	L	10.69	3.93	0.071	0.9771	1.91E-03	2.72
	4	W	8.83	3.33	0.084	0.9748	1.67E-03	2.78
	8	W	6.34	2.35	0.060	0.9837	1.31E-03	2.88
	12	W	5.18	1.79	0.041	0.9904	7.28E-04	3.14

[a] *F:* fitted functions where L refers to logit function and W to Weibull function, [b] pEC_{50}: $-\log EC_{50}$.

Table S2a The model parameters (α and β), some statistics (*RMSE* and *R*), and median effective concentration (EC_{50}) of the binary mixture rays of Cd and Pb in five time points

Ray	Time/h	*F*	α	β	*RMSE*	*R*	EC_{50}	pEC_{50}
Cd-Pb-R1	0.25	L	8.85	2.61	0.044	0.9860	4.07E-04	3.391
	2	L	7.92	2.38	0.027	0.9933	4.70E-04	3.328
	4	L	7.3	2.01	0.021	0.9962	2.33E-04	3.632
	8	L	6.9	1.83	0.016	0.9975	1.70E-04	3.770
	12	L	7.04	1.79	0.023	0.9950	1.17E-04	3.933
Cd-Pb-R2	0.25	L	7.08	2.15	0.056	0.9738	5.09E-04	3.293
	2	L	6.35	2.01	0.043	0.9801	6.93E-04	3.159
	4	L	7.49	2.1	0.052	0.9790	2.71E-04	3.567
	8	L	6.19	1.77	0.039	0.9843	3.18E-04	3.497
	12	L	6.22	1.81	0.025	0.9932	3.66E-04	3.436
Cd-Pb-R3	0.25	L	7.08	2.15	0.056	0.9738	5.09E-04	3.293
	2	L	5.39	1.81	0.056	0.9606	1.05E-03	2.978
	4	L	7.14	2.14	0.055	0.9754	4.61E-04	3.336
	8	L	5.29	1.72	0.041	0.9773	8.40E-04	3.076
	12	L	5.62	1.93	0.041	0.9754	1.22E-03	2.912
Cd-Pb-R4	0.25	L	5.45	1.70	0.074	0.9443	6.22E-04	3.206
	2	L	4.15	1.44	0.042	0.9691	1.31E-03	2.882
	4	L	6.38	1.98	0.052	0.9746	5.99E-04	3.222
	8	L	4.17	1.51	0.036	0.9729	1.73E-03	2.762
	12	L	3.23	1.27	0.036	0.9586	2.86E-03	2.543
Cd-Pb-R5	0.25	L	5.79	1.76	0.077	0.9460	5.13E-04	3.290
	2	L	4.78	1.49	0.067	0.9438	6.19E-04	3.208
	4	L	6.54	2.02	0.040	0.9859	5.79E-04	3.238
	8	L	4.19	1.58	0.032	0.9780	2.23E-03	2.652
	12	L	4.90	1.73	0.032	0.9833	1.47E-03	2.832

Table S2b The model parameters (α and β), some statistics (*RMSE* and *R*), and median effective concentration (EC_{50}) of the binary mixture rays of Cd and Mn in five time points

Ray	Time/h	*F*	α	β	*RMSE*	*R*	EC_{50}	pEC_{50}
Cd-Mn-R1	0.25	L	14.98	4.50	0.063	0.9791	4.69E-04	3.329
	2	W	14.98	4.47	0.067	0.9852	3.63E-04	3.440
	4	W	9.75	2.81	0.046	0.9914	2.33E-04	3.633
	8	W	8.43	2.39	0.045	0.9908	1.92E-04	3.718
	12	W	6.13	1.60	0.030	0.9941	7.92E-05	4.101
Cd-Mn-R2	0.25	W	8.62	2.88	0.035	0.9929	7.11E-04	3.148
	2	L	15.00	4.47	0.047	0.9941	4.41E-04	3.356
	4	L	13.94	3.97	0.042	0.9939	3.08E-04	3.511
	8	L	13.68	3.83	0.044	0.9924	2.68E-04	3.572
	12	L	9.17	2.26	0.034	0.9911	8.76E-05	4.058
Cd-Mn-R3	0.25	L	13.09	4.30	0.027	0.9973	9.03E-04	3.044
	2	L	15.00	4.63	0.077	0.9887	5.76E-04	3.240
	4	L	15.00	4.37	0.064	0.9891	3.69E-04	3.432
	8	L	15.00	4.38	0.024	0.9979	3.76E-04	3.425
	12	L	12.36	3.34	0.024	0.9973	1.99E-04	3.701
Cd-Mn-R4	0.25	L	13.41	4.52	0.029	0.9970	1.08E-03	2.967
	2	L	12.62	4.11	0.047	0.9912	8.50E-04	3.071
	4	L	12.10	3.71	0.048	0.9905	5.48E-04	3.261
	8	L	14.99	4.48	0.056	0.9905	4.51E-04	3.346
	12	W	6.76	1.96	0.033	0.9933	2.13E-04	3.671
Cd-Mn-R5	0.25	L	13.73	4.75	0.054	0.9904	1.29E-03	2.891
	2	W	12.56	4.26	0.084	0.9868	9.11E-04	3.041
	4	W	7.80	2.54	0.080	0.9747	5.76E-04	3.240
	8	W	12.63	4.13	0.076	0.9873	6.95E-04	3.158
	12	W	9.17	2.85	0.018	0.9987	4.21E-04	3.376

Table S2c The model parameters (α and β), some statistics (*RMSE* and *R*), and median effective concentration (EC_{50}) of the binary mixture rays of Pb and Mn in five time points

Ray	Time/h	*F*	α	β	*RMSE*	*R*	EC_{50}	pEC_{50}
Pb-Mn-R1	0.25	L	5.42	1.65	0.090	0.9249	5.19E-04	3.285
	2	L	4.51	1.49	0.057	0.9560	9.40E-04	3.027
	4	L	6.40	2.05	0.027	0.9937	7.55E-04	3.122
	8	W	3.03	1.24	0.034	0.9750	1.91E-03	2.719
	12	W	2.64	1.06	0.080	0.8772	1.53E-03	2.816
Pb-Mn-R2	0.25	L	4.14	1.26	0.110	0.8397	5.18E-04	3.286
	2	L	4.84	1.57	0.059	0.9595	8.26E-04	3.083
	4	L	6.72	2.02	0.070	0.9648	4.71E-04	3.327
	8	L	5.19	1.51	0.061	0.9574	3.66E-04	3.437
	12	W	2.97	0.90	0.062	0.9444	1.79E-04	3.746
Pb-Mn-R3	0.25	L	4.29	1.34	0.103	0.8677	6.29E-04	3.201
	2	L	5.58	1.79	0.064	0.9627	7.63E-04	3.117
	4	L	7.01	2.16	0.059	0.9745	5.68E-04	3.245
	8	L	5.83	1.76	0.064	0.9623	4.87E-04	3.313
	12	W	2.89	0.90	0.057	0.9517	2.16E-04	3.664
Pb-Mn-R4	0.25	L	4.72	1.53	0.084	0.9225	8.22E-04	3.085
	2	L	5.66	1.84	0.034	0.9884	8.39E-04	3.076
	4	L	7.16	2.19	0.053	0.9800	5.38E-04	3.269
	8	W	4.12	1.39	0.074	0.9554	5.41E-04	3.267
	12	W	3.21	1.02	0.068	0.9456	2.79E-04	3.555
Pb-Mn-R5	0.25	L	4.90	1.70	0.091	0.9223	1.31E-03	2.882
	2	L	5.57	1.93	0.055	0.9731	1.31E-03	2.882
	4	L	7.57	2.62	0.069	0.9688	1.29E-03	2.889
	8	W	4.31	1.58	0.064	0.9690	1.00E-03	3.000
	12	L	6.62	1.94	0.073	0.9558	3.87E-04	3.412

Table S3 The model parameters (α and β), some statistics (*RMSE* and *R*), and median effective concentration (EC_{50}) of the ternary mixture rays of Pb, Cd and Mn in five time points.

Ray	Time/h	*F*	α	β	*RMSE*	*R*	EC_{50}	pEC_{50}
Pb-Cd-Mn-R1	0.25	L	13.59	4.44	0.036	0.9942	8.69E-04	3.061
	2	L	14.03	4.51	0.036	0.9948	7.74E-04	3.111
	4	L	14.99	4.50	0.048	0.9921	4.66E-04	3.331
	8	L	10.56	3.03	0.057	0.9854	3.27E-04	3.485
	12	L	9.98	2.80	0.060	0.9825	2.73E-04	3.564
Pb-Cd-Mn-R2	0.25	L	15.00	4.71	0.052	0.9892	6.54E-04	3.185
	2	L	15.00	4.73	0.043	0.9942	6.74E-04	3.171
	4	L	13.88	4.08	0.062	0.9872	3.96E-04	3.402
	8	L	8.91	2.42	0.686	0.9735	2.08E-04	3.682
	12	L	9.47	2.53	0.061	0.9803	1.81E-04	3.743
Pb-Cd-Mn-R3	0.25	L	5.73	1.84	0.074	0.9544	7.67E-04	3.114
	2	L	7.53	2.38	0.038	0.9909	6.86E-04	3.164
	4	L	8.49	2.61	0.054	0.9842	5.58E-04	3.253
	8	L	6.38	1.91	0.072	0.9590	4.56E-04	3.340
	12	L	6.22	1.78	0.071	0.9561	3.20E-04	3.494
Pb-Cd-Mn-R4	0.25	L	5.60	1.67	0.065	0.9583	4.43E-04	3.353
	2	L	5.91	1.86	0.041	0.9838	6.64E-04	3.177
	4	L	6.43	1.92	0.043	0.9837	4.47E-04	3.349
	8	L	5.89	1.69	0.035	0.9874	3.27E-04	3.485
	12	L	5.48	1.46	0.028	0.9897	1.76E-04	3.753
Pb-Cd-Mn-R5	0.25	L	7.01	2.19	0.054	0.9795	6.29E-04	3.200
	2	L	8.33	2.65	0.024	0.9962	7.18E-04	3.143
	4	L	8.20	2.51	0.045	0.9876	5.41E-04	3.267
	8	L	6.70	1.98	0.049	0.9804	4.13E-04	3.384
	12	L	5.75	1.54	0.048	0.9727	1.84E-04	7.734

Table S4a The concentration of a single component in the mixture of Cd-Pb

Rays	components	C_1[c]	C_2	C_3	C_4	C_5	C_6	C_7	C_8	C_9	C_{10}	C_{11}	C_{12}
Cd-Pb-R1	Cd	4.622E-04	3.143E-04	2.137E-04	1.453E-04	9.883E-05	6.720E-05	4.570E-05	3.107E-05	2.113E-05	1.437E-05	9.771E-06	6.644E-06
	Pb	5.859E-04	3.984E-04	2.709E-04	1.842E-04	1.253E-04	8.518E-05	5.793E-05	3.939E-05	2.678E-05	1.821E-05	1.239E-05	8.422E-06
Cd-Pb-R2	Cd	3.431E-04	2.333E-04	1.586E-04	1.079E-04	7.335E-05	4.988E-05	3.392E-05	2.306E-05	1.568E-05	1.067E-05	7.252E-06	4.932E-06
	Pb	1.088E-03	7.400E-04	5.032E-04	3.422E-04	2.327E-04	1.582E-04	1.076E-04	7.317E-05	4.975E-05	3.383E-05	2.301E-05	1.564E-05
Cd-Pb-R3	Cd	2.349E-04	1.597E-04	1.086E-04	7.386E-05	5.022E-05	3.415E-05	2.322E-05	1.579E-05	1.074E-05	7.302E-06	4.965E-06	3.376E-06
	Pb	1.488E-03	1.012E-03	6.883E-04	4.680E-04	3.182E-04	2.164E-04	1.472E-04	1.001E-04	6.805E-05	4.627E-05	3.146E-05	2.140E-05
Cd-Pb-R4	Cd	1.430E-04	9.721E-05	6.610E-05	4.495E-05	3.056E-05	2.078E-05	1.413E-05	9.611E-06	6.535E-06	4.444E-06	3.022E-06	2.055E-06
	Pb	1.813E-03	1.233E-03	8.381E-04	5.699E-04	3.876E-04	2.635E-04	1.792E-04	1.219E-04	8.287E-05	5.635E-05	3.832E-05	2.606E-05
Cd-Pb-R5	Cd	6.561E-05	4.461E-05	3.034E-05	2.063E-05	1.403E-05	9.539E-06	6.486E-06	4.411E-06	2.999E-06	2.040E-06	1.387E-06	9.431E-07
	Pb	2.069E-03	1.407E-03	9.566E-04	6.505E-04	4.423E-04	3.008E-04	2.045E-04	1.391E-04	9.458E-05	6.431E-05	4.373E-05	2.974E-05

[c] C: The concentration of the mixture components

Table S4b The concentration of a single component in the mixture of Cd-Mn

Rays	components	C_1	C_2	C_3	C_4	C_5	C_6	C_7	C_8	C_9	C_{10}	C_{11}	C_{12}
Cd-Mn-R1	Cd	4.829E-04	3.284E-04	2.233E-04	1.518E-04	1.032E-04	7.021E-05	4.774E-05	3.246E-05	2.208E-05	1.501E-05	1.021E-05	6.941E-06
	Mn	7.030E-04	4.780E-04	3.251E-04	2.210E-04	1.503E-04	1.022E-04	6.950E-05	4.726E-05	3.214E-05	2.185E-05	1.486E-05	1.010E-05
Cd-Mn-R2	Cd	4.259E-04	2.896E-04	1.970E-04	1.339E-04	9.107E-05	6.193E-05	4.211E-05	2.864E-05	1.947E-05	1.324E-05	9.004E-06	6.123E-06
	Mn	1.551E-03	1.054E-03	7.170E-04	4.876E-04	3.315E-04	2.254E-04	1.533E-04	1.042E-04	7.089E-05	4.820E-05	3.278E-05	2.229E-05
Cd-Mn-R3	Cd	3.562E-04	2.422E-04	1.647E-04	1.120E-04	7.615E-05	5.178E-05	3.521E-05	2.394E-05	1.628E-05	1.107E-05	7.529E-06	5.120E-06
	Mn	2.592E-03	1.763E-03	1.199E-03	8.151E-04	5.543E-04	3.769E-04	2.563E-04	1.743E-04	1.185E-04	8.058E-05	5.480E-05	3.726E-05
Cd-Mn-R4	Cd	2.682E-04	1.824E-04	1.240E-04	8.434E-05	5.735E-05	3.900E-05	2.652E-05	1.803E-05	1.226E-05	8.339E-06	5.670E-06	3.856E-06
	Mn	3.904E-03	2.654E-03	1.805E-03	1.227E-03	8.346E-04	5.675E-04	3.859E-04	2.624E-04	1.785E-04	1.213E-04	8.252E-05	5.611E-05
Cd-Mn-R5	Cd	1.538E-04	1.046E-04	7.110E-05	4.835E-05	3.288E-05	2.236E-05	1.520E-05	1.034E-05	7.029E-06	4.780E-06	3.250E-06	2.210E-06
	Mn	5.605E-03	3.811E-03	2.592E-03	1.762E-03	1.198E-03	8.149E-04	5.542E-04	3.768E-04	2.562E-04	1.742E-04	1.185E-04	8.057E-05

Table S4c The concentration of a single component in the mixture of Pb -Mn

Rays	components	C_1	C_2	C_3	C_4	C_5	C_6	C_7	C_8	C_9	C_{10}	C_{11}	C_{12}
Pb-Mn-R1	Pb	2.076E-03	1.411E-03	9.598E-04	6.526E-04	4.438E-04	3.018E-04	2.052E-04	1.395E-04	9.489E-05	6.453E-05	4.388E-05	2.984E-05
	Mn	4.768E-04	3.242E-04	2.205E-04	1.499E-04	1.019E-04	6.932E-05	4.714E-05	3.205E-05	2.180E-05	1.482E-05	1.008E-05	6.854E-06
Pb-Mn-R2	Pb	1.836E-03	1.249E-03	8.492E-04	5.774E-04	3.927E-04	2.670E-04	1.816E-04	1.235E-04	8.395E-05	5.709E-05	3.882E-05	2.640E-05
	Mn	1.055E-03	7.172E-04	4.877E-04	3.316E-04	2.255E-04	1.533E-04	1.043E-04	7.091E-05	4.822E-05	3.279E-05	2.230E-05	1.516E-05
Pb-Mn-R3	Pb	1.568E-03	1.066E-03	7.251E-04	4.931E-04	3.353E-04	2.280E-04	1.550E-04	1.054E-04	7.169E-05	4.875E-05	3.315E-05	2.254E-05
	Mn	1.801E-03	1.225E-03	8.329E-04	5.664E-04	3.851E-04	2.619E-04	1.781E-04	1.211E-04	8.235E-05	5.600E-05	3.808E-05	2.589E-05
Pb-Mn-R4	Pb	1.242E-03	8.445E-04	5.742E-04	3.905E-04	2.655E-04	1.806E-04	1.228E-04	8.349E-05	5.677E-05	3.861E-05	2.625E-05	1.785E-05
	Mn	2.854E-03	1.941E-03	1.320E-03	8.974E-04	6.102E-04	4.149E-04	2.822E-04	1.919E-04	1.305E-04	8.872E-05	6.033E-05	4.102E-05
Pb-Mn-R5	Pb	7.906E-04	5.376E-04	3.656E-04	2.486E-04	1.690E-04	1.150E-04	7.817E-05	5.315E-05	3.615E-05	2.458E-05	1.671E-05	1.137E-05
	Mn	4.541E-03	3.088E-03	2.100E-03	1.428E-03	9.709E-04	6.602E-04	4.489E-04	3.053E-04	2.076E-04	1.412E-04	9.599E-05	6.527E-05

Table S5 The concentration of a single component in the mixture of Cd-Pb-Mn

Rays	components	C_1	C_2	C_3	C_4	C_5	C_6	C_7	C_8	C_9	C_{10}	C_{11}	C_{12}
Cd-Pb-Mn-R1	Cd	3.685E-04	2.506E-04	1.704E-04	1.159E-04	7.879E-05	5.358E-05	3.643E-05	2.477E-05	1.685E-05	1.146E-05	7.790E-06	5.297E-06
	Pb	2.590E-04	1.761E-04	1.198E-04	8.143E-05	5.537E-05	3.765E-05	2.560E-05	1.741E-05	1.184E-05	8.051E-06	5.475E-06	3.723E-06
	Mn	2.090E-03	1.421E-03	9.664E-04	6.572E-04	4.469E-04	3.039E-04	2.066E-04	1.405E-04	9.555E-05	6.497E-05	4.418E-05	3.004E-05
Cd-Pb-Mn-R2	Cd	8.070E-04	5.488E-04	3.732E-04	2.538E-04	1.726E-04	1.173E-04	7.979E-05	5.426E-05	3.689E-05	2.509E-05	1.706E-05	1.160E-05
	Pb	4.069E-04	2.767E-04	1.882E-04	1.280E-04	8.701E-05	5.917E-05	4.023E-05	2.736E-05	1.860E-05	1.265E-05	8.602E-06	5.850E-06
	Mn	5.469E-04	3.719E-04	2.529E-04	1.720E-04	1.169E-04	7.952E-05	5.407E-05	3.677E-05	2.500E-05	1.700E-05	1.156E-05	7.862E-06
Cd-Pb-Mn-R3	Cd	1.045E-03	7.104E-04	4.830E-04	3.285E-04	2.234E-04	1.519E-04	1.033E-04	7.023E-05	4.776E-05	3.247E-05	2.208E-05	1.502E-05
	Pb	9.795E-05	6.660E-05	4.529E-05	3.080E-05	2.094E-05	1.424E-05	9.684E-06	6.585E-06	4.478E-06	3.045E-06	2.070E-06	1.408E-06
	Mn	1.918E-03	1.304E-03	8.870E-04	6.031E-04	4.101E-04	2.789E-04	1.896E-04	1.290E-04	8.769E-05	5.963E-05	4.055E-05	2.757E-05
Cd-Pb-Mn-R4	Cd	1.125E-03	7.649E-04	5.202E-04	3.537E-04	2.405E-04	1.636E-04	1.112E-04	7.563E-05	5.143E-05	3.497E-05	2.378E-05	1.617E-05
	Pb	8.810E-05	5.991E-05	4.074E-05	2.770E-05	1.884E-05	1.281E-05	8.711E-06	5.923E-06	4.028E-06	2.739E-06	1.862E-06	1.266E-06
	Mn	9.841E-04	6.692E-04	4.550E-04	3.094E-04	2.104E-04	1.431E-04	9.729E-05	6.616E-05	4.499E-05	3.059E-05	2.080E-05	1.415E-05
Cd-Pb-Mn-R5	Cd	1.115E-03	7.581E-04	5.155E-04	3.505E-04	2.384E-04	1.621E-04	1.102E-04	7.495E-05	5.097E-05	3.466E-05	2.357E-05	1.603E-05
	Pb	1.759E-04	1.196E-04	8.132E-05	5.530E-05	3.760E-05	2.557E-05	1.739E-05	1.182E-05	8.040E-06	5.467E-06	3.718E-06	2.528E-06
	Mn	1.280E-03	8.707E-04	5.921E-04	4.026E-04	2.738E-04	1.862E-04	1.266E-04	8.608E-05	5.854E-05	3.981E-05	2.707E-05	1.841E-05

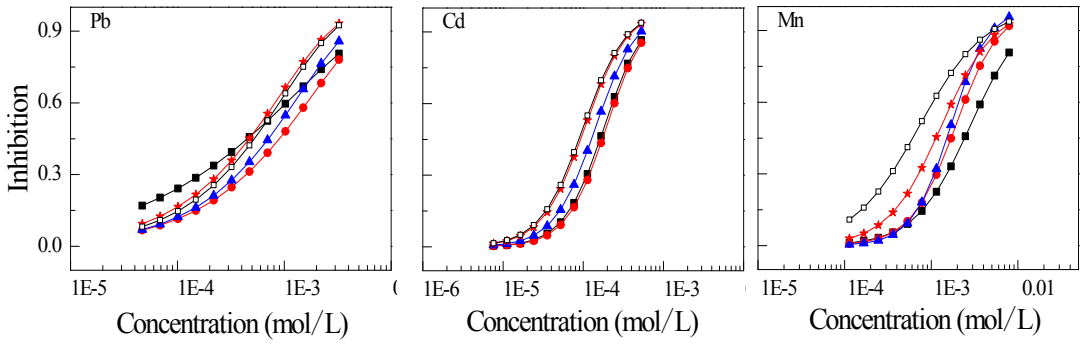

Fig. S1 Concentration-response curves of three heavy metals at different time points for Q67 where ■, ꩜, ▲, 🡻, and □ refer to 0.25, 2, 4, 8 and 12 h.

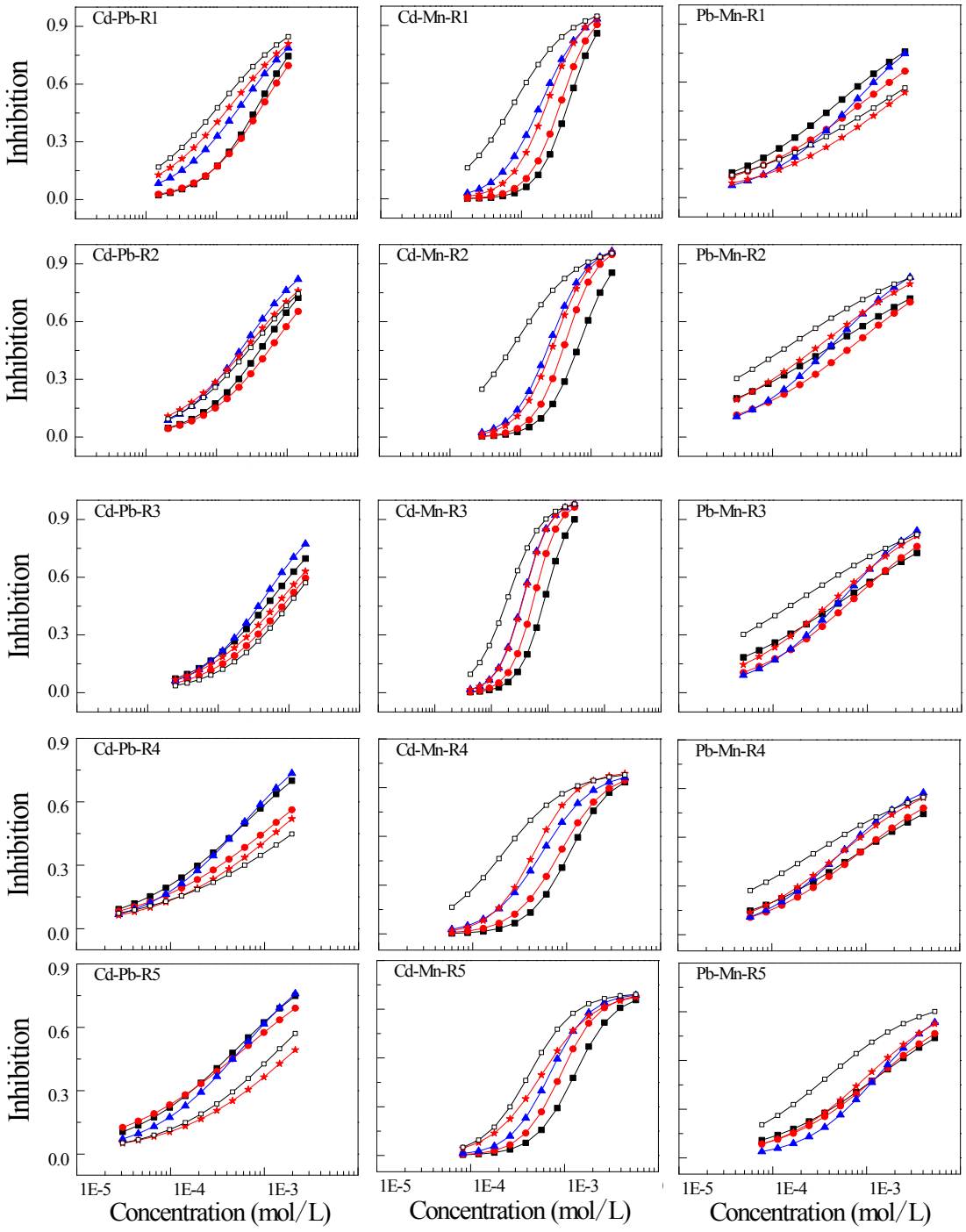

Fig. S2 The concentration-response curves of the three binary mixture systems of three heavy metals on Q67 where ■, ᔓ, ▲, 🔻 and □ refer to 0.25, 2, 4, 8 and 12 h.

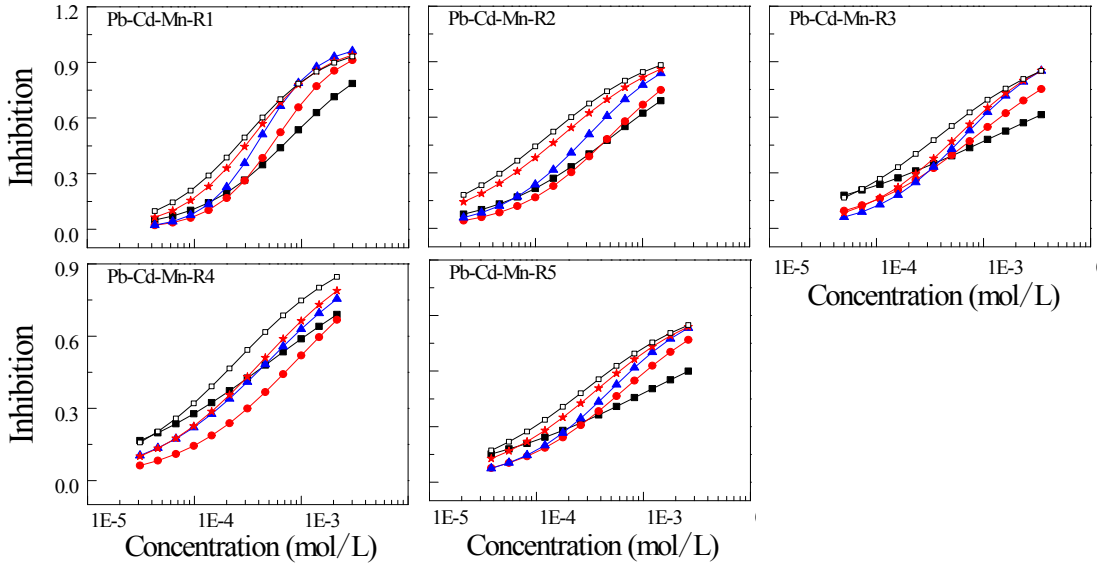

Fig. S3 The concentration-response curves of the ternary mixture systems of three heavy metals on Q67 where ■, ℘, ▲, 🡻 and □ refer to 0.25, 2, 4, 8 and 12 h.

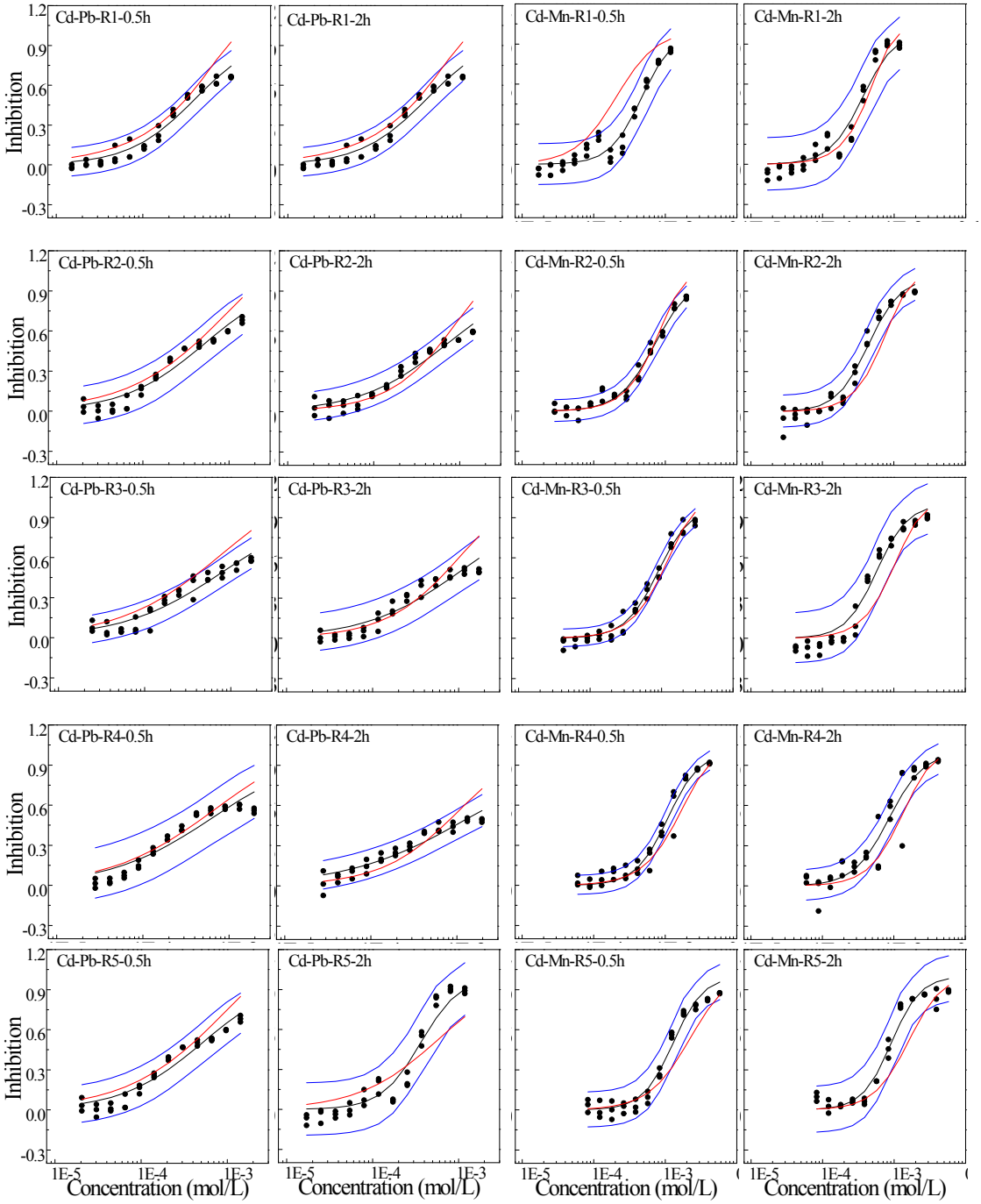

Fig. S4a The concentration-response relationship of ten rays in Cd-Pb and Cd-Mn binary mixture systems towards Q67 in two exposure times of 0.25 and 2 *h* where the black scatters refer to the experimental points, blue lines to the 95% confidential intervals, black solid lines to the fitted CRCs, and red solid line to the CRCs predicted by CA.

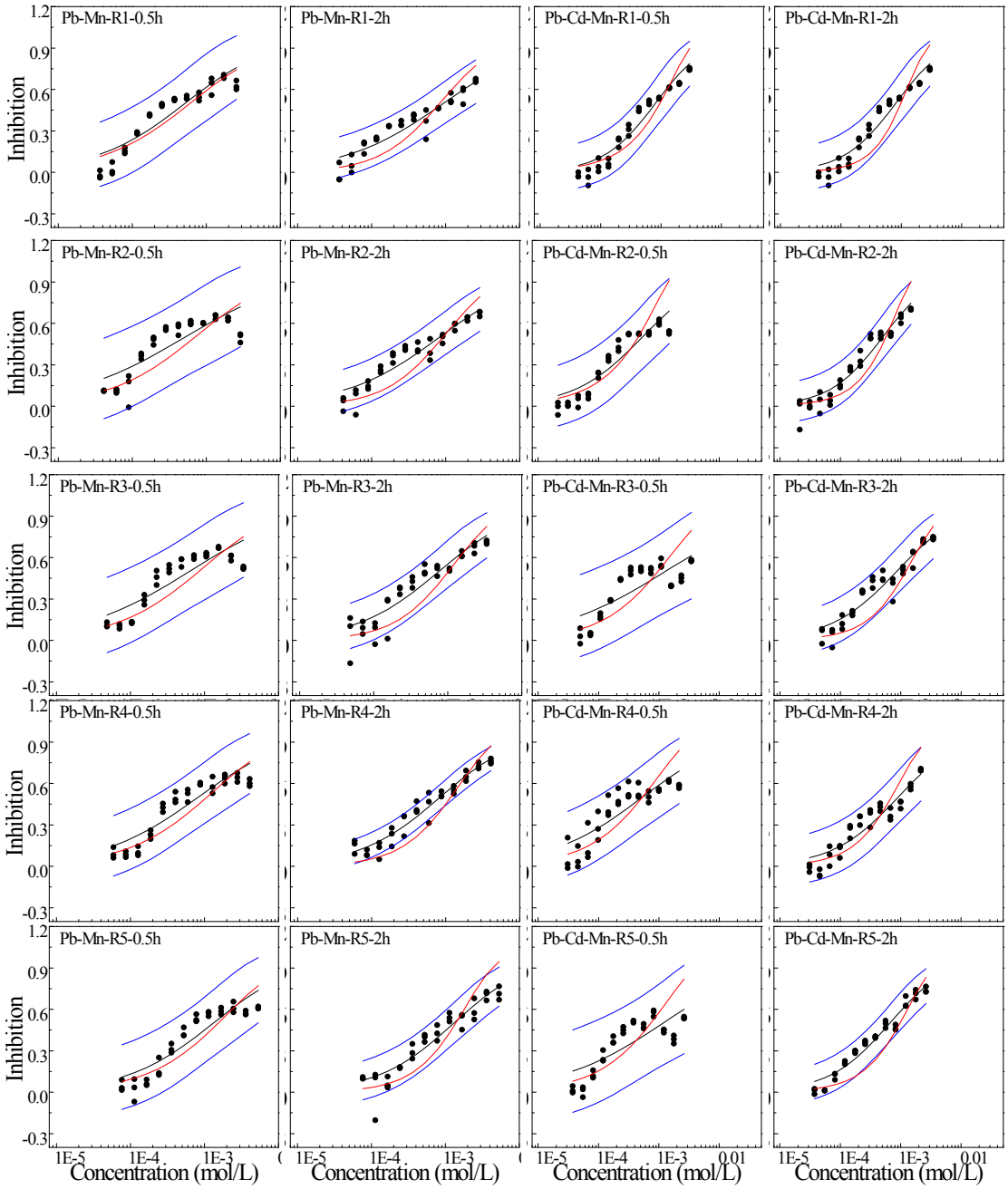

Fig. S4b The concentration-response relationship of ten rays in Pb-Mn binary and Pb-Cd-Mn ternary mixture systems towards Q67 in two exposure times of 0.25 and 2 h where the black scatters refer to the experimental points, blue lines to the 95% confidential intervals, black solid lines to the fitted CRCs, and red solid line to the CRCs predicted by CA.