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INTRODUCTION

Continues advancement and rapid development of techniques operating at the nanoscale open new opportunities to revise and question commonly accepted nucleation and crystal growth theories. Atomic Force Microscopy (AFM) has been successfully involved in various aspects of active pharmaceutical ingredient (API) characterization including crystal growth, stability of solid dispersions, surface morphology, phase changes and dissolution [1]. Recent studies conducted on proteins crystallization at nanoscale show even more dispersed previously accepted Classical Nucleation Theory (CNT) [2] (Fig. 1 a) [2]. Currently, dense liquid droplets [3] seen in protein crystallisation and ‘pre-nucleation clusters’ [Fig. 1 b] [3] seems in inorganic salt crystallisation, are two main concepts of non-classical nucleation theory, although no significant progress has been made towards better understanding of mechanisms controlling heterogeneous nucleation in small organic molecules systems, what is in particular interest, as an epitaxial ordering phenomenon is frequently used to enhance nucleation rates and control properties of materials.

Our studies present a new light on heterogeneous nucleation and the epitaxial growth mechanisms based epitaxial growth of olanzapine dihydrate D on the surface of olanzapine form I (OZPN I) both in high humidity conditions and water solution. Results obtained from Peak Force Quantitative Nanomechanical Mapping Atomic Force Microscopy (PF-QNM-AFM) [4] indicate the presence of intermediate dense liquid-like phase in process of dihydrate D nucleation.

METHODS

PeakForce-QNM-AFM opens new opportunities for nanocaracterisation of the mechanical surface properties. This mode enables force curves separation in order to obtain Young’s modulus, adhesion force between the tip and the sample, energy dissipation, and maximum deformation (Fig. 4) [4].

RESULTS

Geometric real-space analysis of crystal epitaxy

Geometric real-space analysis of crystal epitaxy (GRACE) [6] calculations revealed significant 2-D lattice registry between (100)OZPN and (001), that is responsible for nucleation and epitaxial growth of dihydrate D on the surface of OZPN I.

CONCLUSIONS

Obtained information about observed nanodroplets both in water and 70% RH agrees with the two-step nucleation theory described by Vekilov and coworkers via dense-liquid droplets [2]. New form growing on (100) OZPN I face was characterised as dihydrate D by Raman spectroscopy.