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Morphology-controlled synthesis of colloidal polyphenol particles from aqueous solutions of tannic acid

Tero Kämäräinen,† Mariko Ago,† Luiz G. Greca,† Blaise L. Tardy,† Markus Müllner,‡ Leena-Sisko Johansson,† Orlando J. Rojas*,†,§

†Department of Bioproducts and Biosystems, Aalto University, Vuorimiehentie 1, Espoo, P.O. Box 16300, FI-00076 Aalto, Finland.

‡Key Centre for Polymers and Colloids, School of Chemistry, and The University of Sydney Nano Institute (Sydney Nano), The University of Sydney, Sydney 2006, NSW, Australia.

§Department of Applied Physics, Aalto University, Puumiehenkuja 2, Espoo, P.O. Box 13500, FI-00076 Aalto, Finland.

Corresponding Author

*E-mail: orlando.rojas@aalto.fi
ABSTRACT

The properties and application of particulate systems can be tailored by gaining control on their morphology. Here, a facile method is described for the bottom-up synthesis of bio-based colloidal particles with varied morphologies by simple aqueous oxidation of tannic acid used as precursor in alkaline solutions. Initial tannic acid concentrations of 1–2 wt% produce the largest crystalline yields, while total precipitate yields (up to 64 %) are achieved at 2 wt%. Structural and thermochemical evaluations are reported from measurements based on X-ray diffraction, thermogravimetry as well as infrared, mass, nuclear magnetic resonance and X-ray photoelectron spectroscopies. The analyses suggest a galloyl-rich composition of the particles with thermal stability up to 450–500 °C. We show that the selection of the base species and pH affords the control of the particle morphologies that include rods, platelets, rhomboids, cuboids and quasi-spherical shapes. The main cause-effect relations are elucidated from principal component analysis of process conditions and particle morphogenetic parameters, which are derived from their physical dimensions and yield. The results indicate an anticorrelation between base counter cation ionic radius and particle volume, whereas base strength and initial solution pH correlate with the total precipitate yield and elongated morphologies, respectively.

KEYWORDS. Tannic acid; polyphenol; crystallization; morphology control; colloidal particles

INTRODUCTION

Gaining morphological control in the synthesis of colloidal particles is imperative to the formation of high surface area and functional materials. The value of structural diversity is also apparent, for instance, in biomineralized composites,1–4 which has motivated research into
naturally abundant inorganic compounds, such as calcium carbonate, and towards uncovering pathways to gain control on particle size and morphology during crystallization (e.g., by utilizing impurities and templating techniques).\textsuperscript{5–9} Progress in bio-based nanoparticle extraction has also enabled a variety of anisotropic particles to be obtained from polymeric building blocks.\textsuperscript{10,11}

Natural polyphenols such as lignins, lignans and tannins represent plant-based building blocks more suitable for bottom-up approaches compared to polysaccharides sourced via a top-down deconstruction of cell walls. The former also add prospects to endow a wide range of properties and health benefits.\textsuperscript{12–14} Although polyphenols have enjoyed less attention compared to their polysaccharide counterparts, colloidal particle preparation routes have facilitated lignin for a broad number of applications in recent years.\textsuperscript{15–18} Lately, crystallization of ellagic acid particles\textsuperscript{19} obtained by sonochemical processing of tannic acid enabled the formation of phenolic microcrystals. Though the syntheses of ellagic acid particles has been scarcely reported, it has been shown to be amenable for the creation of objects with morphologies resembling rod-like,\textsuperscript{20} planar\textsuperscript{21} and cuboidal\textsuperscript{22} shapes via antisolvent precipitation.
Figure 1. Overview of polyphenolic particle synthesis from aqueous solution of tannic acid and schematic representation of results obtained by using principal component analysis (top right), where the arrow links the effect of increasing the associated variable (solution pH–particle elongation, base conjugate acid $pK_a$–yield and base counter cation ionic radius $R$–particle volume).

In this communication, we introduce a new and simple route for the conversion of tannic acid into polyphenolic particles while gaining control over their morphology, ranging from rods to planar to cuboidal and quasi-spherical (Figure 1). Note: see Experimental Section in the Supporting Information document. The approach is based on agitation-induced oxidation of tannic acid under basic conditions. The simplicity of the process points to excellent prospects for scalability. We emphasize the relationship between morphology and the conditions in the reaction media using principal component analysis (PCA, Figure 3b, PCA Section in Supporting Information). The results point to the specificity of base type and pH to tailor the crystallization process and to obtain particles of oxidized tannic acid (OTA) with given morphologies.
RESULTS AND DISCUSSION

The particles of oxidized tannic acid, OTA, were produced at room temperature under stirring from aqueous 2 wt% tannic acid solutions adjusted to pH 7.8, 9 or 11 by using KOH, NaOH, LiOH, Na$_3$PO$_4$ or NH$_4$OH (Figure 1). The reactions proceeded for a time ranging between ca. 14 h and 1 week, during which tannic acid, a mixture of gallotannins, was hydrolyzed and likely oxidatively converted into ellagitannins and hexahydroxydiphenic acid units. No direct evidence of the formation of ellagic acid was obtained. The hydrolysis of tannic acid resulted in a decrease in oxidant concentration as the reaction proceeded due to the generation of gallic acid ($pK_a$ of the carboxylic acid and phenolic OH-groups: 4.4, 8.2, 10.7 and 13.1). The change in reaction medium pH after 14 h and 1 week show qualitatively similar decreasing trends between the different bases apart from NH$_4$OH at pH 11 (Figure 3a). A more detailed study of the evolution of pH with NaOH and KOH points to an equilibrium value at ~100 h starting from pH 7.8 and at ~20 h with an initial pH 11 (Figure S1). For the strongest bases, KOH and NaOH, the particle yield increased with increasing pH, whereas the highest yield was achieved at the initial pH 9 with LiOH and NH$_4$OH. The yield with Na$_3$PO$_4$ was constant across the experimented pH range, suggesting the importance of the hydroxide base in defining the morphology type.
Figure 2. Scanning electron microscopy images of oxidized tannic acid particles with given morphologies. (a) KOH pH 7.8, 2 wt% (in tannic acid), 14 h with washed particle morphology (inset). (b) LiOH pH 9, 2 wt%, 1 week with a close-up showing ca. 50 nm nanostructure (inset). (c) LiOH pH 7.8, 2 wt%, 1 week. (d) NaOH pH 7.8, 0.4 wt%, 1 week. (e) LiOH pH 7.8, 2 wt%, 14 h. (f) NH₄OH pH 9, 2 wt%, 14 h. (g) NaOH pH 7.8, 2 wt%, 14 h. (h) LiOH pH 9, 2 wt%, 14 h. (i) LiOH pH 11, 2 wt%, 14 h. (j) Na₃PO₄ pH 7.8, 2 wt%, 1 week. (k) NaOH pH 11, 2 wt%, 14 h. (l) KOH pH 11, 2 wt%, 14 h. (m) Na₃PO₄ pH 7.8, 2 wt%, 14 h. (n) KOH 2 wt%, pH 9, 14 h (washed). (o) NH₄OH pH 11, 2 wt%, 14 h. (p) KOH pH 11, 2 wt%, 14 h with washed particle
morphology (inset). See Figures S2–S6 in Supporting Information for additional related morphologies.

A collection of particle morphologies produced by the given reaction conditions is shown in Figure 2 containing scanning electron microscopy (SEM) images (see also Figures S2–S6 for SEM images of related morphologies). The structures included cuboidal and odd-shaped particles with varying number of smooth and faceted faces (Figure 2a–e,h), oblate plates (Figure 2f–g, j–k) and needle and rod-like particles (Figure 2i, l–p). With increasing pH (KOH), the OTA particle morphology changed from rhombus-like at pH 7.8 (Figure 2a) to twinned needle structures at pH 9 (Figure 2n) and further to high axial ratio rods at pH 11 (Figure 2p) with a small portion of dumbbell-like particles with constituents reminiscent of the morphology obtained at pH 9 (Figure 2l). Upon washing, the rods (pH 11) disintegrated into cuboidal particles with two opposing rough faces (Figure 2p, inset) and loose bundles of rod-like constituents (see Figure S2 for a comparison), while at pH 7 the washing uncovered a roughness encompassing the whole particle (Figure 2a, inset), in stark contrast to the anisotropic nanostructure found in a 3D morphology produced by LiOH (Figure 2b, inset). As the pH was increased in the presence of NaOH, the crystalline shapes of OTA shifted into increasingly larger oblate plates (Figure 2g,k; see the intermediate size at pH 9 in Figure S3). At pH 9 and 11, the particles formed large twinned structures with individual planar components meeting at large angles also having much larger width-to-thickness ratio compared to those obtained at pH 7.8. In LiOH, the OTA morphologies were more diverse. At pH 7.8, precipitates formed ca. 50 µm wide odd-shaped, quasi-spherical particles after 14 h (Figure 2e) and angular 3D constructs after 1 week (Figure 2c), whereas at pH 9 the crystals formed a roughly 50/50 % mixed population of rods and elongated cuboids (Figure 2h). At pH 11, the particles comprised thin rod-like plates
tapering at both ends of their largest physical dimension (Figure 2i). The change in morphology was more drastic compared to others after 1 week, whereby the low to mid-range pH displayed irregular 3D structures, while at pH 11 the narrow plates transformed mostly into bundles and dumbbells (Figure S4). In the presence of Na₃PO₄, the OTA evolved into oblate plates at pH 7.8, which developed into twinned oblate plates after 1 week (Figure 2j and Figure S5). At pH 9, the population contained needle-like particles (Figure 2m), which after 1 week formed twinned oblate plates. Twinned plate-like and almond-shaped precipitates were acquired at pH 11 (Figure S5). With NH₄OH, OTA particles formed twinned structures in the whole pH range, comprising irregular clusters (Figure S6), plates (Figure 2f) and rods (Figure 2o) at pH 7.8, 9 and 11, respectively.

To determine how the process conditions affected the ensuing particle morphology, a PCA with a varimax rotation (see Supporting Information for details) was conducted based on the base counter cation ionic radius ($R$), base conjugate acid $pK_a$, the initial solution pH and the resulting morphology by evaluating morphogenetic parameters consisting of ratios derived from the particle physical dimensions ($d_2/d_1$ and $d_3/d_2$, where $d_1$, $d_2$, $d_3$ are average dimensions in descending order of particles prepared from 2 wt% tannic acid in 14 h measured from SEM images), volume ($V = d_1d_2d_3$) and total yield ($Y$, after 1 week). The following salient morphogenetic remarks can be construed from the PCA correlation circles (Figure 3b) of the three principal components (PCs) accounting approximately 81 % of the total variance (see Figure S7): Firstly, an anticorrelation exists between the counter cation size and particle volume without a significant linear dependence with yield points due to a plausible inhibitory influence of increasing $R$ on the secondary nucleation rate of the hydrolysis products. Secondly, the effect of weaker base diminishing the rate of hydrolysis of tannic acid is entailed in the correlation
between pKₐ and total yield. Thirdly, a moderate correlation with initial pH and d₃/d₂ in conjunction with anticorrelation with d₂/d₁ suggests that increased pH promotes elongated morphologies, possibly through differing concentration dependencies of the growth rates of the associated crystal planes (see summary in Figure 1).

**Figure 3.** (a) Tannic acid (TA, 2 wt% solution) pH (bar plot) and the corresponding yield of OTA precipitate (square markers) in the presence of the respective base, as indicated. (b) Correlation circles of the varimax-rotated principal component (RPCs) pairs with eigenvalues > 1 (ca. 81 % explained variance) based on the base counter cation ionic radius (R), base conjugate acid pKₐ, initial solution pH, ratios of mean particle characteristic dimensions (d₂/d₁ and d₃/d₂), mean particle volume (V = d₁d₂d₃) and total yield (Y). (c) Powder X-ray diffractograms of oxidized tannic acid (OTA-NaOH) particles formed after 14 h at given TA solution concentrations and their corresponding morphologies (SEM images, 2 µm scale bar). (d) Mass-loss rate from thermogravimetric analysis (TGA) of TA and OTA-NaOH/KOH precipitates (2 wt% TA) after 14 h at different initial pH with the char content at 600 °C (inset) and their corresponding morphologies prior to TGA (SEM images).
The effect of tannic acid concentration on crystallinity was evaluated with NaOH using powder X-ray diffraction (PXRD). Tannic acid powder displayed an amorphous structure, lacking any well-defined peaks in the diffractogram (data not shown). In the 1–2 wt% tannic acid concentration range, precipitates with the highest crystallinity were produced after 14 h (PXRD and SEM; Figure 3c). Intense peaks at 2θ values mainly between 20–30° were observed, indicative of a crystalline form of the particles.\textsuperscript{20,24,25} No residual NaOH crystals were observed based on the lack of strong diffraction bands in the range 30–40°,\textsuperscript{26} while the amorphous background differed in shape from that of tannic acid’s. After prolonging the reaction time to 1 week, the smallest verified tannic acid concentration that yielded amorphous precipitates was 0.2 wt% (Figure S8). An increased amount of well-defined cuboidal particles developed at 0.4 wt% TA after 1 week (Figure 2d), which we attribute to primary and secondary nucleation induced by the increasing concentration of hydrolyzed tannic acid.

The matrix-assisted laser desorption/ionization (MALDI) mass spectra of OTA-NaOH particles revealed species with a repeating unit of 152 m/z identified as a galloyl residue (Figure S9).\textsuperscript{27,28} An explanation to the apparent intensity attenuation at high m/z with increasing pH is explained as harsher NaOH and KOH hydrolysis conditions resulting in smaller molecular weight compounds. Gel permeation chromatography measurements support a crystallization-driven mechanism of OTA-KOH particle formation, as the elugrams did not show polymer build-up during OTA-KOH particle formation (Figure S10). After partially dissolving OTA-KOH particles in dimethylacetamide (DMAc) no significant higher molecular weight material could be detected. It was further noted that the OTA-NaOH and OTA-KOH particles (94 h reaction time, prepared at pH 7.8 and 11) were generally poorly soluble in toluene, chloroform, acetone, dimethylformamide (DMF), dimethyl sulfoxide (DMSO), ethanol and water when
assessed from the supernatant and sediment characteristics after vortex shaking and centrifugation (Figure S11). Only DMSO yielded a sediment-free spin down with OTA-KOH (pH 7.8).

The Fourier-transform infrared (FTIR) spectroscopy gives further support to the chemical makeup of the OTA-NaOH precipitates as suggested by MALDI, showing peaks corresponding to galloyl-rich species (Figure S12).24,29,30 In the OTA-NaOH FTIR spectrum, 3552 cm\(^{-1}\) and the broad band around 3100 cm\(^{-1}\) were attributed to O–H stretch, while 1614, 1580 and 1510 cm\(^{-1}\) correspond to aromatic C=C–C vibrations. 1326, 1256 and 1194 cm\(^{-1}\) were assigned to C–O stretch, whereas 1111 and 1054 cm\(^{-1}\) were assigned to the aromatic in-plane C–H stretch. A particularly weak band is associated to the C=O carbonyl stretch found typically around 1722–1702 cm\(^{-1}\),30 visible as a shoulder alongside 1692 cm\(^{-1}\) at 1714 cm\(^{-1}\).

The X-ray photoelectron spectroscopy (XPS) survey spectra showed the expected elemental bands for tannic acid and OTA-NaOH (14 h, pH 7.8) (Figure S13a). The relative amounts of carbon and oxygen did not change markedly (tannic acid: O/C = 0.43 ± 0.01, OTA-NaOH: O/C = 0.41 ± 0.04), and similarly, changes in the oxidation state of carbon atoms were marginal (Figure S13b). The \(^{13}\)CCP/MAS NMR spectroscopy of OTA-NaOH showed notable differences in the ester/carboxyl band (C=O region) and in the phenolic -COH and aromatic bands between pH 7.8 and pH 9/11, indicating a possible transition in the nature of the carbon composition at higher pH (Figure S14).31 This could manifest in the observed pH/morphology dependencies as indicated by the PCA.

Thermogravimetric analyses of OTA-NaOH/KOH particles showed a notable increase in the onset of thermal degradation, from ca. 220 to 450 °C (Figure 3d) compared to tannic acid, attributed to chemical and structural changes.19 With OTA-KOH, the two mass loss events in the
decomposition region for OTA-NaOH were more distinct. Although the decomposition temperatures remained similar, the needle/rod-like OTA-KOH particles (pH 9 and 11) had a much higher char content at 600 °C compared to other morphologies (Figure 3d, inset), suggesting a stronger cohesion of the assemblies or higher crystalline particle content since variation in the residual alkali did not likely contribute to such extent.

In summary, we offer a simple and effective approach to achieve morphological control under given process conditions. One can speculate that the various morphologies, and possible crystalline forms, contribute to given surface chemical properties such as morphology-dependent antioxidant activity.32 It may be also possible that they endow some level of tunability and delivery control, especially if one considers the inherent properties of polyphenols, including anti-inflammatory, antimicrobial, antimitogenic, anticarcinogenic and antioxidative effects.12–14 However, determination of such properties and their connection with crystallographic data, yet to be acquired, is needed. This can play a pivotal role in the rich morphological varieties acquired, including concentration dependencies of the secondary precipitation on different crystalline faces. The current results and discussion provide guidelines for such future studies. Moreover, further relevance in material processing can be expected. The reproducibility of the method with respect to the tannic acid source (mass spectrometry) needs to be evaluated in detail. Efforts to reproducibly and systematically produce desired particle geometries of given size and chemistry has been challenging unless made synthetically. The introduced route gives the research community an unprecedented possibility for polyphenolic particle preparation by using facile, bottom-up approach from an organic precursor.

CONCLUSIONS
Polyphenol-based particles with a variety of tailorable morphologies were produced from tannic acid using a facile synthesis method. PCA results indicated an anticorrelation between base counter cation ionic radius and particle volume, while base strength and pH correlated with the total precipitate yield and particle elongation, respectively. Thermochemical analyses suggested a galloyl-rich composition possessing an elevated thermal stability, a testament to the successful fragmentation of the tannic acid precursor followed by their nucleation and crystallization. The facile, bottom-up synthesis of particles with fine control over their morphology is expected to expand the utilization of such bio-based materials. This is not only important in reducing the negative environmental impact incurred by current manufacturing processes but also in forming materials bearing new and enhanced properties.

ASSOCIATED CONTENT

Supporting Information

The following files are available free of charge: Experimental section including particle synthesis protocol, reaction medium pH time dependence plots, PCA explained variance, additional SEM images, MALDI mass spectra, GPC elugrams, particle solubility test figures, FTIR spectra, XPS spectra and $^{13}$CCP/MAS NMR spectra (PDF).

AUTHOR INFORMATION

ORCID

Tero Kämäräinen: 0000-0001-8333-4900
Mariko Ago: 0000-0001-5258-4624
Blaise L. Tardy: 0000-0002-7648-0376
Markus Müllner: 0000-0002-0298-554X
Leena-Sisko Johansson: 0000-0003-0428-8155
Author Contributions

The manuscript was written through contributions of all authors. All authors have given approval to the final version of the manuscript.

Notes

The authors declare no competing financial interest.

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SYNOPSIS. Polyphenolic particles with a rich variety of morphologies were produced from tannic acid using a simple, green method.