

Potential of mechanochemistry in the preparation of novel multicomponent supramolecular systems containing praziquantel

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Praziquantel (**PZQ**), a broad-spectrum therapeutic drug used to treat schistosomiasis is included in the WHO Model List of Essential Medicines [1,2]. Its high efficacy, coupled with the risk of drug resistance from long-term use, fully justifies the need for research on this substance. 5-Hydroxyisophthalic acid (**5HIP**), benzene-1,3,5-tricarboxylic acid (**TRI**) and (*E,E*)-muconic (**MUC**) acid were used for cocrystallization experiments with **PZQ** (Fig. 1). The potential of mechanochemistry was applied to develop repeatable syntheses, leading to the formation of suitable crystalline phases. The use of these acids resulted in the identification and characterization of eight new multicomponent systems, including three cocrystals and five cocrystal solvates. Growing single crystals enabled X-ray structural analysis, focusing on the formation of specific supramolecular synthons responsible for the arrangement of molecules in the crystal. Among the identified phases, two of them are hydrogen-bonded organic frameworks (HOFs) composed of **PZQ** and **5HIP** in a 1:4 stoichiometric ratio, in which the **5HIP** acid molecules are arranged in layers, forming hexagonal channels in which **PZQ** and solvent molecules are located.

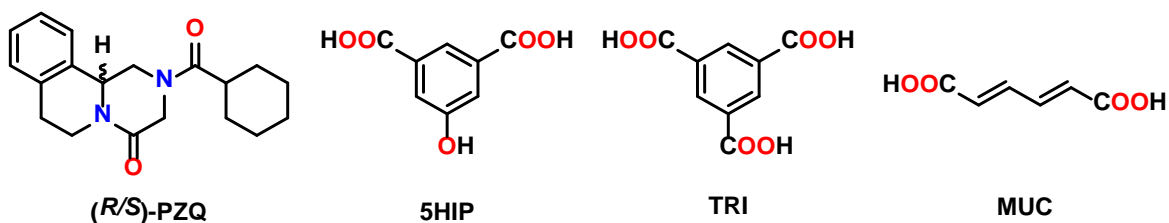


Figure 1. Chemical structure of (*R/S*)-**PZQ** and coformers used (5-hydroxyisophthalic acid, **5HIP**, benzene-1,3,5-tricarboxylic acid, **TRI**, (*E,E*)-muconic acid, **MUC**).

Simultaneous thermal analysis indicated high thermal stability of the studied systems compared to pure **PZQ**, particularly for obtained cocrystal solvates. UV-Vis spectroscopic studies demonstrated the effect of cocrystallization on the solubility of **PZQ**.

This study demonstrates the essence of mechanochemistry as an effective way to obtain multicomponent supramolecular systems selectively, in a short time and with minimal use of solvents. Moreover, the additional characterization of the studied **PZQ** cocrystals shows the influence of cocrystallization on important physicochemical properties, such as solubility and thermal stability.

[1] W. H. O. = O. mondiale de la Santé, *Weekly Epidemiological Record = Relevé épidémiologique hebdomadaire* (2020) **95**, 629–640.

[2] WHO Model Lists of Essential Medicines, <https://www.who.int/groups/expert-committee-on-selection-and-use-of-essential-medicines/essential-medicines-lists> (accessed May 7, 2025).

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