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INTRODUCTION

Controlled drug delivery systems are investigated to increase the chemical stability of the drug and to eliminate the side effects caused by the systemic administration via the circulatory system. Functionalized silica and titania xerogels are emerging as a new category of drug host systems. In the treatment of neurological disorders, which occur primarily in the central nervous system, a ceramic device can be implanted directly near a damaged tissue, thus avoiding passage through the blood brain barrier and reducing the necessary drug doses. Valproic acid (VPA), an often used anticonvulsant drug, encapsulated within a titania device has been successfully tested on mice as a therapy for epileptic disorders and is necessary to understand how to control the kinetics of drug release by changing the synthesis parameters.

EXPERIMENT AND RESULTS

Three different samples of TiO_2-VPA were prepared with alkoxide:water molar ratios of 1:4, 1:8, and 1:16, with a constant alkoxide:solvent molar ratio (1:8) at 30 mg VPA/g TiO_2. VPA was dissolved in a mixture of *t*-butanol and water. Titanium *n*-butoxide was added drop-wise, maintaining the mixture under constant stirring at 30 °C. The solution was stirred for 24 h. Finally, alcohol was evaporated and the titania-VPA materials were dried at 30°C for three weeks. The Raman spectra of the powders were recorded with 632.8 nm light by a Jobin-Yvon Labram micro-Raman apparatus. The laser power on the sample was kept below 1 mW by the insertion of optical filters.

The Raman spectra in the 2600-3000 cm^{-1} region (Fig. 1- left) show features due to the stretching C-H vibrations of -CH, $-CH_2$, and $-CH_3$ groups of VPA. In the

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low wave-number region (Fig.1- right), three broad bands typical of amorphous titania at about 200, 430, and 630 cm^{-1} are evident. Pure VPA shows a feature at 314 cm^{-1}. The Raman spectra suggest that the crystals must be smaller than 5 nm for all three water/alkoxide ratios.

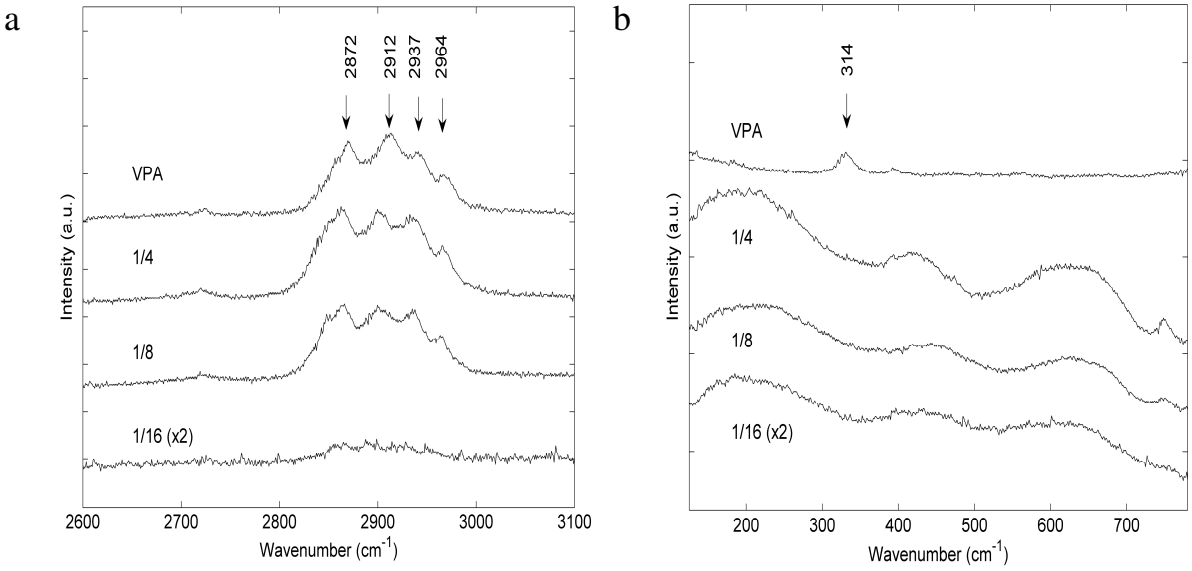

FIGURE 1. (a) High and (b) low frequency Raman spectra in TiO_2-VPA system prepared at different alkoxide:water molar ratios.

Usually, sol-gel TiO_2 synthesized under acid conditions at RT produces a mixture of the three forms of crystalline titania, i.e. brookite, anatase, and rutile: our results suggest that the addition of valproic acid seems to favour the formation of amorphous titania. Hydrogen bridges such as TiO–·HO=C–R could hinder the formation of crystallites.

The surface areas, obtained by BET measurements, are five times larger than those of conventional titania: the increased acidity of the initial sol produces larger pore sizes and areas in the final product, compatible with 5 nm nanosized titania as estimated by Raman measurements. The pore diameter and the surface concentration of hydroxyl groups control the rate of drug release. Titania surface hydroxylation should lead to greater interaction between titania and the valproic acid, thus decreasing the rate of drug release. Increasing the water/alkoxide ratio may lead to a decrease of surface hydroxylation and therefore to a reduction of titania drug interaction and to increasing rate of drug release from the titania reservoir. A further decrease in surface hydroxylation by increasing the water/alkoxide ratio is however accompanied by a decrease in pore size thus reducing the rate of drug release.

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