Supplementary Material

Synthesis, *In Vitro*, and *In Silico* Analysis of the Antioxidative Activity of Dapsone Imine Derivatives †

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DDS and its derivatives were subjected to their anticancer activity prediction through the CLC-pred server ((http://www.way2drug.com/Cell-line/index.php) [44]. For a given compound, this tool predicts the spectrum of cytotoxicity based on the structure-cytotoxicity relationship analysis for more than 50 000 active compounds on 278 human cancer cell lines. As can be observed in Table S1, the result is given as probability of activity (Pa) and probability of inactivity (Pi). For a compound, the probability to be active is considered when Pa > Pi. Otherwise, when Pa values > 0.5 a high probability to have anticarcinogenic activity is considered.

Table S1. *In silico* prediction of cytotoxicity for tumor cell lines.

Compound	Cell Line	Cell Line Full Name	Pa*	Pi**
DDS	A2780	Ovarian Carcinoma	0.625	0.005
1	LoVo	Colon adenocarcinoma	0.681	0.004
2	LoVo	Colon adenocarcinoma	0.473	0.006
3	LoVo	Colon adenocarcinoma	0.421	0.008
4	LoVo	Colon adenocarcinoma	0.539	0.005
5	LoVo	Colon adenocarcinoma	0.451	0.007
6	LoVo	Colon adenocarcinoma	0.572	0.005
7	LoVo	Colon adenocarcinoma	0.434	0.008
8	LoVo	Colon adenocarcinoma	0.534	0.005
9	LoVo	Colon adenocarcinoma	0.477	0.006
10	YAPC	Pancreatic carcinoma	0.391	0.112

*Pa (0 – 1) represents the bioactivity probability of a given compound based on structural similarity respect to an active molecule database. **Pi (0 – 1) represents the bioinactivity probability of a given compound based on structural similarity respect to an active molecule database.

In silico acute-oral toxicity

The acute-oral toxicity of the synthetized compounds was evaluated based on the Environmental Protection Agency (EPA) and Globally Harmonized System (GHS) categorization, which have been well accepted for the evaluation of the organic compound toxicity by considering the 50% Lethal Dose (LD_{50}) values. The prediction was performed by using the software SiliS-PTOXRA (http://tomocomd.com/apps/ptoxra) developed by the Marrero group [45]. As can be observed in Table S2, only one compound (**4**) was found to be out of the applicability domain and consequently its prediction was not determined. All other compounds were satisfactorily evaluated, and the results suggest that all of them are in class III of the EPA category, and class IV and V in the GHS category, suggesting that these compounds have, in general, low toxicity. This categorization was obtained for compounds with $300 < LD_{50} < 5000$ mol/kg.

Table S2. Classification of the compounds in terms of the EPA and GSH categories for the evaluation of acute oral toxicity.

		Acute-Oral Toxicity	
Compound	Applicability domain*	EPA category	GHS category
1	IN	III	V
2	IN	III	V
3	IN	III	IV
4	OUT	---	---
5	IN	III	IV
6	IN	III	V
7	IN	III	V
8	IN	III	IV
9	IN	III	V
10	IN	III	IV
DDS	IN	III	IV

*The labels "IN" and "OUT are used for those cases when the structures fall or do not fall within the model applicability domain, used for the prediction.