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Research Article

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Selective fabrication of gamma-polymorphs of glycine by novel metal particles

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ABSTRACT

Crystallization of stable polymorphs of glycine was carried out from aqueous solution in the presence of novel metal nanaoparticles. Even lower concentration of novel metal nanaoparticles yield α and γ mixed nucleation. When the silver nanoparicles volume concentration reached 10%, the solution yield γ nucleation totally. The UV-vis spectra and Raman spectra have proved that glycine interact with the negative silver with amino cation. The interaction effectively prevent the formation of glycine alpha crystal type double-layer structure, thus inhibiting the formation of alpha crystal form, promotes the formation of gamma crystalline.

Key words: Glycine, polymorphism, additive, novel metal paricles

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INTRODUCTION

Polymorphism is the ability of a compound to crystallize in different crystalline forms. Each form has the same chemical structure but different arrangements of the molecules in the crystal lattice. Polymorphism is a crucial issue in the development of the process for pharmaceutical and fine-chemical manufacture, as polymorphs may exhibit different functionalities and physical properties, such as bioavailability, stability, melting point, structural energy, density, solubility, dissolution rate, morphology of the particles, etc. Hence, it is essential to develop a manufacturingprocess to controll polymorphism [1].

In industrial crystallization systems, impurities that are structurally related to the solute molecule are often present in solutions from upstream processes. In several cases, designer additives are intentionally added either to modify crystal habits, stabilize a polymorphor control the solution mediated phase transformation. These additives/impurities are known to interact with the crystalline phase stereochemically,and in the process, they influence the nucleation and growth kinetics. This type of interaction mechanism has been established through studies on stereoselective habit modification and nucleation control in molecular crystals with “tailor-made” additives [2].Based on an adsorption-based mechanism, the impact of impurities on nucleation could be two fold: first, the adsorption on specific crystal faces could influence the interfacial tension between the crystal nuclei and the supersaturated solution and, therefore, alter the nucleation kinetics[2]; second, the impurities could block the active growth sites on the embryonic nucleus surface and, hence, inhibit its development to the critical size.In some cases, impurities could alter the solution thermodynamics (primarily the solubility) and, therefore, influence the effective supersaturation available for nucleation.However,compare to these studies, the effect of nanoparticlesas additive on crystal growth study has rarely reported. It is well known that the metallic nanoparticles are currently a subject of intense interest because of their attractive physical, chemical, catalytic, and spectroscopic properties.The aim of the present work was to check if the metallic nanoparticles can serve as the additive to control crystal polymorph.

To get a better understanding of the mechanism of formation and transformation of the selected polymorphs during the crystallization process, the simplest amino acid, glycine (NH_2CH_2COOH), is chosen as the model compound in this study. Glycine is known to have at least three polymorphs: α-, γ- and β-forms[2]. γ-form is the thermodynamically most stable form among the three known glycine polymorphs under ambient conditions.However in an aqueous glycine solution, the α-form is the commercially available form because it spontaneously crystallizes from neutral aqueous solutions under normal conditions.The *γ*form apparently only appears whencrystallization takes placefrom acidic or basic solutions, from aqueous solutions by addition of electrolytes,from supersaturated solution irradiatedwith plane-polarized laser light,from neutral aqueous solutions through careful control of the solvent evaporation by using microporous membranes, and from emulsions, microemulsions and lamellar phases by surfactants, etc[3].The least stable β-glycine crystallizes from alcohol-water solutions, but it rapidly transforms to the metastable α-glycine when in contact with water.In the present study, the selective crystallization ofγ-form glycine in the presence of silver nanoparticles and the crystal growth mechanism of the additives were also investigated.

EXPERIMENTAL SECTION

In 200 ml of redistilled deionized water, 36 mg of silver nitrate was dissolved and the solution was heated to boiling. The 4ml of a 1% trisodium citrate aqueous solution was added into the boiling silver nitrate solution dropwise, accompanied with vigorous stirring. The mixed solution was kept boiling for a further 30 min. Finally, green–gray silver colloid was obtained. The size of the silver colloid we prepared was about 70 nm. The SEM image of silver colloid is shown in the supporting information.

Silver colloid /aqueous glycine mixtures were prepared by preweighing the nanopartilces and adding warm (above 50 °C) aqueous glycine solution. This mixtureswere placed in a bathat 50ºC for 30 min. After mixed, the samples were transferred to a water bath at 25 °C and left to crystallize. Four different silver colloid concentrations were used, 0.5, 1,5 and 10% v/v respectively. The concentration of glycine aqueous solutions were 280mg/ml.

Raman spectroscopy was employed to monitor the solid-phase composition. However, because the Raman scattering effect results from both the solid and liquid phases, Raman spectroscopy can also be applied for solute monitoring. In this work, a RA 400 Raman spectrometer from Mettler-Toledo (Greifensee, Switzerland) equipped with a 250 mW frequency-stabilized laser diode at 785 nm and a thermoelectrically cooled CCD detector was used.Raman spectra were collected at a laser intensity of 150 mW in the 800 to 1800 cm^{-1} range with a resolution of 0.5 cm^{-1} and were averaged over 10 scans using an exposure time of 5 s.The crystal morphology was observed by an OlympusBX51 microscope with an attached CCD video camera(Olympus, Japan). Powder XRD patterns of glycine crystals were determinedat room temperature using a Bruker D8 advancediffractometer with Cu-Ka radiation at 40 mA, 40 kV.

RESULTS AND DISCUSSION

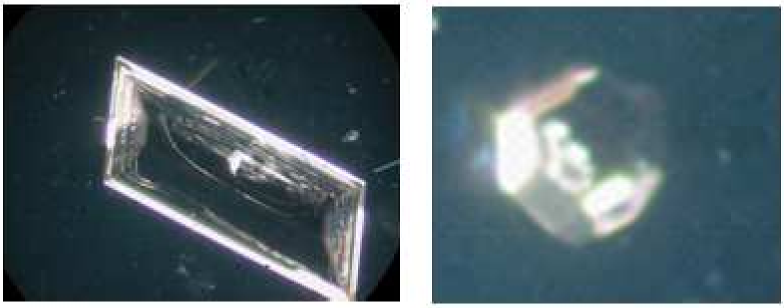

Fig. 1. Optical microscopy images of prepared crystals (a) from pure water -formed, (b) from a 10v % silver colloid-in-water

The dissociation of silver colloids in solutionis accompanied by speciation of glycine cations, and hence apH changeswhile the pH of pure glycine solution was measuredas ca. 6.2, in the presence of silver colloids, the solution pH increased to ca. 7.5. Glycine crystals with the αpolymorph usually grow fromsolutions in the pH range 3.8-8.9[3].Fig.1a shows anexample of an αglycine crystal grown from a neutral solution.It has the expected prismatic morphology. When the silver nanoparticles were introduced into the solution, the crystal displays different morphologies.

XRD patterns of glycine crystals formed under different experimental conditions are shown in Fig. 2. Comparison of the powder pattern with those expected from the single crystal structures of α-, β-, and γ-glycine revealed the exclusive formation of α-glycine in the pH=7.5, with no detectable amounts of the other two forms (Fig. 2). In contrast, even in a relatively low concentration of silver nanoparticles, glycine crystals revealed the presence of γ-glycine. When the concentration reach 10% v/v, the XRD result shows the exclusive formation of γ-glycine crystal.

It is clearly found that even in a relatively low concentrations, silver nanopartilces can still affect the crystal nucleate.

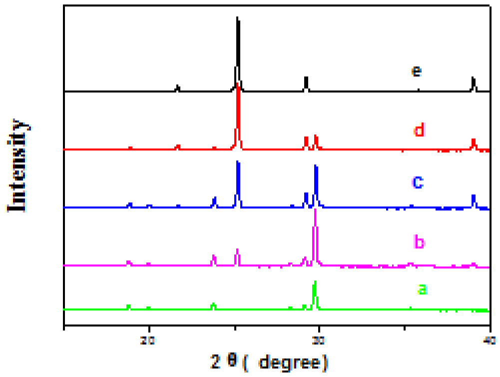

Fig. 2 Glycine crystals grown from aqueous solutions in theabsence and the presence of silver colloids: (a) α-Glycine, no additive;(b) α and γ-Glycine from 0.5% (v/v of silver colloid) ; (c) α and γ-Glycine from 1% (v/v of silver colloid) ;(d) α and γ-Glycine from 5% (v/v of silver(colloid);(e) γ-Glycine from 10% (v/v of silver colloid)

Many references have been reported on the application of additives to stabilize crystal forms. Currently, it is believed that additives operate by adsorption onto crystal facets, which consequently changes the surface free energy and may block sites which are necessary for incorporation of solute into the crystal lattice. This may ultimately result in kinetic and morphological changes

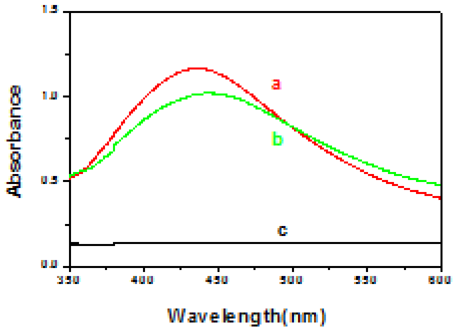

Fig . 3. A representative UV/vis absorption spectra of a :silver colloid (red) , b: glycine aqueous solutions in the presence of 10 % v/v of silver colloid and c : pure glycine solutions

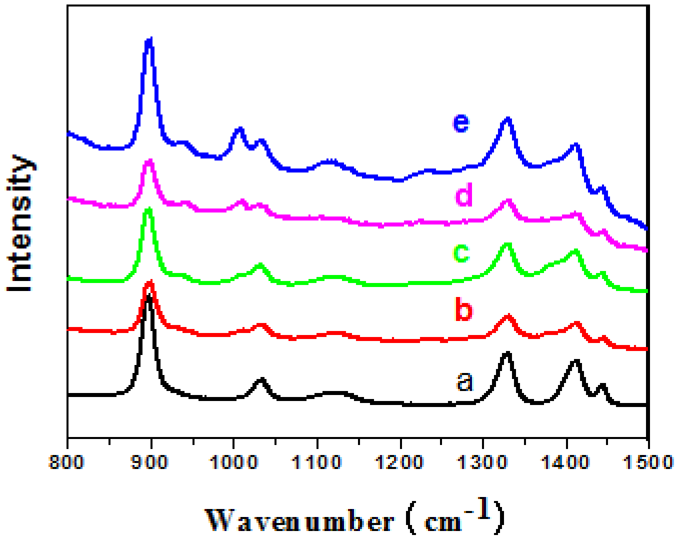

Fig. 4 Raman spectra of aqueous solutions in theabsence and the presence of silver colloids: (a) Glycine solution , no additive;(b) Glycinesolution (0.5% v/v of silver colloid) ; (c) Glycinesolution(1% v/v of silver colloid) ; (d) Glycine solution (5%v/v of silver(colloid);(e)Glycine solution (10% v/v of silver colloid)

The UV–visible adsorption spectra of the silver colloid, glycinesolution before and after the addition of silver colloid are shown in Fig.3. The adsorption spectrum of the silver colloidshows a single sharp molar extinction maximum at 432nm, which is due to the resonant excitation of plasma oscillations in the confined electron gas of the particles.After the addition of the colloids to the glycine solution,the adsorption spectrum showsλmax shift from 432 to 445 nm. The appearance of the red shifted band isascribed to the adsorption of the glycine molecules on the surfaces of the silver nanoparticles. From the above discussion, it indicates that the glycine molecules have an interaction with the metal nanoparticle.

Another important evidence for the silver colloids affect nucleate glycine growth was shown in Fig. 4. Fig. 4b-4e show the raman spectra of glycine mixed with different silver colloids volume, while 4a depicts a raman sepctrum of glycine solution of the same concentration without the colloid solutions. Spectra b-e were measured after mixing of the glycine solution with the silver colloids. The band assignments for raman spectra of glycine in various states have been well established [4].The spectra of glycine solution mixed with the silver colloid were very different from that of the α glycine form aqueous solution.For example, Fig. 4b-4e all show an intense band at 1003 cm^{-1}, but the corresponding bands are not identified in the glycine solution spectrum. Clearly appearances of the NH_3^+ asymmetric and symmetric stretching modes at 1608 and 1490cm^{-1} and the intense band at 1003 cm^{-1} due to the C-N streching mode are also good evidence for the interaction of the NH_3^+ group with the silver surface. On the basis of this observation we conclude that the amino groups can interact strongly with the negatively charged silver surface. The protonated acid species are present in solution they may join the surface and in doing so modify the charged nature of the interface preventing the further addition of zwitterions. These ions would thus act as selective tailor-madeadditives to inhibit the crystallization of α. At the same time they could not totally inhibit the appearance of the more stable γ form. The slow growing +c will be inhibited fast growing -c direction will be available for growth and hence that the crystallization of γ cannot be completely inhibited by these charged species. Therefore, it is quite reasonable thus signifying a unidirectional growth inthe-c direction as clearly shown in Fig.1.

CONCLUSION

In this short communication we demonstrate that silver nanoparticles can be used as additives to affect the crystal growth. Based on employing characterization techniques such as X-ray diffraction, UV-vis, and Raman spectrum, we proved that γ form of glycine crystallized in the exist silver colloids opposed to the α form, which crystallized in neutral solution. It is clearly obtained form Raman and UV-vis data that strong interaction between the glycine molecular and silver colloid play a crucial role in the glycine crystal polymorphism mechanism. The possibility of creating silver colloids as crystal seeds or additives with a variety of sizes, architectures and chemical functionalities opens new experimental opportunities for synthesizing the controllable crystal.

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