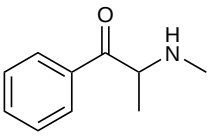
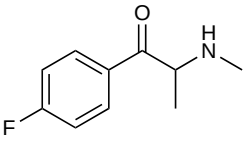
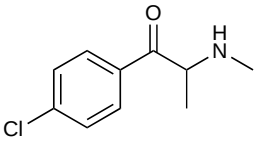
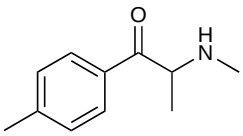
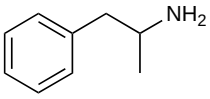
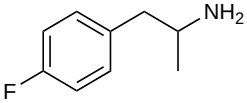
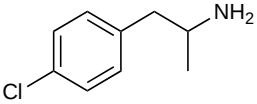
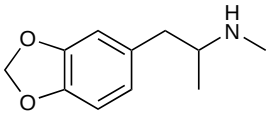
MC	**4-FMC**	**4-CMC**	**4-MMC**
			
Amphetamine	**4-FA**	**PCA**	**MDMA**
			

Figure S1. Chemical structures of amphetamine and methcathinone derivatives.

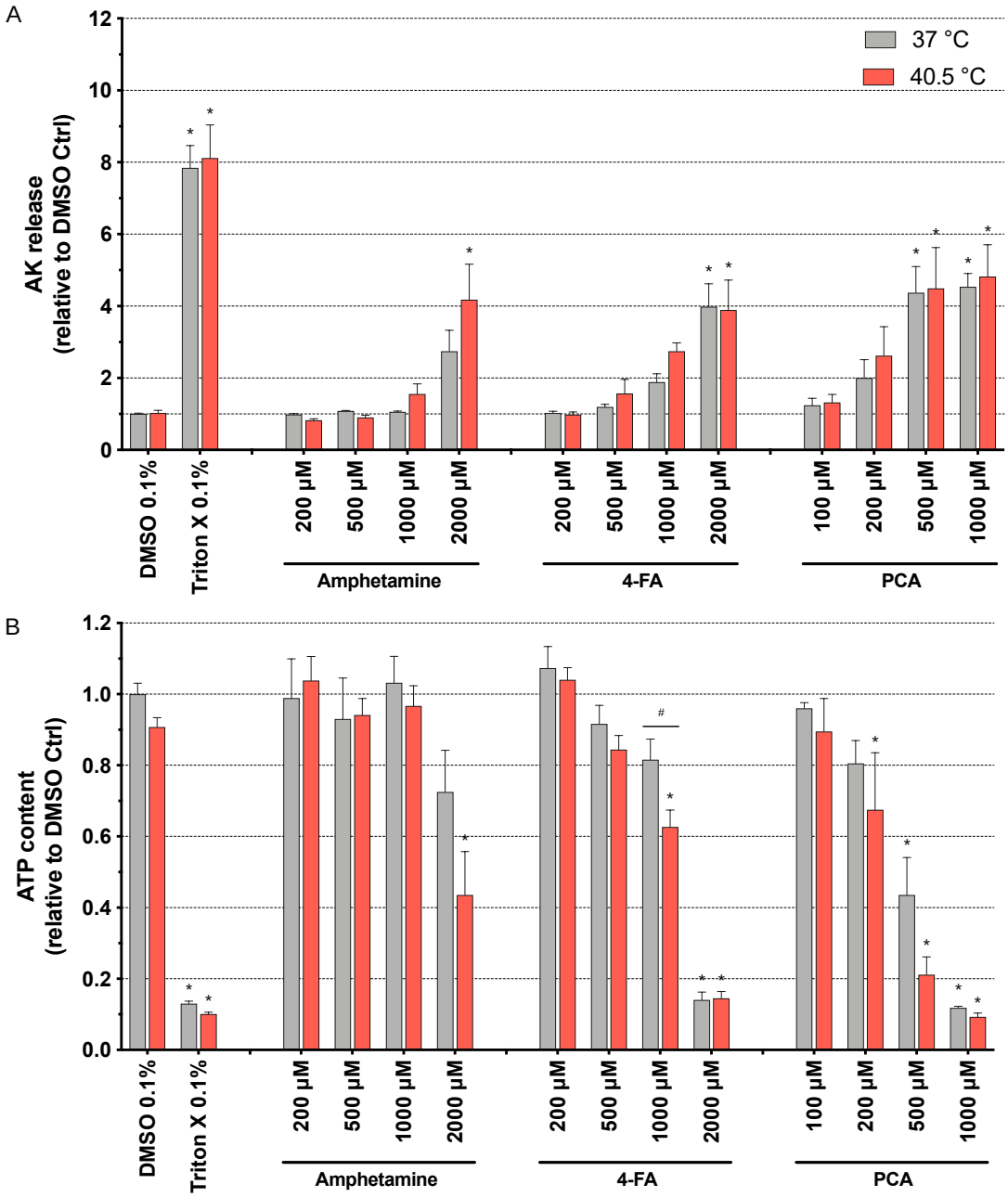


Figure S2. (**A**) Plasma membrane integrity and (**B**) intracellular ATP content assessed in SH-SY5Y cells after 24 h of exposure at 37 °C and 40.5 °C to amphetamine, 4-FA (200–2000 µM), and PCA (100–1000 µM). DMSO and Triton X were used as negative and positive controls, respectively. Data are expressed relative to DMSO control incubations as mean ± SEM of eight independent experiments run in quadruplicate. Statistical comparisons were performed with one-way ANOVA followed by *t*-tests (*$P \leq 0.05$ *versus* control at the same temperature; $^{\#}P \leq 0.05$ *versus* the same concentration at different temperature).

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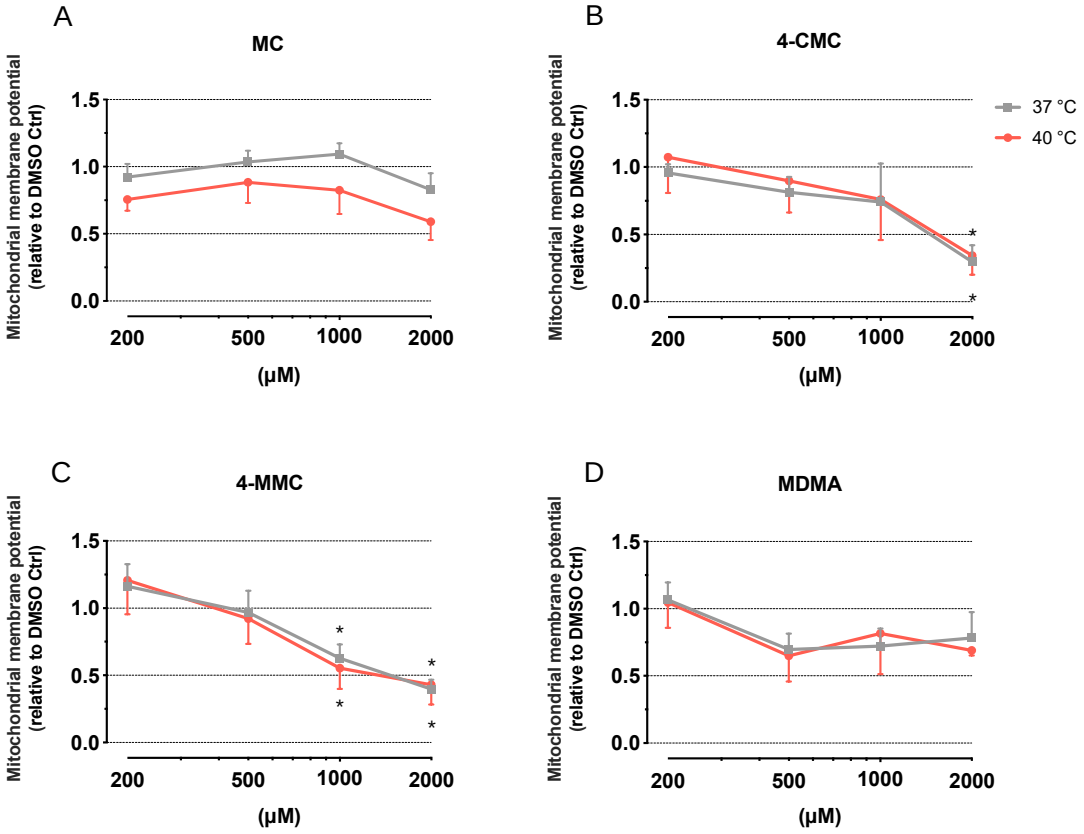

Figure S3. Mitochondrial membrane potential in SH-SY5Y cells. The mitochondrial membrane potential was measured after 24 h of exposure at 37 °C or 40.5 °C to MC, 4-CMC, 4-MMC, and MDMA (200–2000 µM). Data are expressed relative to DMSO control cells as mean ± SEM of three independent experiments run in quadruplicate. Statistical comparisons were performed with one-way ANOVA followed by *t*-test (*$P \leq 0.05$ *versus* control at the same temperature).

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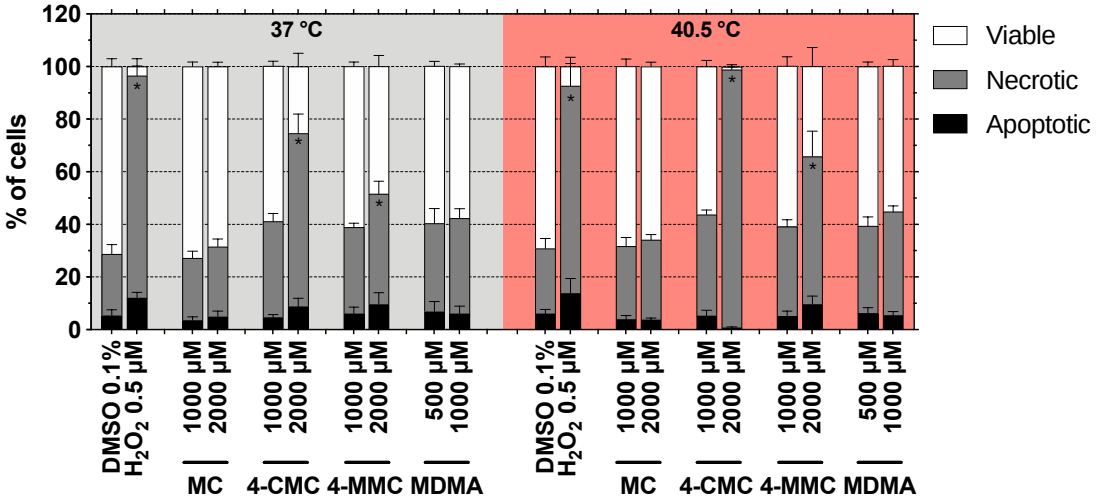

Figure S4. Percentage of viable, necrotic and apoptotic cells after 24 h of exposure to test compounds. SH-SY5Y cells were exposed to MC, 4-CMC, 4-MMC (1000 µM and 2000 µM), and MDMA (500 µM and 1000 µM) for 24 h at 37 °C or 40.5 °C. DMSO and H_2O_2 were used as negative and positive controls, respectively. Data are expressed as mean ± SEM of six independent experiments. Statistical comparisons were performed with one-way ANOVA followed by *t*-tests (**P* ≤0.05 *versus* control at the same temperature).

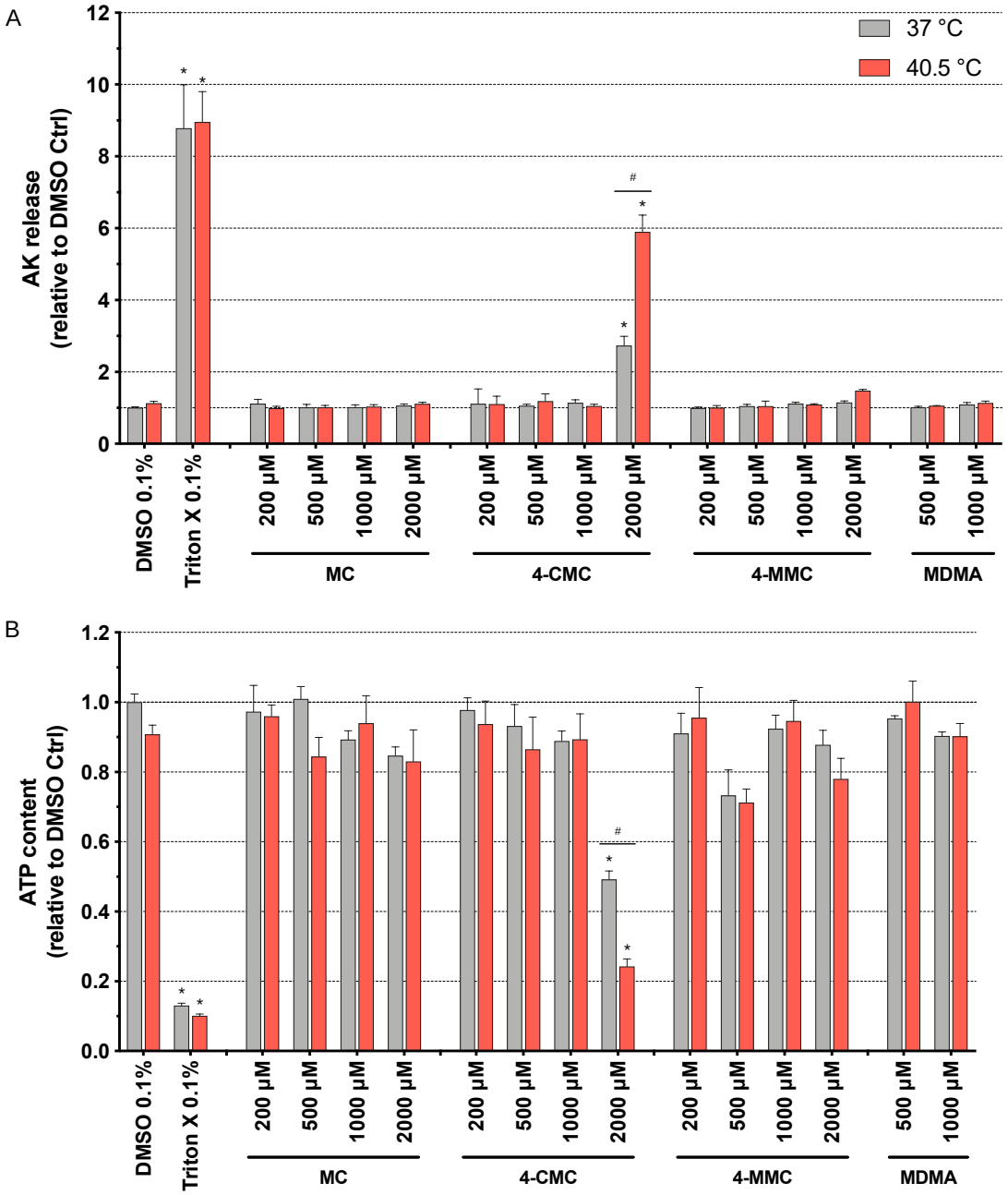

Figure S5. (**A**) Plasma membrane integrity and (**B**) intracellular ATP content assessed in SH-SY5Y cells after 6 h of exposure at 37 °C and 40.5 C to MC, 4-CMC, 4-MMC (200–2000 µM), and MDMA (500 µM and 1000 µM). DMSO and Triton X were used as negative and positive controls, respectively. Data are expressed relative to DMSO control incubations as mean ± SEM of eight independent experiments run in quadruplicate. Statistical comparisons were performed with one-way ANOVA followed by *t*-tests (**P* ≤0.05 *versus* control at the same temperature; #*P* ≤0.05 *versus* the same concentration at different temperature).

Table S1. Quantification (IC_{50}) of membrane toxicity (MT) and ATP depletion (ATP) by methcathinones at 37 °C and 40.5 °C in SH-SY5Y cells.

	37°C			**40.5°C**		
	MC (mM)	4-CMC (mM)	4-MMC (mM)	MC (mM)	4-CMC (mM)	4-MMC (mM)
MT IC_{50}	>2	>2	>2	>2	1.94	1.57
ATP IC_{50}	>2	1.30	>2	>2	0.77	0.86