

**MS31-P12****Liquid essential oils tamed in the solid forms by cocrystalization: from the design to the industrial application**Paolo Mazzeo<sup>1</sup>, Claudia Carraro<sup>1</sup>, Silvia Agazzi<sup>1</sup>, Federica Bianchi<sup>1</sup>, Alessia Bacchi<sup>1</sup><sup>1</sup>. Dipartimento di Chimica, della Vita e della sostenibilità ambientale, University of Parma, Parma, Italy**email:** [paolopio.mazzeo@unipr.it](mailto:paolopio.mazzeo@unipr.it)

Co-crystals are multicomponent crystalline materials in which different molecular entities are stoichiometrically kept together within the same crystal lattice. Their properties are a blend of single component characteristics, tuned by internal interactions. In modern times, cocrystals are of great interest in the pharmaceutical context because they are able to modify the chemo-physical properties of the pure drug by appropriate selecting a suitable coformer. However, some important molecules for human health are liquid at room temperature, which may influence the efficacy of their formulation since they tend to be less stable than solid forms. For this reason, the stabilization of liquid APIs is of enormous interest not only for the final delivery of the drug product but also for its storage, transportation and handling. Within this project we address the problem of taming liquid essential oils (EOs) in crystalline forms at ambient conditions and assess their applicability in the agro-food industrial arena. In addition to their widespread use as flavouring agents, EOs represent a “green” alternative in pharmaceutical, nutritional and agricultural fields due to their reported antimicrobial, antimycotic and antioxidant properties. The use of EOs in industrial context is anyhow limited by their low-melting point, which negatively affects their chemical stability. As proof of concept, we here successfully forced the enthalpic stabilization of EOs, such as eugenol (a major component of clove oil), carvacrol (extracted from the oregano essential oil) and thymol (present in the oil of thyme) by providing a new efficient intermolecular network in the solid state, co-crystallizing them with different N-based cofomers. Cofomers were appropriately chosen among a list of regulated substances apt for agro-food industries.

All products have been fully characterized and their properties – i.e. solubility and EOs release in air and in simulant media – described in relation to their three-dimensional structure with particular emphasis on the role of the coformer used.

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**Keywords:** Cocrystals, Essential-oils, Crystal-Engineering**MS31-P13****Insights into Weak C-H...F-C Interactions in C<sub>6</sub>F<sub>6</sub>:C<sub>6</sub>H<sub>6-n</sub>Me<sub>n</sub> co-crystals using a combination of powder neutron and X-ray diffraction, single-crystal diffraction, and DSC**Jeremy Karl Cockcroft<sup>1</sup><sup>1</sup>. Department of Chemistry, University College London (UCL), London, United Kingdom**email:** [j.k.cockcroft@ucl.ac.uk](mailto:j.k.cockcroft@ucl.ac.uk)

Powder X-ray and neutron diffraction (PXRD and PND) are ideal tools for the study of solid-solid phase transitions, especially when complemented by DSC measurements. Similarly, single-crystal X-ray diffraction (SXD) is the method of choice for structure determination, especially given the capabilities of modern X-ray equipment (focussed micro-source X-rays with 2D detectors) combined with state-of-the-art data processing (CrysAlisPro) and analysis (Olex2) software. In addition, variable temperature (VT) crystallography can provide a more detailed understanding of the interactions between molecules than the static one-shot single temperature approach. Combining all of these methods has improved our understanding of the co-crystal system C<sub>6</sub>F<sub>6</sub>:C<sub>6</sub>H<sub>6-n</sub>Me<sub>n</sub> for n=0 to 3.

The structure of phase IV of the prototype material C<sub>6</sub>F<sub>6</sub>:C<sub>6</sub>H<sub>6</sub> was solved from combined neutron and synchrotron X-ray powder diffraction a quarter of a century ago<sup>[1]</sup>, but a detailed understanding of the other 3 phases has remained elusive until now: new laboratory PXRD and SXD data has resulted in the determination of the crystal structures of the unknown phases and a better understanding of the transitions, particularly when combined with DSC measurements<sup>[2]</sup>. Furthermore, due to the combined use of PXRD, DSC and SXD techniques, the origins of the phase transitions in the related system C<sub>6</sub>F<sub>6</sub>:C<sub>6</sub>H<sub>3</sub>Me<sub>3</sub> co-crystal system have now been fully understood<sup>[3]</sup>. More recent studies of C<sub>6</sub>F<sub>6</sub>:C<sub>6</sub>H<sub>4</sub>Me<sub>2</sub> (p-xylene) using a similar approach has reveal subtleties in the structure of this adduct as a function of temperature which have not previously been seen; it exhibits similarities in structural behaviour to that of the C<sub>6</sub>F<sub>6</sub>:C<sub>6</sub>H<sub>3</sub>Me<sub>3</sub> adduct. Finally, a preliminary PXRD study combined with low temperature DSC on C<sub>6</sub>F<sub>6</sub>:C<sub>6</sub>H<sub>5</sub>Me (toluene) shows that this system is more similar to the prototype material. In each case, an understanding of the changes in symmetry as a function of temperature is essential to solving the structures.

Variable temperature crystallography provides a tool for studying the competing intermolecular interactions in these systems. In all cases, there is a very strong electrostatic interaction from the equal and opposite quadrupolar force between the C<sub>6</sub>F<sub>6</sub> and C<sub>6</sub>H<sub>6-n</sub>Me<sub>n</sub> rings leading to columns of molecules stacked like dinner plates, but subtle changes in the C-H...F-C interactions between columns of molecules as a function of temperature lead to a variety of phase formations.

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**Keywords:** Variable temperature powder diffraction, C-H...F-C Interactions, Co-crystals

**MS31-P14****Co-crystallisation of energetic materials with reduced sensitivity**

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Insensitive explosives have attracted significant interest in the past three decades owing to their potential application in numerous energetic materials. Research of the explosive of low impact sensitivity and high explosive performance is the vital problem in the energetic materials, which has not been solved yet (1-4). Efforts have been made to diminish this through synthesis of new molecules, however this is usually a complex, need to time consuming process cost-effective production methods, extensive validation, and requirements to meet increasing challenging performance target (5). Co-crystallisation is new an effective technique to improve the solubility, bioavailability physical and chemical stability properties of drugs without altering their chemical structure, and it is extensively used for the pharmaceutical industry (6-9). Therefore, co-crystallization may supply a new method to possibility of tuning the performance and sensitivity of an energetic material without requiring complex preparation or synthesis of novel compounds (10-13). To modify and improve the properties of energetic materials, via co-crystallisation between TNT, Picric Acid with non-energetic materials were studied. Co-crystallisation studies including characterization (single crystal X-ray data, Powder X Ray diffraction), thermal behavior (Differential Scanning Calorimetry), impact sensitivity (BAM Fall Hammer), and intermolecular interactions were carried out in detail. And also we analysed the crystal packing and show how this may influence sensitivity to impact.

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**Keywords:** Sensitivity, Inter molecular interaction, Co-crystallisation