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Flavonoid adsorption and stability on titania-functionalized silica nanoparticles

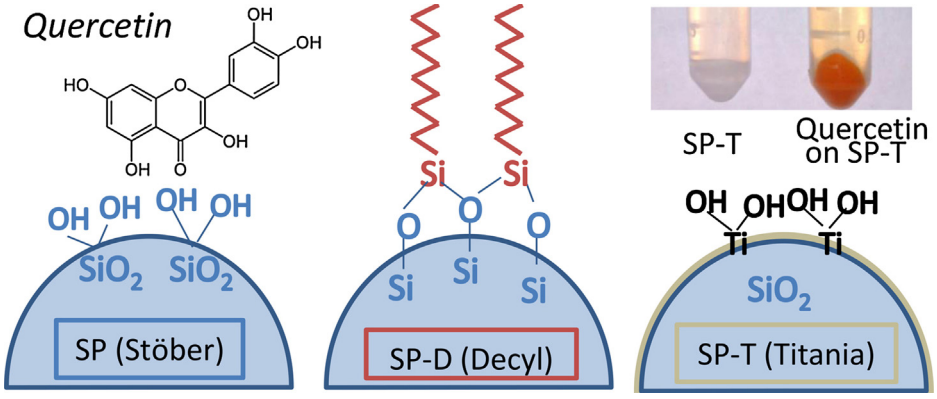
Daniel M. Schlipf, Cory A. Jones, Marie E. Armbruster, Elliott S. Rushing, Kaitlyn C. Wooten, Stephen E. Rankin, Barbara L. Knutson*

Department of Chemical and Materials Engineering, University of Kentucky, 177 F. Paul Anderson Tower, Lexington, KY 40506-0046, United States

HIGHLIGHTS

- Quercetin adsorption isotherms on non-functionalized and functionalized particles.
- Demonstration of tunable titania grafting densities on Stöber particles.
- Titania density-dependent adsorption of quercetin from solution.
- Quercetin retains antioxidant activity after chelation to titania coated particles.

GRAPHICAL ABSTRACT



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ABSTRACT

The interaction of flavonoids with silica surfaces is of interest for separation and recovery of these natural products with potential anti-oxidant and anti-inflammatory properties. The benefit of tailored silica materials for natural product separation is based on the ability to readily tune their surface functionality and pore structure. In this work, the adsorption of quercetin, a model plant-derived flavonoid, was measured on silica particles (450 nm diameter) that were non-functionalized, hydrophobically functionalized (16.2 mg decyl groups/g) or titania modified (0.33–9.83 mg TiO_2/g). Quercetin interactions with these functionalized silica particles were interpreted from adsorption measurements on nonporous silica particles, which eliminate the potential diffusional and steric constraints of pores. Titania functionalized particles are found to exhibit significantly increased adsorption capacities compared to non-functionalized and decyl functionalized materials, presumably due to binding of quercetin to the metal oxide, and this capacity increased linearly with surface coverage of titania. The ability to recover the activity of bound quercetin is demonstrated using a 2,2-diphenyl-1-picrylhydrazyl (DPPH) assay. This investigation provides guidelines for the surface modification of both porous and nonporous silica for the recovery of natural product flavonoids, taking advantage of the binding properties of the functionalized silica surface.

* Corresponding author. Tel.: +1 859 257 5715; fax: +1 859 323 1929.
E-mail address: bknut2@uky.edu (B.L. Knutson).

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1. Introduction

Quercetin is a common secondary plant metabolite possessing a variety of therapeutic medicinal uses. It has been shown to reduce the effects of oxidative stress on a variety of cell lines by scavenging free radical oxygen species [1,2]. Quercetin has been investigated for disease prevention, for example its roles in modulating signal transduction pathways associated with carcinogenesis as well as Alzheimer's disease [3,4]. The anti-thrombosis and anti-inflammatory effects of quercetin may aid in the reduction of obesity [5]. Secondary metabolites produced by plants, such as quercetin, are of high value, although traditional methods of metabolite recovery are expensive, detrimental to plant cells and require large quantities of plant cell tissue [6]. A common method of recovery is exudation, or altering of the cell membrane permeability for release of produced molecules [7]. An alternative proposed method is the use of nanoparticles for recovery of metabolites in plant cell cultures [8]. Understanding the interaction of nanoparticle systems with plant metabolites is a crucial first step in designing nano-particle based metabolite scavenging systems.

Silica nanoparticles are increasingly investigated for the loading of therapeutics and for topical delivery applications [9,10]. Silica materials are robust, employ well known aqueous-based synthesis protocols and are widely used in the fields of catalysis, chromatography and therapeutics delivery [11–13]. Versatile synthesis techniques have been developed for silica thin films and particles of controlled pore structure, and pore size. Using modified silanes, hydrophilic silica can be functionalized with a variety of organic moieties to modify surface properties including charge and hydrophobicity [14,15]. Deposition of reactive metal oxide precursors on the silica surface results in different metal oxide coatings, including titania [16]. Titania coated silica nanocomposites, in particular, have been identified as an alternative to pure titania particles because the ability to control particle properties (porosity, morphology, and particle size) is better established in silica than titania [17–19].

Quercetin is a hydrophobic, polar polyphenolic flavonoid, with an octanol/water partition coefficient of 1.82 [20]. Quercetin shows an unusually low solubility in both octanol and water, which is why high uptake and bioavailability of free quercetin is difficult to achieve [20]. As a model antioxidant, the adsorption of quercetin onto nanoparticles has been investigated, primarily with a focus on the delivery of therapeutics and metal chelation [15,21–23]. Previous investigations of quercetin adsorption examined its interactions with silica or silica modified with pharmaceutical binders. The adsorption of quercetin drastically increased on silica modified with the pharmaceutical binder polyvinylpyrolidone (PVP, terminated with carboxylic acids) as compared to unmodified silica (terminated in hydroxyl groups), due to the increase in quercetin hydrogen bonding sites and stabilization within the polymer [23]. With hydrogen bonding playing a direct role in quercetin binding, a clearer comparison of quercetin adsorption between hydrophilic and hydrophobic surfaces, such as unmodified and alkyl chain modified silica, respectively, is needed.

The binding of quercetin and titania provides a strong interaction for the design of adsorbents. Quercetin possesses a diol, and therefore can act as a bidentate ligand to interact with available titanium on the surface of the particles, potentially in a manner similar to chelation [8]. Bulk titania, while possessing powerful optical, catalytic and binding properties, has an isoelectric point near pH = 6.5 [24], which is expected to lead to particle flocculation near plant physiological pH values (5.5–7.5). In contrast, silica has an isolectric point near pH = 2.0 [25] and would be expected to remain colloidally stable near pH 7.0. In addition, titania is polymorphic and may undergo phase transformations upon aging in aqueous solution or heating during regeneration, whereas titania dispersed on silica spheres has significantly increased thermal stability and catalytic activity properties [26,27]. Pure nonporous titania nanoparticles (2.8 ± 1.4 nm) have been investigated for the recovery of quercetin in plant cells [8]. Quercetin binding to the metal oxide TiO_2 was indicated by a noticeable color shift in the adsorbate. Quercetin, which is light yellow in solution, turns dark orange upon adsorption to a titania surface, corresponding to a readily measurable bathochromic shift [8]. This coloration shift has been employed in TiO_2 modified silica xerogel materials for the spectroscopic detection of a variety of polyphenolic compounds including catechol, quercetin, rutin, gallic, caffeic and ferulic acids [28]. Quercetin has also been demonstrated to stabilize silica from hydrolysis when investigated on a quercetin-functionalized, titania-capped silica, used for mercury chelation and removal [22].

This work examines the interaction of the model antioxidant, quercetin, with modified silica surfaces for the design of silica platforms for flavonoid recovery. Non-porous silica particles, synthesized by the Stöber method [29] with average particle diameters of 450 nm, were functionalized by post-synthesis grafting with decyl groups (using n-decyltriethoxysilane silane) or with a reactive titania precursor (titanium(IV) ethoxide). While non-porous particles do not have the high surface area of mesoporous silica, they allow for the investigation of solute–surface interactions in the absence of steric and diffusional limitations of pores, with evenly accessible exterior particle surfaces for functionalization, solute adsorption and activity assays [30]. The titania precursor concentration was varied to achieve lightly functionalized to near-monolayer coverage of titania on nonporous silica, as verified by a colorimetric titania dissolution assay. The quercetin loading of unmodified, hydrophobically modified, and titania coated particles was measured via solution depletion experiments. The ability to recover the antioxidant activity of quercetin adsorbed on titania-coated silica particles was demonstrated using a 1,1-diphenyl-2-picryl-hydrazyl reduction assay. The results provide a basis for tuning silica surfaces with titania for the recovery of active antioxidants from solution, and can be extended to mesoporous silica platforms with high surface area for the selective separation and recovery of antioxidant compounds.

2. Experimental

2.1. Materials

Ethanol (200 proof), de-ionized ultra purified water and ammonium hydroxide (14.8 M, ACS grade) were purchased from Fisher Scientific. Tetraethyl orthosilicate (TEOS) (98%) was purchased from Acros Organics. n-Decyltriethoxysilane (D-TEOS) was purchased from Gelest, Morrisville PA. Quercetin (≥95%), titanium(IV) ethoxide (TEO, technical grade) and anhydrous toluene (99.8%) were purchased from Sigma–Aldrich. 2,2-Diphenyl-1-picrylhydrazyl (DPPH, 95%) was purchased from Alfa-Aesar.

2.2. Materials synthesis

2.2.1. Stöber particle (SP) synthesis

Stöber particles were synthesized using a modified Stöber method [29]. Particles were prepared by mixing ethanol (58.22 g), concentrated ammonium hydroxide (9.8 mL), DIUF water (10.8 g) and TEOS (5.26 g). Turbidity was seen after 10 min. Particles solutions were stirred for 24 h and the particles were recovered from solution by centrifugation at 5000 rpm. After centrifugation, particles were dried in an oven at 80 °C for 12 h. After drying, particles were washed 3 times in ethanol (20 mL) followed by repeated