

## Stability and thermoconversion of vitamin D<sub>3</sub> on aerosil surfaces

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**Abstract.** Stability of vitamin D<sub>3</sub> on aerosil surfaces has been studied by UV- and IR-spectroscopy. The difference in the thermobehaviour of vitamin D<sub>3</sub> in the adsorbed state at low and high surface coverages has been observed and discussed in terms of the competition between vitamin D<sub>3</sub> molecules and their thermoisomers for the adsorption sites.

**Keywords.** Vitamin D<sub>3</sub>; aerosil surfaces; thermostability; thermoisomerization.

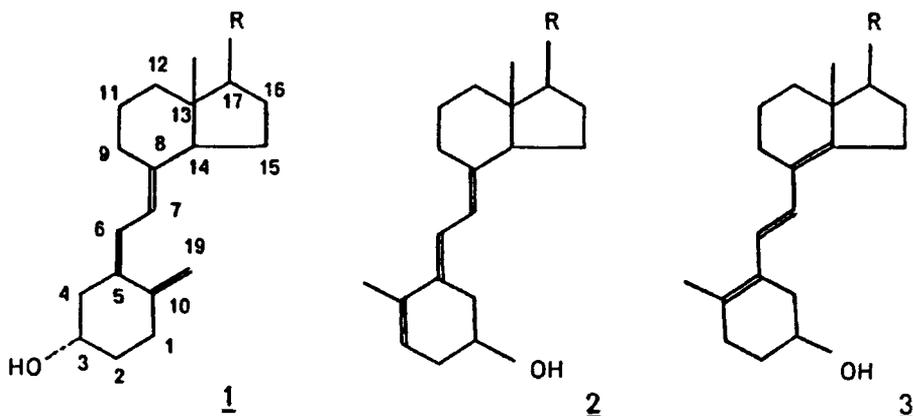
### 1. Introduction

It has long been known (Takahashi and Yamamoto 1969) that vitamin D in powders dispersed in various dispersive solids such as talc, aluminium silicate, calcium phosphate, silica gel etc. that have pronounced surface acidity, is readily isomerized yielding “isoproducts”—isovitamin D and isotachysterol (figure 1). In hexane solution the same reactions can be initiated by iodine and by boron trifluoride (Kobayashi and Adachi 1973).

The comparative studies of vitamin D thermoconversion on the surface of porous and non-porous dispersive SiO<sub>2</sub> (silica gel and aerosil, respectively) at pre-monolayer coverages have revealed a marked difference. In contrast to the reaction on silica gel, the above mentioned isomerizations into “isoproducts” are not observed on non-porous aerosil surfaces (Dmitrenko *et al* 1994). It was supposed that due to unique structural features such as high conformational flexibility (Havinga 1973; Hofer *et al* 1993) and presence of conjugated triene system with exocyclic double bonds, the vitamin D molecule possesses an exceptional sensitivity to spatial factors (which are different for silica gel and aerosil surface) that, in turn, gives rise to the difference in thermobehaviour.

For explaining silica surface effects in the chemistry of adsorbed organic compounds, aerosil is the most appropriate dispersive carrier due to its sufficiently homogeneous surface structure and low content of impurities. This fact, and especially its potential in pharmaceutical applications, make it interesting to study vitamin D stability in such a system in more detail.

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**Figure 1.** Vitamin D<sub>3</sub> (1) and products of its thermoisomerization in presence of acid agents, isovitamin<sub>3</sub> (2) and isotachysterol<sub>3</sub> (3). R=C<sub>8</sub>H<sub>17</sub>.

In this paper, we present the results of IR- and UV-absorption spectroscopic studies on stability of vitamin D adsorbed by aerosil and its thermobehaviour at two cases of surface coverage: low (pre-monolayer) and high (far greater than monolayer).

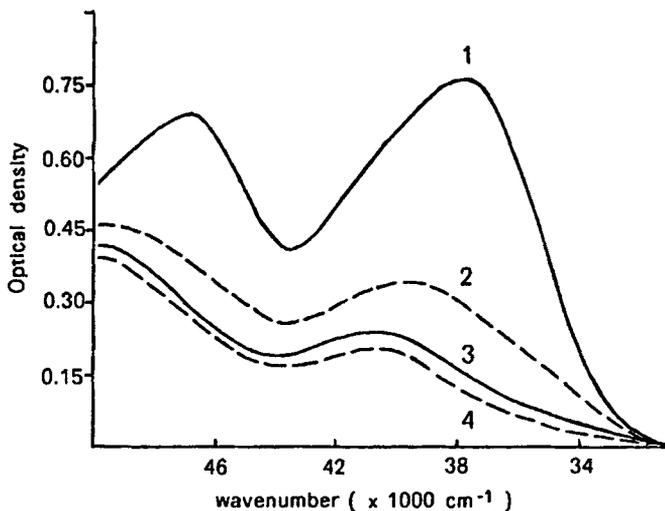
## 2. Experimental

For this work we used A-300 aerosil ("Hlorvinil", Kalush, Ukraine) with a surface area 260 m<sup>2</sup> g<sup>-1</sup>. Thin pressed transparent tablets weighing 10 mg cm<sup>-2</sup> were prepared from the aerosil for further samples preparations. The IR- and UV-spectra were recorded on a IR-75 Specord and UV-Vis Specord spectrophotometers respectively. The vitamin D<sub>3</sub> aerosil samples were prepared by impregnation of aerosil tablets with concentrated solution of vitamin D<sub>3</sub> in CCl<sub>4</sub>. Solution spectrum of vitamin D<sub>3</sub> was recorded in CCl<sub>4</sub> in 0.15 cm pathlength NaCl microcell at concentration 0.01 M. The UV absorption spectrum of adsorbed vitamin D<sub>3</sub> was measured in aerosil-hexane system prepared in 0.1 cm quartz cell by using aerosil tablet and hexane solution of vitamin D<sub>3</sub> at concentration 0.0005 M.

Stability of vitamin D<sub>3</sub> on aerosil surface and its thermoconversion was controlled analogously to the procedure described earlier (Perminova 1990) by recording the UV absorption spectra of transparent product solutions obtained by washing with ethanol of the dried samples.

## 3. Results and discussion

UV absorption spectrum of vitamin D measured in aerosil-hexane matrix is 2 nm red-shifted in comparison with the one in homogeneous solution. In contrast to a number of organic compounds (for example, ketones, Leermakers and Thomas 1965) the shift observed cannot be attributed to the effect of increased microenvironment polarity. In solvents of different polarity vitamin D has the same absorption maximum at 265 nm. Thus, one may assume that the spectral shift obtained in aerosil-hexane matrix is dictated by the changes in the chromophore geometry, which, in turn, can be

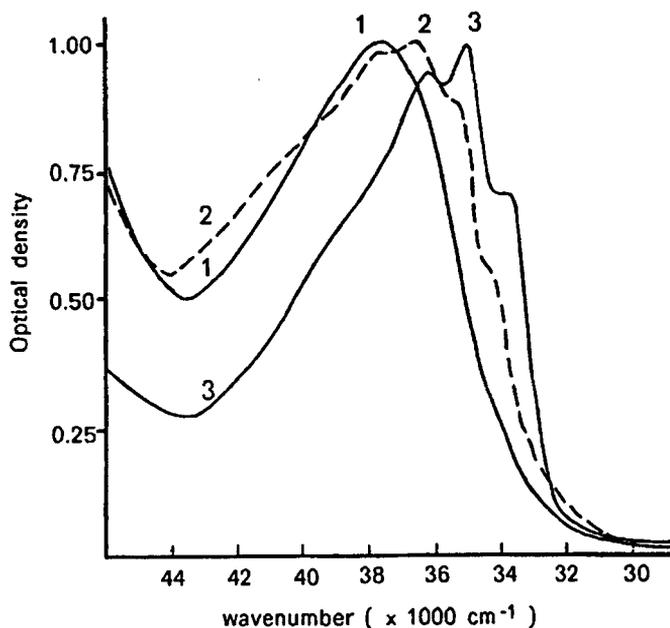


**Figure 2.** UV absorption spectrum of vitamin D<sub>3</sub>(1) and its time-dependent transformation in samples kept at room temperature: (2) after 2 days, (3) after 4 days, (4) after 6 days.

caused by the conformational redistribution in favour of certain conformation due to hydrophobic and electrostatic interactions (Terenetskaya *et al* 1990, 1995). Participation of  $\pi$ -electrons of steroid triene in the formation of adsorption complex also may affect the molecular structure, thereby changing the absorption properties.

Naturally, one may expect vitamin D stability and its thermobehaviour in the adsorbed state to be altered as compared to that in solution. Figure 2 shows the temporal changes in the UV-spectrum of vitamin D adsorbed on aerosil observed when the samples are kept at room temperature. Significant decrease of optical density and a blue shift of the absorption maximum over a period of a few days indicates the dramatic degradation in the vitamin D molecule caused by the aerosil surface. It has also been revealed that evacuation of the samples does not affect vitamin D stability on aerosil and the spectral changes occurring in it are quite similar to that obtained in air. It is extremely likely that the geometry of the adsorption complex, probably a more planar molecular structure, and the close contact of the most reactive part of the vitamin D molecule with surface active sites, favours the degradation reactions.

The change in the vitamin D absorption spectrum at higher temperatures, (up to 100°C) is very nearly the same as that shown in figure 2. The rate of vitamin D degradation increases significantly with increase in temperature. The situation markedly changes when passing from the low coverages used in the previous experiments ( $< 2 \times 10^{-6} \text{ mol g}^{-1}$ , pre-monolayer) to higher ones ( $> 3 \times 10^{-3} \text{ mol g}^{-1}$ ). It has been shown that heating of samples with high adsorbate coverage under vacuum at 90°C over 50 min produces the reaction product mixture with the specifically structured UV absorption spectrum in comparison with pure vitamin D spectrum when washing with ethanol (figure 3, curves 1 and 2, respectively). Washing the sample with CCl<sub>4</sub> leads to a product mixture with a spectrum (curve 3, figure 3) characteristic of a mixture of "isoproducts", (2) and (3) (figure 1). According to Holick



**Figure 3.** Normalized UV absorption spectra of vitamin D<sub>3</sub>(1) and the product mixtures obtained by washing off the vitamin D<sub>3</sub>/aerosil sample after its thermotreating at 90°C during 50 min with ethanol (1) and with CCl<sub>4</sub> (2).

*et al* (1973), isotachysterol (3) has UV absorption spectrum with maxima at 302, 290 and 280 nm whereas isovitamin (2) spectrum is slightly shifted (300, 288 and 278nm). Because ultraviolet absorption spectra for isotachysterol and isovitamin are so similar, it is very difficult to distinguish one isomer from the other. Polymeric OH vibrations at  $3330\text{ cm}^{-1}$  obtained in the IR spectrum in CCl<sub>4</sub> solution indicate the predominance of isovitamin in the CCl<sub>4</sub> product mixture (Takahashi and Yamamoto 1969).

The spectrum represented by curve 2 (figure 3) can be considered as resulting from the overlapping of the individual spectra of 1, 2, 3 and unknown degradation products (absorbing short wave length radiation) in a certain proportion determined by stages of the reaction.

The fact that two products of thermoisomerization (2) and (3), in contrast to vitamin D, can be easily removed from the surface by CCl<sub>4</sub>, indicates that their interaction with the adsorption sites is weaker in comparison to that of vitamin D. This may explain the observed difference in the thermobehaviour of vitamin D on aerosil. At the pre-monolayer coverage, all the vitamin D molecules directly interact with the surface. In contrast, at a sufficiently high coverage, there should be competition for the adsorption sites. On heating, molecules in contact with the surface ("first" layer) undergo conversion into isovitamin and isotachysterol and then are forced out by other more polar molecules of vitamin D. As a consequence of this competition, the accumulation of "isoproducts", 2 and 3, is observed. Returning to the case of low surface coverage, we may assume that all molecules of vitamin D are prone to thermoconversion and fast sequential or simultaneous degradation processes.

### 3. Conclusions

Accumulation of isovitamin D and isotachysterol observed at high adsorbate coverage and attributed to the competition between molecules that have reacted and those that have not, demonstrates significant mobility of vitamin D molecules near the surface.

We believe that the competition for the adsorption sites takes place in the case of vitamin D thermoconversion into "isoproducts" on silica gel surfaces despite the low adsorbate concentrations used (Dmitrenko 1994). Detailed studies on the temperature and pore size effects are in progress.

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