Chemical reactivity of paraquat with the previously validated antidote, sodium salicylate

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Sodium salicylate (NaSAL) has been showing to be a promising antidote for the treatment of paraquat (PQ) poisonings. The modulation of the pro-oxidant and pro-inflammatory pathways, as well as the anti-thrombogenic properties of NaSAL are probably essential features for the healing effects provided by this drug. Nevertheless, a possible direct chemical reactivity between PQ and NaSAL is also a putative pathway to be considered, this hypothesis being the objective of the present study. In accordance, it is shown, for the first time that PQ and NaSAL react immediately in aqueous medium and within 2–3 min in the solid state. Photographs and scanning electron photomicrographs indicated that a new chemical entity is formed when both compounds are mixed. This assumption was corroborated by the evaluation of the melting point, and through several analytical techniques, namely ultraviolet/visible spectroscopy, nuclear magnetic resonance spectroscopy, gas chromatography/mass spectrometry/mass spectrometry (GC/MS/MS), liquid chromatography/electrospray ionization/mass spectrometry/mass spectrometry (LC/ESI/MS/MS) and infrared spectroscopy, which revealed that stable charge-transfer complexes are formed when PQ is mixed with NaSAL. LC/ESI/MS/MS allowed obtaining the stoichiometry of the charge-transfer complexes. In order to increase resolution, single value decomposition, acting as a filter, showed that the charge-transfer complexes with m/z 483, 643 and 803 correspond to the pseudo-molecular ions, respectively 1:2, 1:3 and 1:4 (PQ:NaSAL). In conclusion, these results provided a new and important mechanism of action of NaSAL against the toxicity mediated by PQ.

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