The HK-2 cells were treated with different concentrations of drugs (cisplatin: 2, 4 μM; cyclosporin: 4, 8 μM; aristolochic acid I: 8, 16 μM; gentamicin: 4, 8 mM) for 6, 24 and 48 h. While no significant difference of albumin, α1-MG, calbindin, Collagen IV, osteoactivin and renin were found in drug treatment groups compared to the vehicle control group (Fig. S1 and S2).

The HK-2 cells were treated with 22 compounds in order to determine the predictive performance of endpoints. The growth inhibition of HK-2 cells induced by 22 compounds was shown in Table. S1. The highest protein levels of KIM-1, osteopontin, clusterin, CysC, NGAL, GSTπ, TIMP-1, LDH and GGT, the lowest level of cell viability were determined (Fig. S3, S4 and S5).

Table. S1 The cell viability (%) of HK-2 cells induced by 22 compounds.

No.	Compound	Concentration (μM)					
		0.01	0.1	1	10	100	1000
1	Cisplatin	99.4	94.3	**90.5**	**50.3**	**18.3**	5.9
2	Cyclosporin	98.2	97.2	**95.3**	**96.4**	**67.4**	15.3
3	Aristolochic acid I	99.3	98.1	**97.2**	**86.1**	**79.3**	30.7
4	Triptolide	**96.3**	**80.4**	**60.3**	40.2	25.2	10.2
5	Rifampicin	**95.2**	**83.4**	**65.2**	46.2	20.3	9.4
6	5-Fluorouracil	**93.2**	**84.9**	**59.3**	48.5	29.3	12.7
8	Tetracycline	**92.1**	**78.3**	**52.8**	36.6	20.1	8.2
9	Ifosfamide	98.4	97.3	**95.3**	**85.4**	**60.3**	40.3
10	Potassium dichromate	**93.7**	**81.9**	**64.8**	50.2	32.1	12.4
11	Tobramycin	99.4	94.8	**96.5**	**88.2**	**65.2**	46.2
12	Cadmium(II) chloride	**95.8**	**86.4**	**69.3**	30.2	18.5	5.8
13	Ibuprofen	99.8	97.2	**96.3**	**86.2**	**67.1**	34.9
14	Furosemide	99.7	97.0	**95.8**	**83.8**	**62.7**	30.5
15	Cyclophosphamide	99.1	98.4	97.1	**97.3**	**88.2**	**68.3**
16	Azathioprine	99.8	98.3	**97.4**	**90.3**	**52.4**	21.2
18	Vancomycin	99.9	98.4	96.5	**94.3**	**86.2**	**67.3**
19	Ciprofloxacin	99.8	99.2	97.8	**95.7**	**85.8**	**64.6**
20	Doxorubicin	**95.6**	**96.8**	**64.7**	40.2	20.7	10.5
21	Levodopa	99.6	97.4	95.2	**94.2**	**90.9**	**87.2**
22	Acarbose	99.8	99.1	98.3	**96.1**	**92.1**	**86.6**

Table. S1 The cell viability (%) of HK-2 cells induced by 22 compounds (continued).

No.	Compound	Concentration (μM)					
		1	10	100	1000	10000	20000
7	Gentamicin	99.1	98.4	97.1	**95.3**	**75.9**	**60.1**
17	Acetaminophen	99.3	97.1	96.3	**92.1**	**81.1**	**54.3**

Note: The concentrations of the bold cell viability were chosen for the predictive performance of biomarkers.

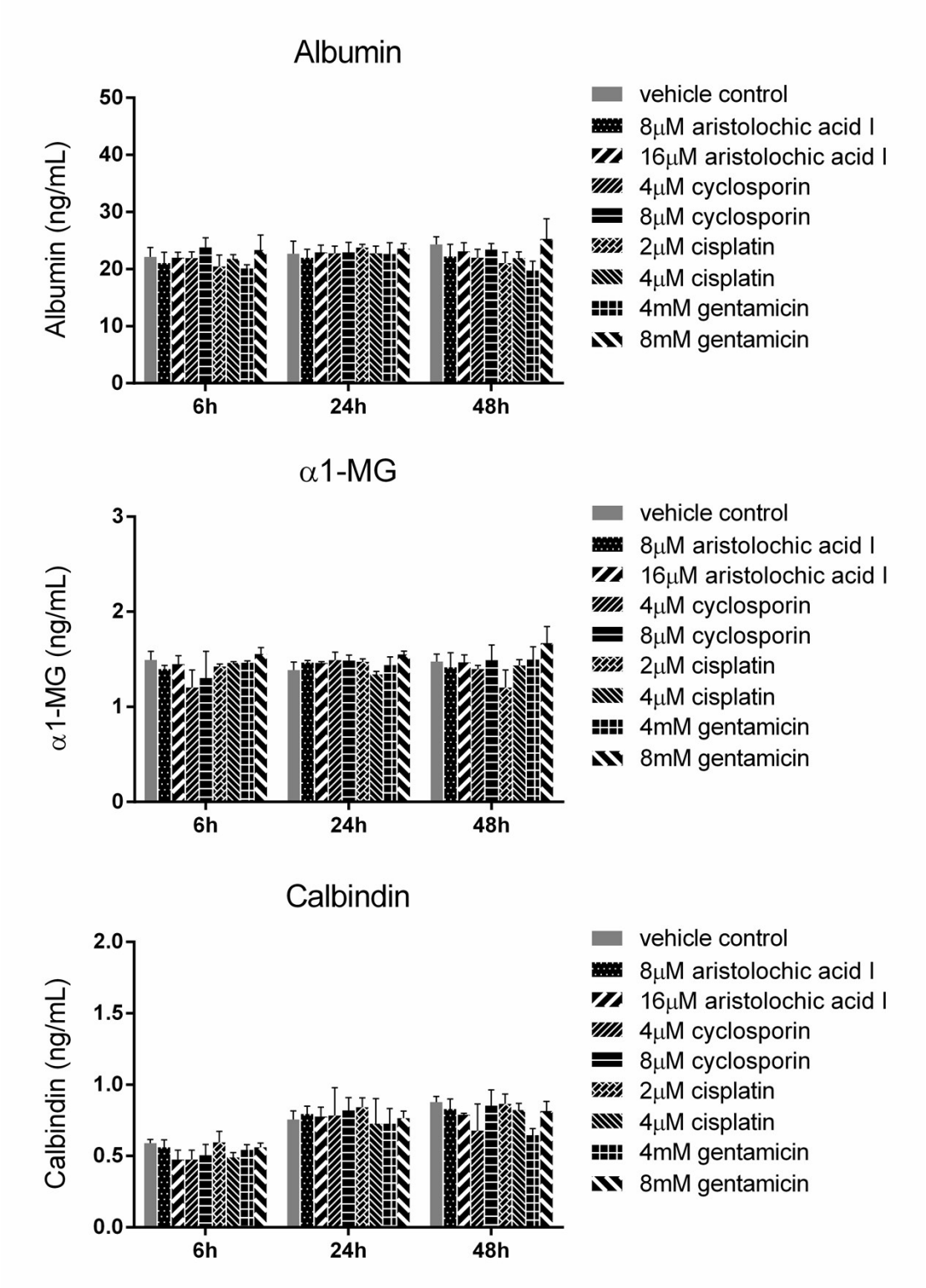

Figure S1. The protein levels of albumin, α1-MG and calbindin in HK-2 cell treated with cisplatin, cyclosporin, aristolochic acid I and gentamicin at 6, 24 and 48 h (mean ± SD, n=3). *Significantly different from the vehicle control value ($p < 0.05$).

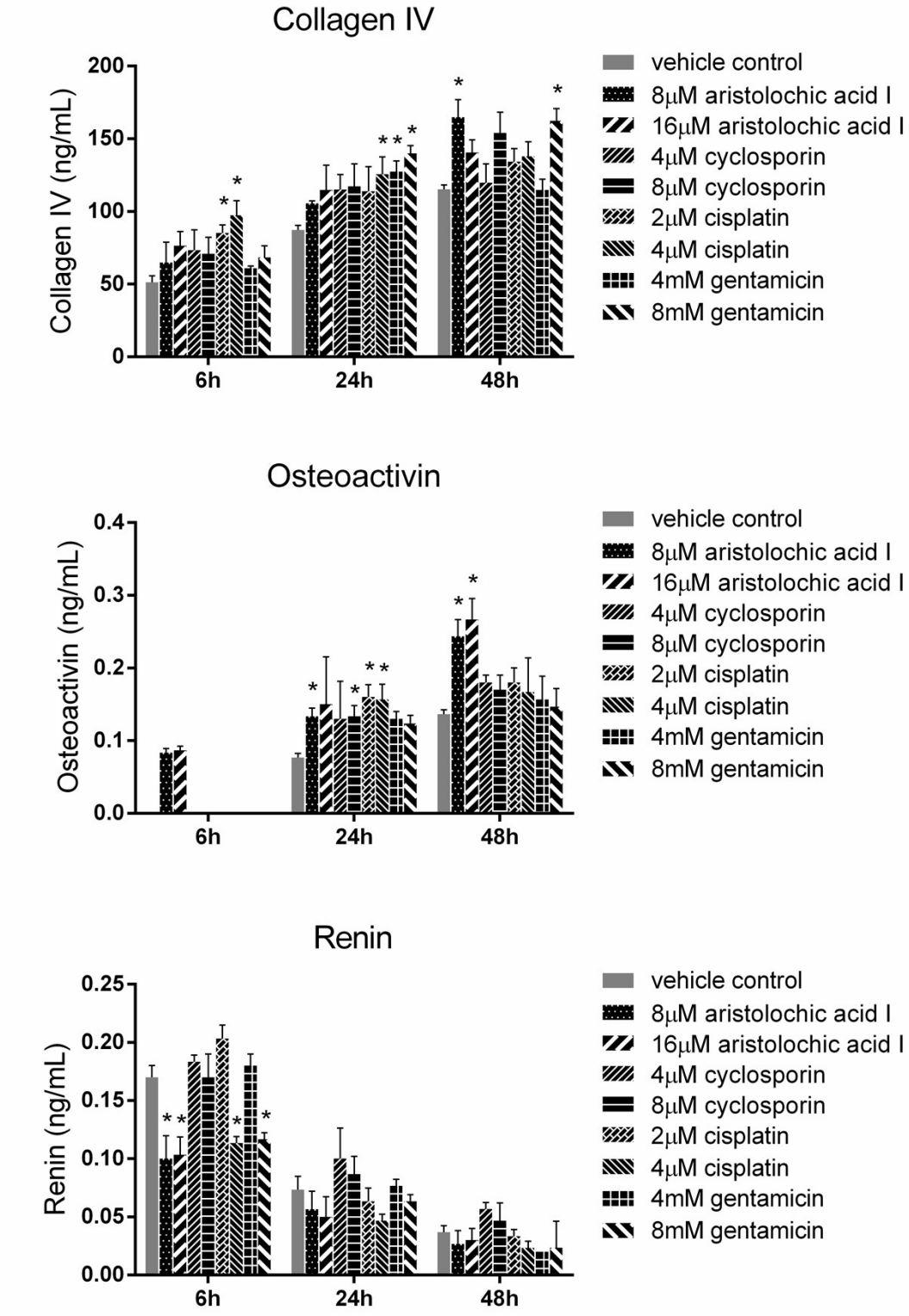

Figure S2. The protein levels of Collagen IV, osteoactivin and renin in HK-2 cell treated with cisplatin, cyclosporin, aristolochic acid I and gentamicin at 6, 24 and 48 h (mean ± SD, n=3). *Significantly different from the vehicle control value ($p < 0.05$).

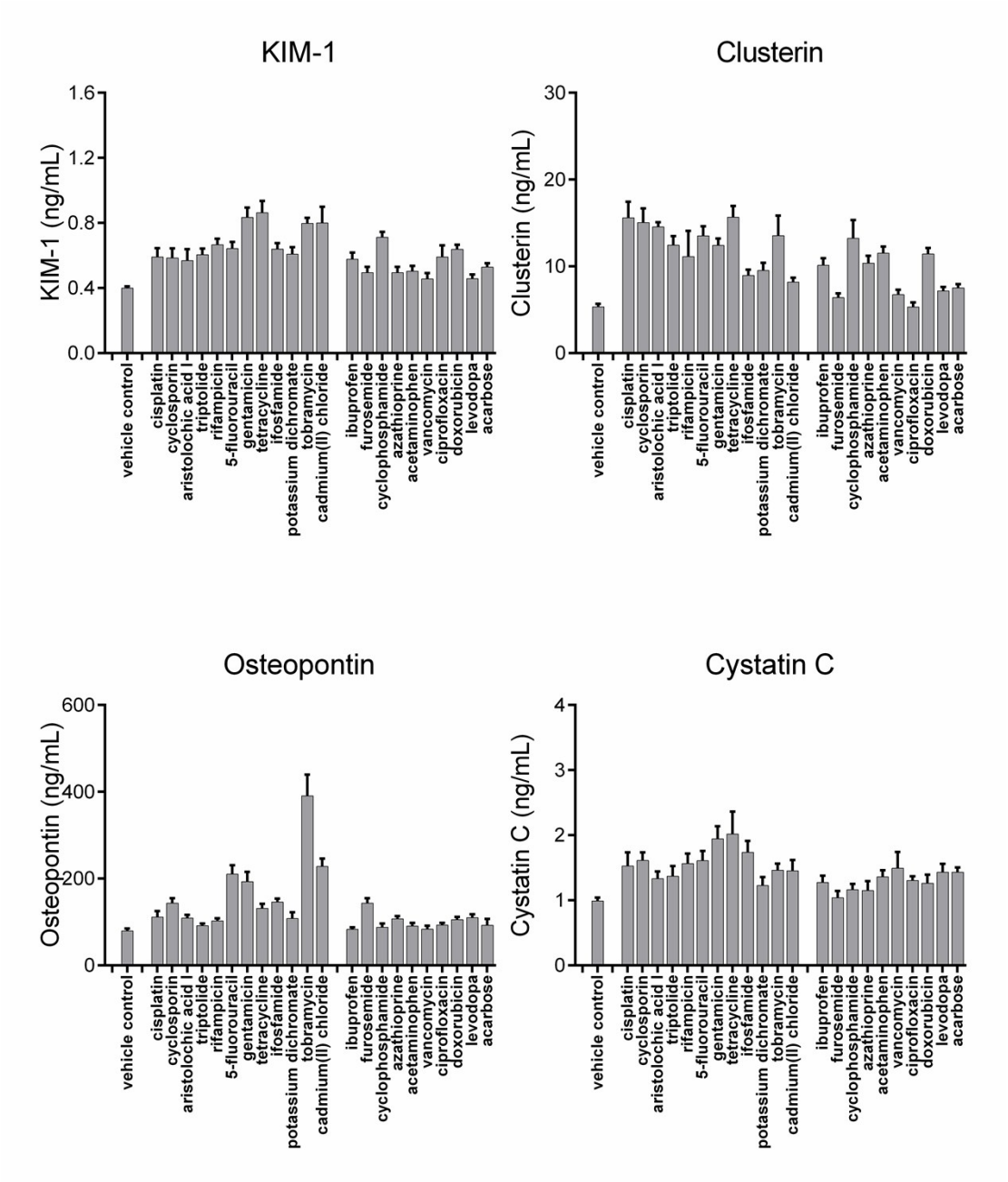

Figure S3. The highest protein levels of KIM-1, osteopontin, clusterin and CysC in the HK-2 cells treated with 22 compounds at 24 h (mean ± SD, n=3).

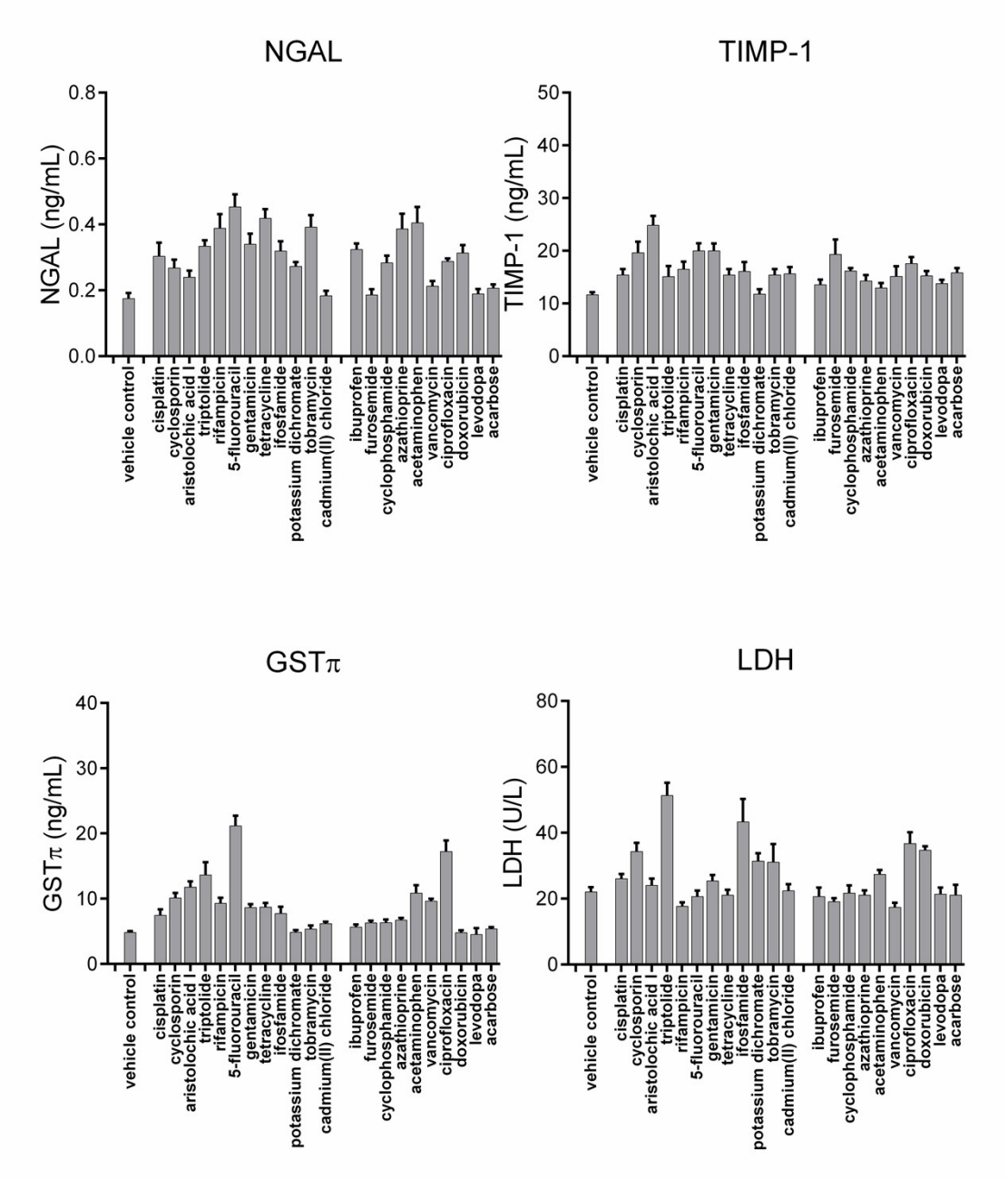

Figure S4. The highest protein levels of NGAL, TIMP-1, GSTπ and LDH in the HK-2 cells treated with 22 compounds at 24 h (mean ± SD, n=3).

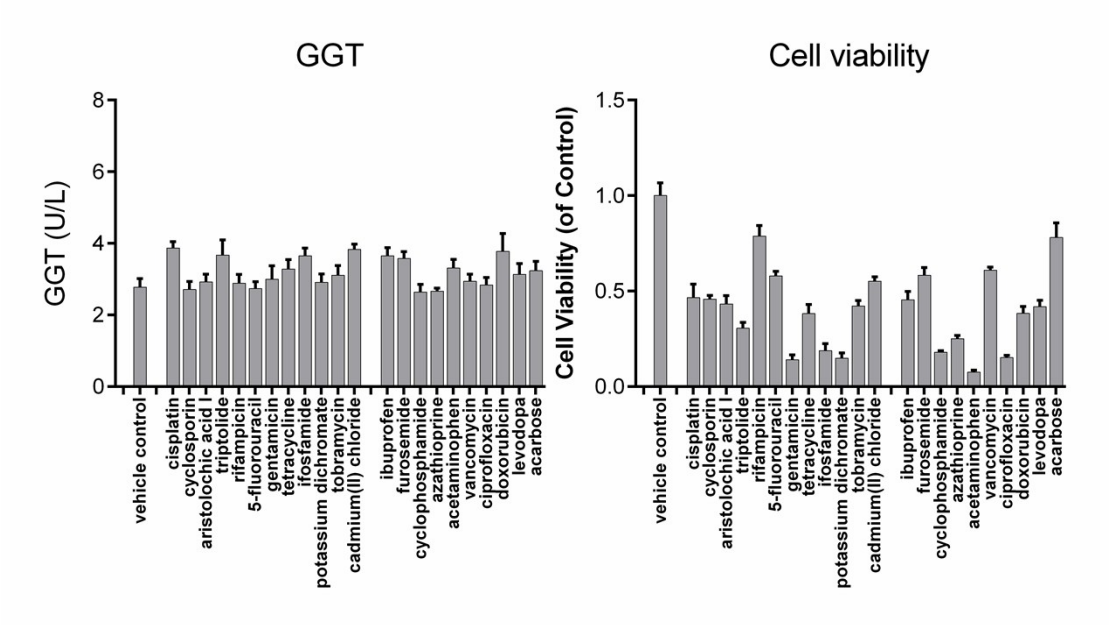

Figure S5. The highest protein levels of GGT and the lowest level of cell viability in the HK-2 cells treated with 22 compounds at 24 h (mean ± SD, n=3).