Electronic Supplementary Material (ESI) for RSC Medicinal Chemistry.

Integrating a Quinone Substructure into Histone Deacetylase Inhibitors to Cope Alzheimer's diseases and Cancer

Melissa Guardigni,[1Δ] Giulia Greco,[2Δ] Eleonora Poeta,[3Δ] Alan Santini,[1] Elisa Tassinari,[1] Christian Bergamini,[3] Chiara Zalambani,[3] Angela De Simone,[4] Vincenza Andrisano,[1] Elisa Uliassi,[3] Barbara Monti,[3] Maria Laura Bolognesi[3*] Carmela Fimognari,[1] Andrea Milelli[1*]

[1] Department for Life Quality Studies, Alma Mater Studiorum-University of Bologna, 47921 Rimini, Italy.

[2] Department of Chemistry "Giacomo Ciamician", Alma Mater Studiorum-University of Bologna, 40129, Bologna, Italy.

[3] Department of Pharmacy and Biotechnology, University of Bologna, 40126 Bologna, Italy.

[4] Department of Drug Science and Technology, University of Turin, 10125 Turin, Italy.

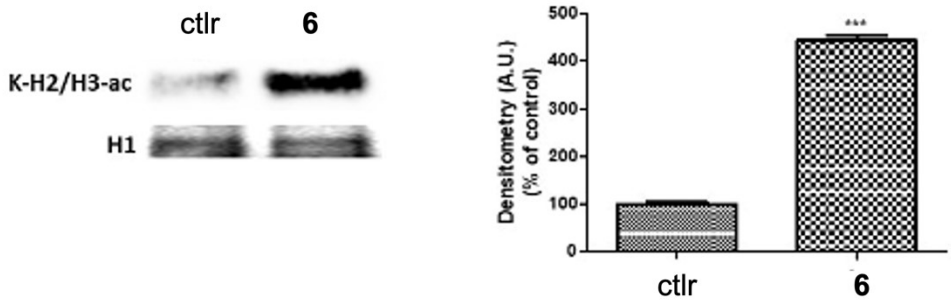


Figure S1. Western blot analysis (left panel) and densitometric quantification (right panel) of lysine (K)-acetylated H2 and H3 hystones extracted from SH-SY5Y cells treated with 5µM of compound **6** or vehicle for 6 hours.

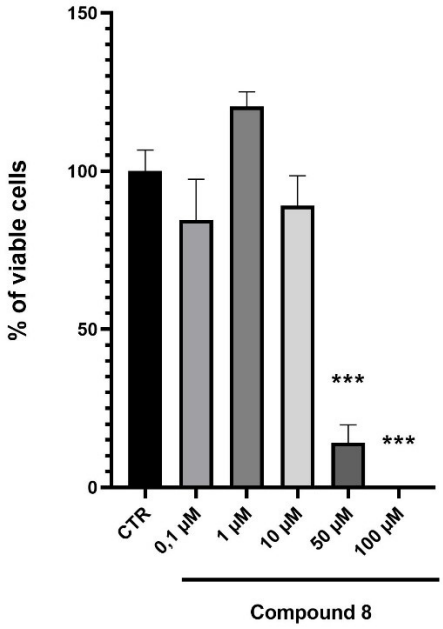


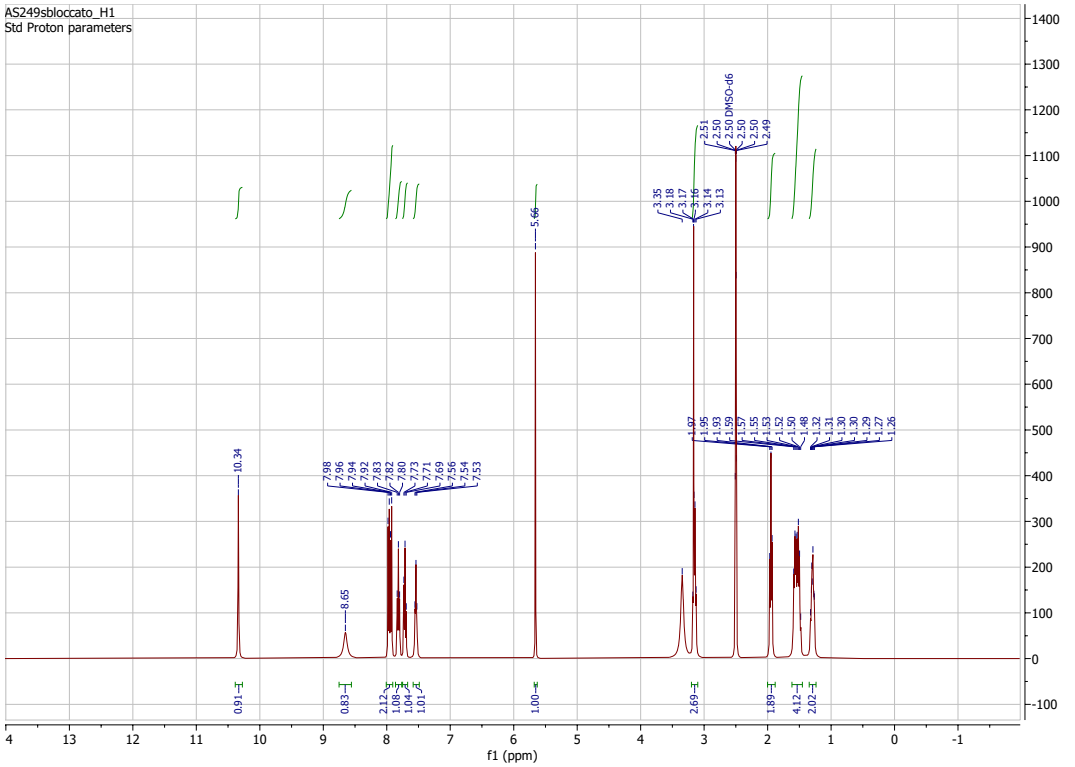
Figure S2. Viability of HepG2 cells after 24 h of incubation with different concentrations of compound **8** assessed by MTT assay (n = 4). Data are expressed as percentage of vehicle-treated viable cells. *** $p \leq 0.001$ (n=4).

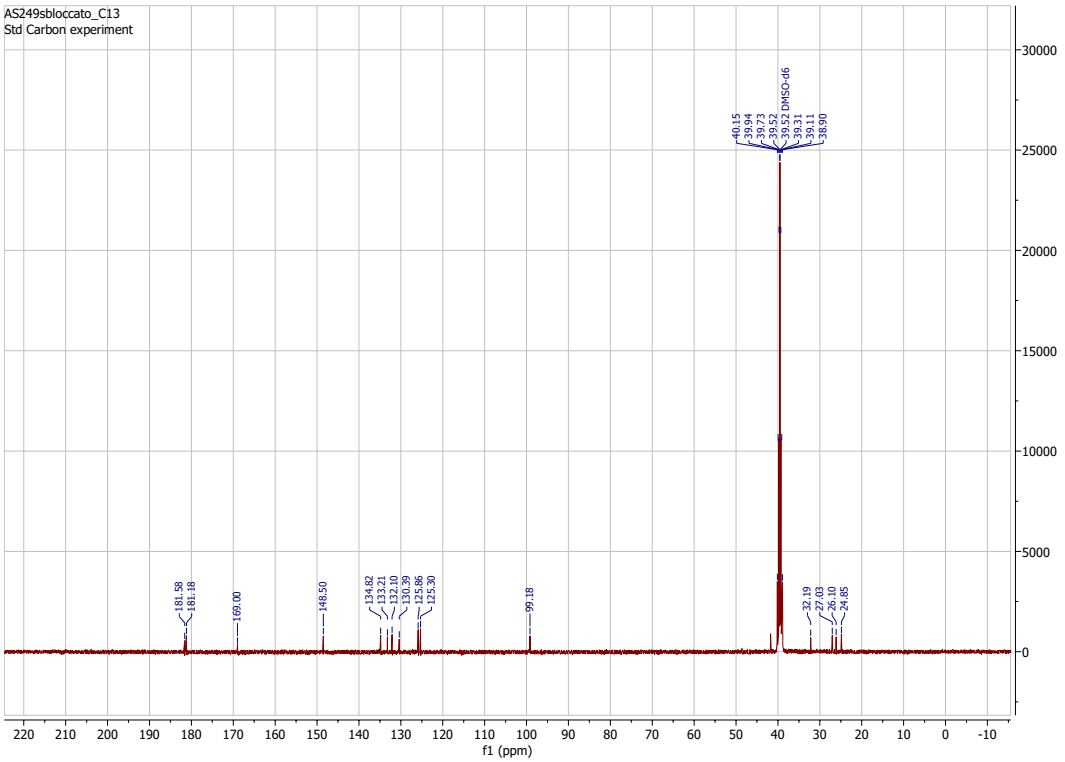
PAINS behavior assessment

We are aware that **1-8** carry a quinone structure, which is recognized as pan assay interference compounds (PAINS). However, different cytotoxicity profiles with SAR were delineated within **1-8**. Moreover, different anti/pro-oxidant abilities (compounds **6** and **8**) were shown. Furthermore, the two more active compounds have menadione, where a methyl group is in the α-position relative to the side substituent and it is not subject to attack by nucleophilic groups of proteins. This seems to suggest that the activity of the reported series is not caused the by pan assay interference.

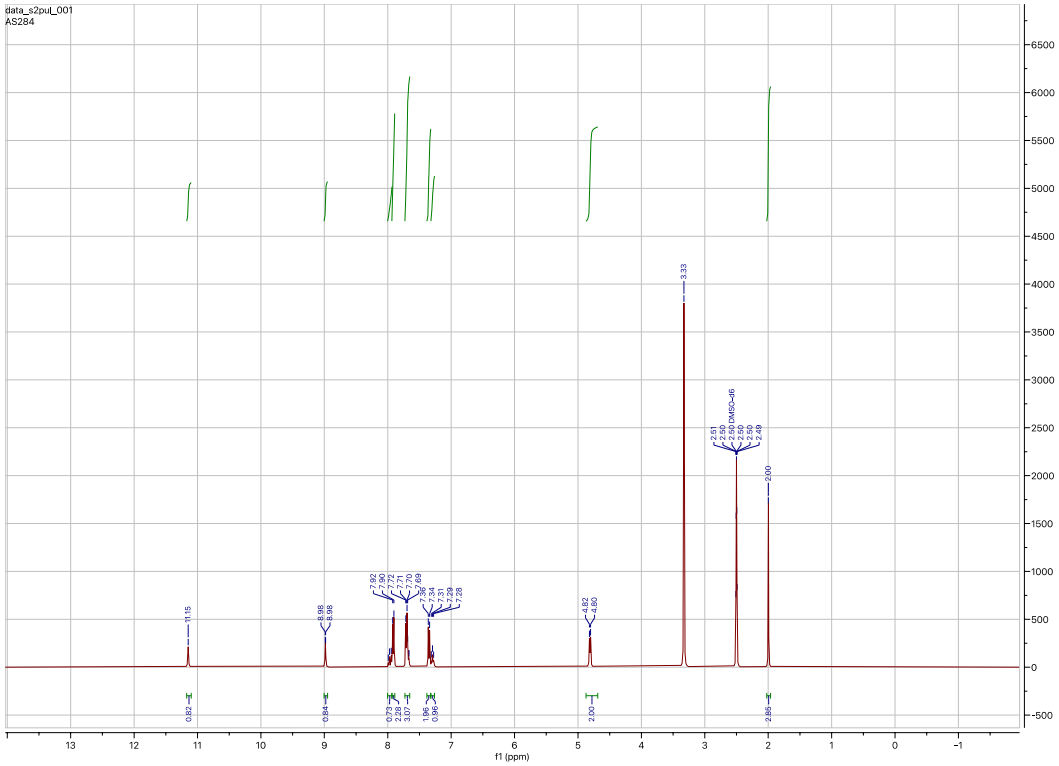
Representative copies of ^{1}H-NMR and ^{13}C-NMR spectra.

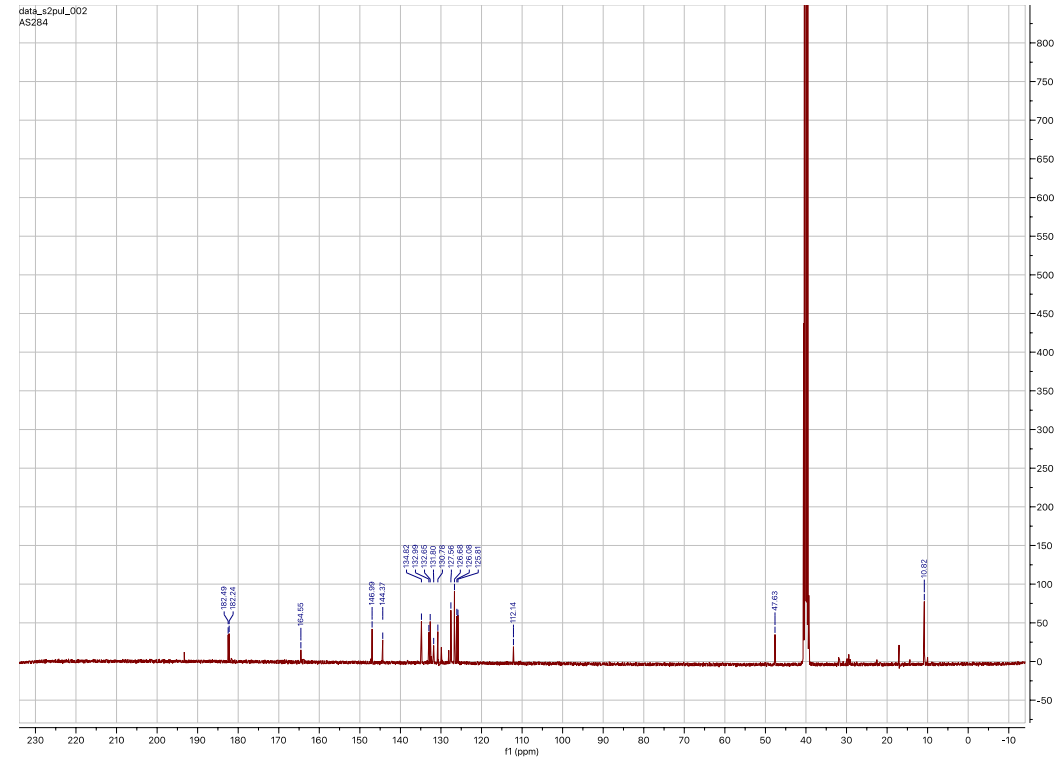
Compound 1. ^{1}H-NMR (400 MHz) and ^{13}C-NMR (100 MHz) in DMSO-d.



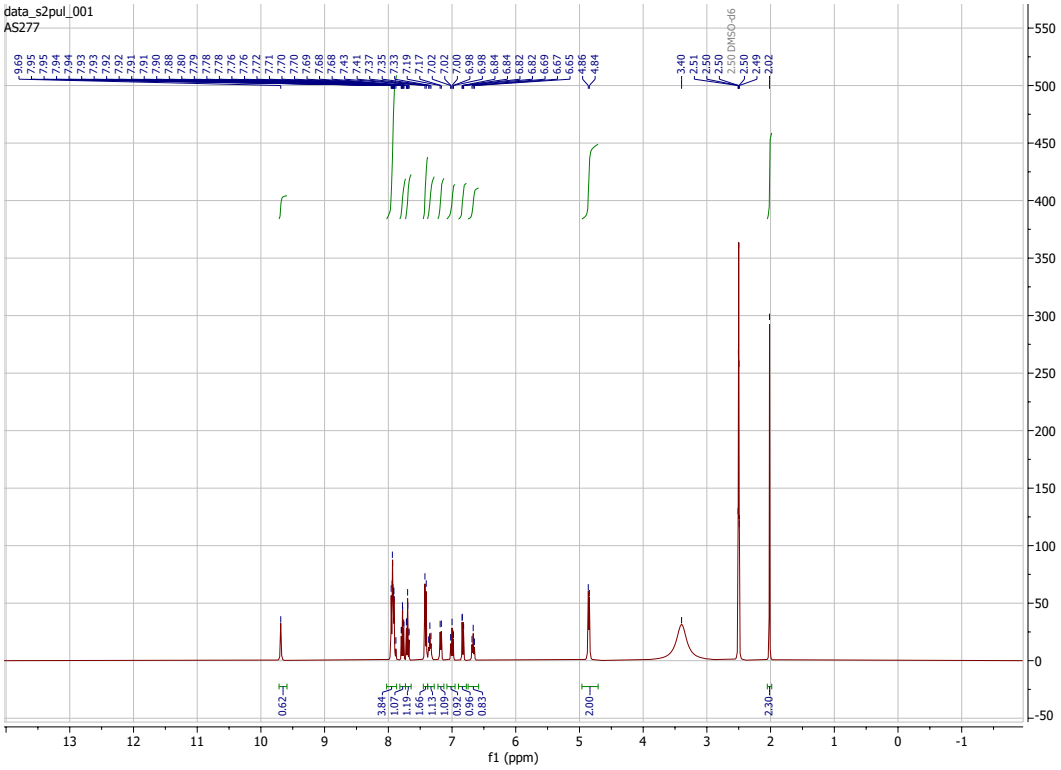


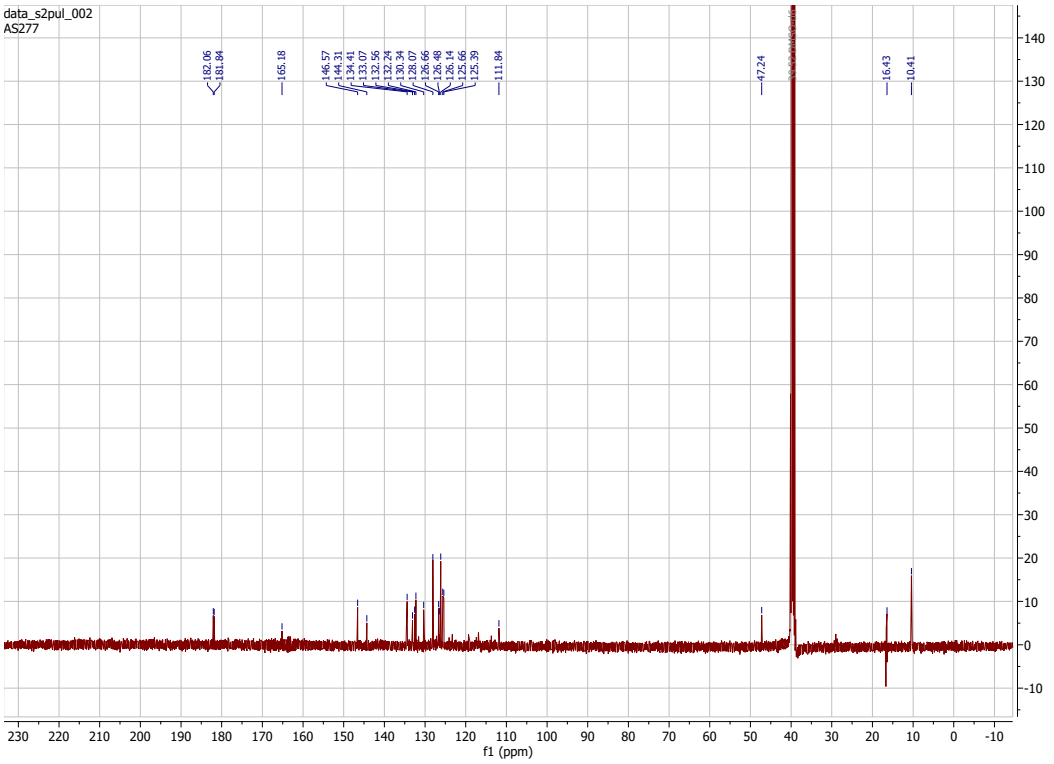
Compound 4. ^{1}H-NMR (400 MHz) and ^{13}C-NMR (100 MHz) in DMSO-d.





Compound 6. ^{1}H-NMR (400 MHz) and ^{13}C-NMR (100 MHz) in DMSO-d.





Compound 8. ^{1}H-NMR (400 MHz) and ^{13}C-NMR (100 MHz) in DMSO-d.