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Experimental and computational investigation of polymorphs and solvates of probucol.

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In this work, we present results on the investigation of the different polymorphs and solvates of the antihyperlipidemic drug probucol (PROB), Figure 1, resulting from crystallization in various solvents. While the PROB intermolecular interactions by hydrogen bonding involving the hydroxyl groups are hindered by the adjacent *t*-butyl fragments, its molecular flexibility is conferred by the sulfanyl chain. Two crystal structures of PROB were already described in literature [1], which are conformational and packing polymorphs.

Using different crystallization conditions, including different solvents, two new PROB polymorphs were identified, as well as five new solvates. Their thermal behaviors were investigated and their crystal structures solved. The kinetics of crystallization in selected solvents and experimental conditions was also accessed.

The conformational landscape of the compound was explored by DFT calculations in dielectric media. Molecular dynamics studies of PROB in selected solvents were used to assist the rationalization of particular solute-solvent interactions and solvent induced conformational preferences influencing the crystallization outcomes.

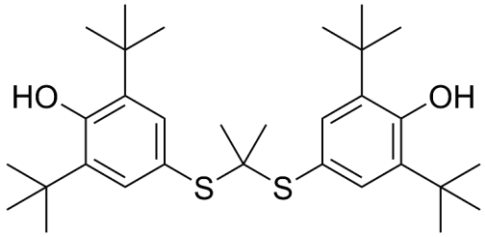

Figure 1- Probucol molecular structure.

References

[1] K. Kawakami, C. Ohba (2017): **Crystallization of probucol from solution and the glassy state,** Int J Pharm 517, 322-328.

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Preferred type of contribution:

☐ **Poster**

☒ **Oral**

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