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Screening Conditions for the Synthesis of Crystalline Spherical Clusters using 5-Hydroxynicotinic Acid

Catarina V. Esteves

1 Centro de Química Estrutural, Institute of Molecular Sciences, Faculdade de Ciências, Universidade de Lisboa, 1749-016 Lisboa, Portugal
2 LAQV-REQUIMTE, Chemistry Department, NOVA School of Science and Technology, NOVA University of Lisbon, 2829-516 Caparica, Portugal
3 Departamento de Engenharia Química e Biológica, Escola Superior de Tecnologia do Barreiro, Instituto Politécnico de Setúbal

INTRODUCTION & AIM

Crystallization is used for product separation and purification in production sectors such as food, agriculture, electronics, and pharmaceuticals.[1] However, a considerable lack of understanding about the molecular mechanisms behind the formation of crystals remains. Systematic crystallization studies on families of compounds are useful to understand how slight changes in molecular structure can impact the crystallization outcome. Building upon previous studies on the hydroxynicotinic acid family (Fig. 1),[2] in this work, novel insights into the optimization of synthetic procedures to obtain crystalline spherical clusters of 5-hydroxynicotinic acid (5HNA) are presented.

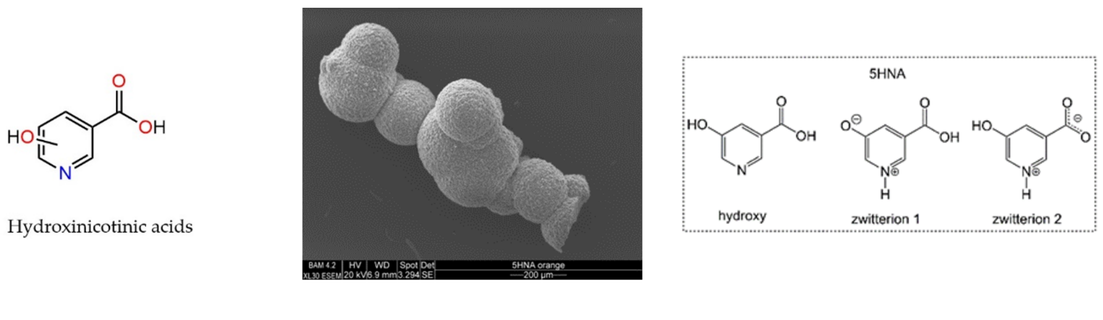
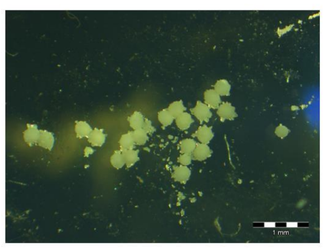
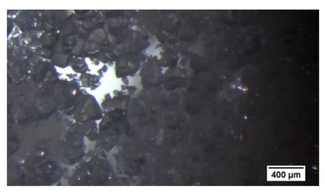
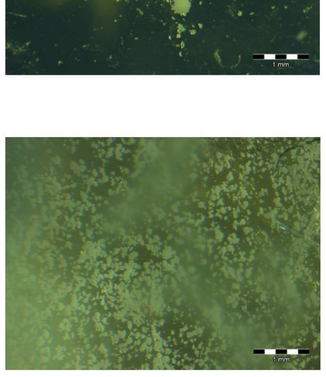
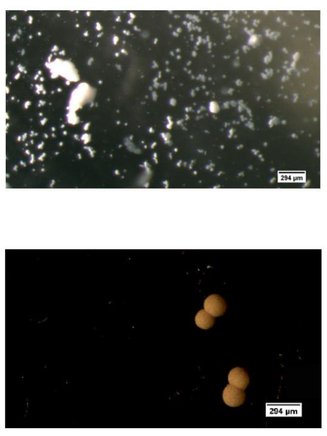
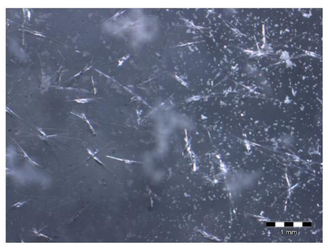
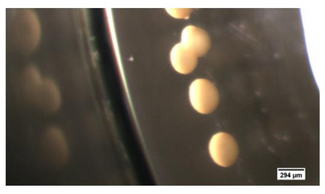


Figure 1. Generic molecular structure of hydroxynicotinic acids (left); one of the obtained SEM images of the 5HNA crystalline spherical clusters (middle, scale bar 200 µm); and the molecular structure of the 5HNA (right).

METHOD

A synthetic method was meticulously explored and identifies the most favourable conditions for producing spherical clusters of 5HNA. The systematic screening of various synthetic conditions has led to the successful formation of these clusters. This work opens new avenues for the potential applications of 5HNA spherical crystalline clusters. Such clusters have diverse diameters depending on the solvent and the synthesis conditions. The clusters were characterized by optical microscopy, scanning electron microscopy (SEM) and powder X-ray diffraction (PXRD).

Table 1. Microscopy images of the 5-hydroxynicotinic acid spherical clusters.

Procedure #1	Water synthesized 5HNA crystalline spherical clusters:	
	DMSO synthesized 5HNA crystalline bulkier clusters	
Procedure #2	Water/DMSO 95:5 (*v*/*v*) synthesized 5HNA crystalline spherical clusters	
	THF/DMSO 95:5 (*v*/*v*) synthesized 5HNA crystalline spherical clusters	
Procedure #3	EtOAc/water 95:5 (*v*/*v*) synthesized 5HNA crystalline spherical clusters	
		

ACKNOWLEDGEMENTS

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RESULTS & DISCUSSION

The clusters were investigated, and the smooth surfaces observed by microscopy (Table 1) proved to be composed of aggregates of several small crystals by means of SEM (Fig. 2) and PXRD (Fig. 3). In the case of the water-derived spherical clusters, the acquired PXRD patterns exhibited a notable resemblance to those previously documented for samples obtained at pH 4.5, as illustrated in a preceding study[1].

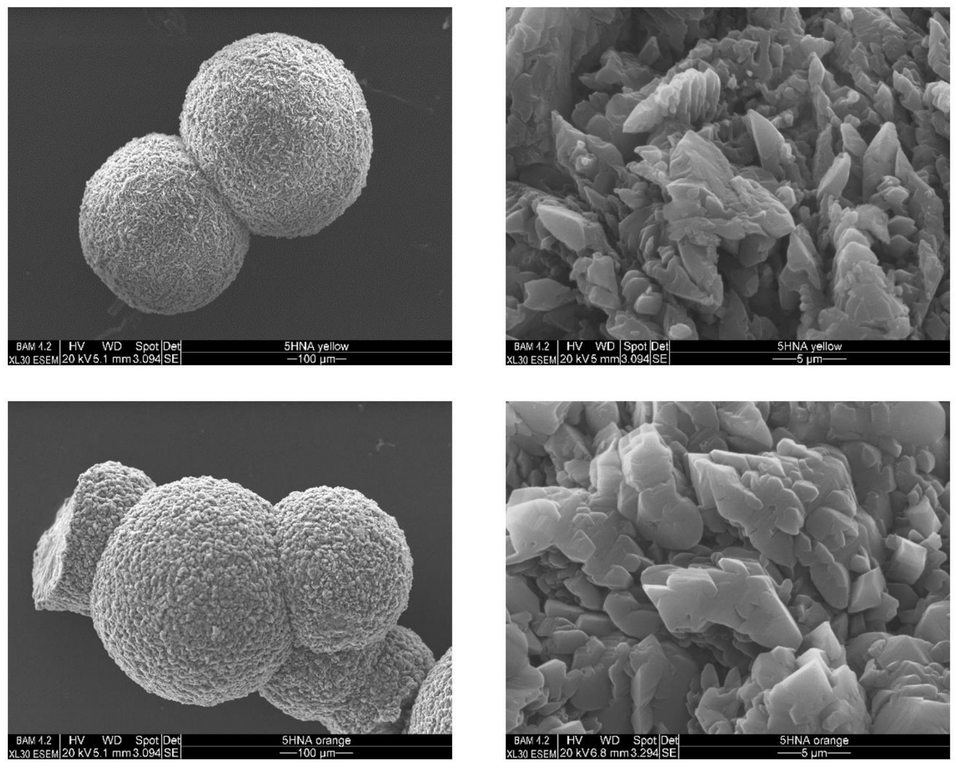

Figure 2. SEM images of the 5HNA crystalline spherical clusters obtained in: Top: THF/DMSO (95:5, *v*/*v*) labelled 5HNA yellow; and Bottom: EtOAc/water (95:5, *v*/*v*) labelled 5HNA orange. Left: scale bar 100 µm; Right: scale bar 5 µm.

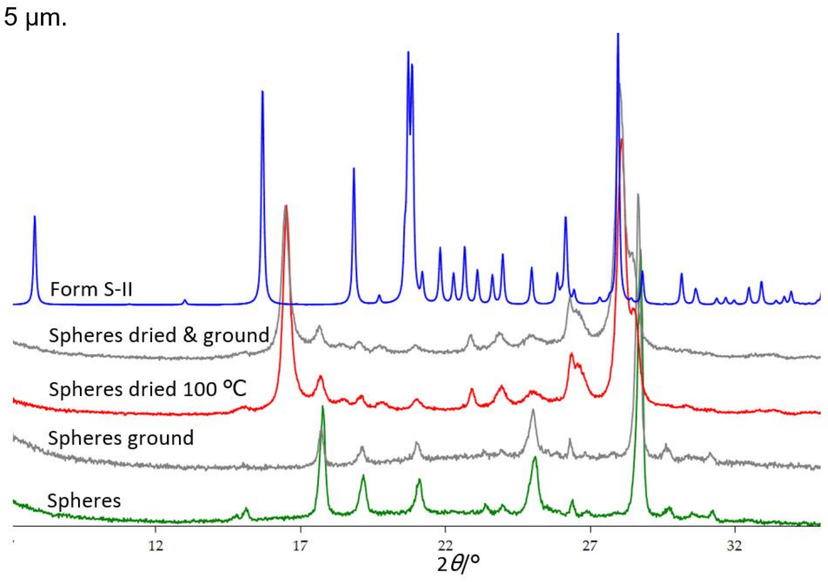

Figure 3. Comparison of the X-ray diffraction patterns, acquired at 293 ± 2 K, for the water/DMSO 95:5 (*v*/*v*) synthesized 5HNA crystalline spherical clusters with the simulated pattern from the crystal structure of the 5HNA DMSO solvate [3] (all the diffractograms were normalized to the peak of highest intensity—I_n).

CONCLUSION

Possibly the clusters were formed by a self-assembly process driven by hydrogen bonding and π-π interactions between the 5HNA molecules. The solvents ought to play a relevant role in such self-assembly process. The clusters exhibit different crystallinity depending on the solvent. Such clusters could be used as building blocks for nanomaterials with potential applications in a multitude of fields.

FUTURE WORK / REFERENCES

To better understand the self-assembly process, computational studies are underway, through collaboration with colleagues from UFRJ (Universidade Federal do Rio de Janeiro).

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3. A. Joseph *et al. Cryst. Eng. Commun.* **2019**, *21*, 2220–2233.