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Synthesis of bioactive materials based on undoped/doped TiO_2 and their nanocrystals with α- / β -cyclodextrins

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Bioactive compounds encapsulating for controlled protection and release is an actuality field, with involved in supra-molecular chemistry, biochemistry, drugs products, cosmetics and food-processing fields. The controlled protection and release of bio-molecules represent a large and actuality field, with application, especially in drugs, cosmetics and food-processing industries. Cyclodextrins were the first studying compounds regarding to complexing behavior and catalytic properties, in order to copy the enzymes. In this paper it was achieved the synthesis of titanium dioxide undoped and doped with metallic ions, silver and iron, through sol-gel method, and also their complexation with α- / β-cyclodextrins through co-crystallization method. The obtained nanomaterials were characterized by X-ray diffraction (XRD), scanning electron microscopy (SEM), energy dispersive X-ray analysis (EDAX), thermogravimetry (TG) and Fourier transform infrared spectroscopy (FT-IR).

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1. Introduction

The complexation of anorganic or organic compounds (as guest molecules) with other molecules which contain cavities, channels or pockets (host molecules) is a very interesting field due to the special properties of the complexes: protection and controlled release of bioactive compounds, obtaining water soluble formulations of hydrophobic or water insoluble compounds, enhancing the targeting of pharmaceutically active compounds. The chemical bases of these processes are known as "host-guest chemistry" or supramolecular chemistry [1].

Cyclodextrins are ones of the first compounds studied as guest molecules and as enzyme mimetic in catalytic processes. They are cyclic oligosaccharides and the representative such compounds are α- and β-cyclodextrin, which are composed by six or seven α-(1→4) bonded glucopyranose moieties [1-3].

The complexation of cyclodextrins with metallic oxides is hard to do due to the dimensions of the inorganic particles, especially metallic oxides [4-6], which must be lower than the inner cavities of cyclodextrins (under 2 nm). On the other hand, metal-organic compounds can be easily encapsulated due to the possibility of hydrophobic interaction between organic moieties of guest compound and the hydrophobic cavity of cyclodextrin [7, 8].

The number of studies on the complexation of titanium dioxide with cyclodextrins is very low, some of them [9] trying to obtain anatase-cyclodextrin nanoparticles (with the dimensions of particles of tens nanometers), using the hydrolysis of tetrabutyltitanate and coordination of the resulting species in the presence of cyclodextrin. Other studies regarding the titanium dioxide are performed in order to enhance the photo-stabilizing and fluorescent properties [10-13].

In this study we try to obtain titanium dioxide/α- and β-cyclodextrin nanoparticles by co-crystalization of micronized TiO_2 undoped or doped with metallic ions, like Au^+, Ag^{2+}, Fe^{2+}. The resulting complexes are previsioned to have enhanced properties (like bioavailability and bioactivity).

2. Materials and Method

2.1 Materials

Undoped and doped titanium dioxide nanocrystals were synthesized by the sol-gel route, using the precursors: titanium isopropoxide, isopropyl alcohol, distilled water, nitric acid, gold (III) chloride trihydrate, silver nitrate and ferrous nitrate. 5 ml of titanium isopropoxide (in drops) were mixed with 30 ml of

isopropyl alcohol, under continuous stirring. After a few minutes of stirring, distilled water was added, continuously controlling the solution pH with nitric acid in order to avoid the precipitation. In the case of Au, Ag, Fe-doped TiO_2 ions, after the adjustment of the pH (2.5 for Au, Ag and 5 for Fe) the previously prepared solutions, precursors for doping were added under continuous stirring. In both cases, the gel was dried and washed in order to remove the secondary reaction products. The calcination was achieved in the oven, at a temperature of 250ºC for undoped TiO_2 and 500ºC for Au, Ag, Fe -doped TiO_2. The obtained materials were characterized by X-ray diffraction (XRD), scanning electron microscopy (SEM) and energy dispersive X-ray analysis (EDAX).

α- and β-Cyclodextrin used for co-crystallization with the TiO_2 were obtained from Fluka Chemie AG and were reagent grade.

2.2 Co-crystallization of titanium dioxide with cyclodextrins

α- or β-Cyclodextrin was dissolved in 1 ml water at 50ºC in a thermocontrolled minireactor equipped with magnetic stirrer and then the nanoparticles of TiO_2 undoped or doped with metallic ions were dispersed in the cyclodextrin solution in 15 minutes in a mass ratio of 0.5 to 1.5 relatively to cyclodextrin. The suspension was then cooled in 30 minutes at room temperature, when the cyclodextrin from solution crystallize on the TiO_2 nanoparticle surfaces. The co-crystallization was perfected at 5ºC for 12 hours. The complex suspension was filtered and dried at room temperature. The quantities and yields of crystallization are presented in Table 1.

2.3 Scanning electron microscopy (SEM) and EDAX

SEM analysis was performed in order to evaluate the morphology and dimensionality of crystals. An Inspect S scanning electron microscopy device was used in this experiment. EDAX analysis was performed for identification of the ions presence in titanium dioxide structure.

Table 1. Quantities and yields for co-crystallyzation of α- and β-cyclodextrin with undoped and doped TiO_2.

No	Complex type*	Code	m_{CD} (g)	m_{TiO2} (g)	CD:TiO_2 (w/w)	Yield (%)
1	TiO_2/aCD	Tn_aCD01	0.054	0.025	0.5	54.3
2	TiO_2/aCD	Tn_aCD02	0.054	0.05	1.0	64.13
3	TiO_2/aCD	Tn_aCD03	0.054	0.075	1.5	63.33
4	TiO_2/bCD	Tn_bCD01	0.067	0.034	0.5	56.14
5	TiO_2/bCD	Tn_bCD02	0.067	0.067	1.0	65.67
6	TiO_2/bCD	Tn_bCD03	0.067	0.102	1.5	72.19
7	TiO_2-Au/aCD	TAu_aCD01	0.054	0.025	0.5	64.18
8	TiO_2-Au/aCD*	TAu_aCD02	0.054	0.05	1.0	-
9	TiO_2-Au/aCD*	TAu_aCD03	0.054	0.075	1.5	-
10	TiO_2-Au/bCD	TAu_bCD01	0.067	0.034	0.5	59.7
11	TiO_2-Au/bCD	TAu_bCD02	0.067	0.067	1.0	61.87
12	TiO_2-Au/bCD*	TAu_bCD03	0.067	0.102	1.5	-
13	TiO_2-Ag/aCD	TAg_aCD01	0.054	0.025	0.5	55.57
14	TiO_2-Ag/aCD	TAg_aCD02	0.054	0.05	1.0	59.23
15	TiO_2-Ag/aCD	TAg_aCD03	0.054	0.075	1.5	62.17
16	TiO_2-Ag/bCD	TAg_bCD01	0.067	0.034	0.5	43.27
17	TiO_2-Ag/bCD	TAg_bCD02	0.067	0.067	1.0	63.36
18	TiO_2-Ag/bCD	TAg_bCD03	0.067	0.102	1.5	83.43
19	TiO_2-Fe/aCD	TFe_aCD01	0.054	0.025	0.5	60.76
20	TiO_2-Fe/aCD	TFe_aCD02	0.054	0.05	1.0	70.77
21	TiO_2-Fe/aCD	TFe_aCD03	0.054	0.075	1.5	76.59
22	TiO_2-Fe/bCD	TFe_bCD01	0.067	0.034	0.5	58.91
23	TiO_2-Fe/bCD	TFe_bCD02	0.067	0.067	1.0	65.45
24	TiO_2-Fe/bCD	TFe_bCD03	0.067	0.102	1.5	92.31

* aCD – α-cyclodextrin; bCD – β-cyclodextrin; TiO_2 – undoped titanium dioxide; TiO_2-Au – Au^+ doped titanium dioxide; TiO_2-Ag – Ag^+ doped titanium dioxide; TiO_2-Fe – Fe^{2+} doped titanium dioxide; TAu-aCD02,3 and TAu-bCD03 could not be performed

2.4 Thermogravimetry analysis (TG)

In order to evaluate the behavior of the TiO_2-cyclodextrin complexes at increasing the temperature up to the decomposition of cyclodextrin a thermogravimetric analysis was performed, using a TG 209 NETZSCH apparatus, with a temperature program of 20-550°C and a heating ratio of 10°C/min. All determinations were performed under nitrogen atmosphere.

2.5 FT-IR analysis

Infrared spectroscopy with Fourier transform (FT-IR) was achieved for the obtained nanoparticles using a JASCO 430 apparatus, the samples being dispersed in KBr.

3. Results and discussion

The X-ray patterns (Fig.1) present the crystallization as *anatase* form of the undoped / Au, Ag, Fe - doped TiO_2, even if the calcination temperatures for the TiO_2 doping surpass the values of 250ºC. From the diffraction spectra it is noticed that the dopants did not present separate peaks, which means that they are distributed uniformly in the crystalline network.

From the surface morphology (SEM) it can be observed that the TiO_2-Au, TiO_2-Ag and TiO_2-Fe nanospheres dimensions range between 20-40 nm (Figs. 2a, 2b, 2c). EDAX analyses (Figs. 2d, 2e, 2f) confirm the presence of Au, Ag, Fe dopants in titanium dioxide structure.

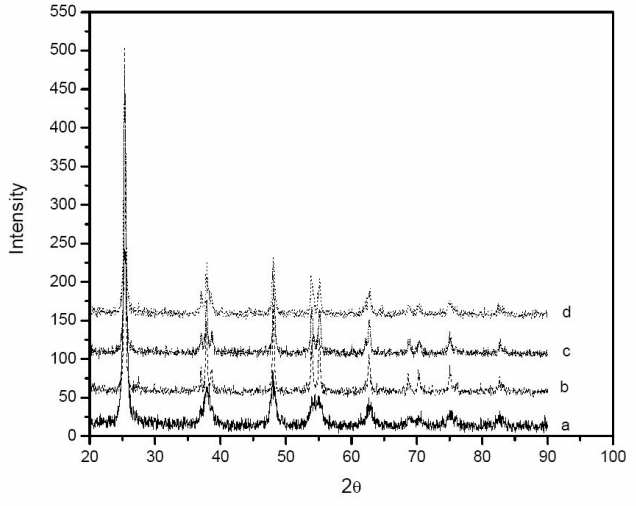


Fig.1. X-ray patterns for TiO_2 undoped (a) and doped TiO_2-Ag (b), TiO_2-Fe (c), TiO_2-Au (d).

The study on the complexation/co-crystallization of titanium dioxide undoped or doped with metallic ions (gold, silver, and iron) with α- and β-cyclodextrin revealed that the yield are higher in the case of β-cyclodextrin (up to 92.3%) but not meaningful correlations were observed according to the type of doping metallic ions. Thus, for the Tn-aCD complex the yield was 54.3-64.1%, for the higher TiO_2/aCD mass ratio the yield value being very close (63-64%). For the undoped TiO_2/bCD complex the yield was higher (56-72%) and a clear correlation between the yield and mass ratio of the components was observed

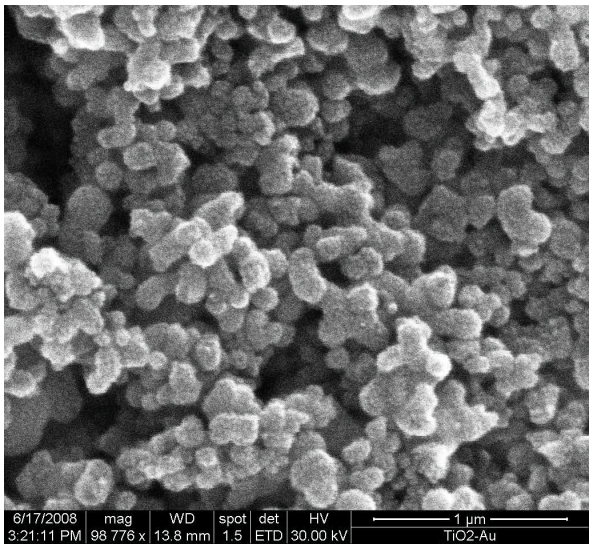
TIn all cases the yields of complexation of doped TiO_2 with cyclodextrins were higher comparatively with the case of undoped titanium oxide. Thus, in the gold case, the complex with aCD was obtained with a yield of 64.2%, and in the case of bCD, this was lower. The situation is inversed in the case of silver and iron ions use for TiO_2 doping. For the TiO_2-Ag/aCD complexes the yield was in the range of 55.5-62.2% and for the same case with bCD this was in the range of 43.3-83.4%. Similar situation is observed in the case of TiO_2-Fe/aCD and TiO_2-Fe/bCD, the yield being 60.8-76.6% for the first case and 58.9-92.3% for the second one.

The SEM analysis of the commercial cyclodextrins and of the undoped or doped TiO_2/cyclodextrin nanoparticles revealed that the morphology of undoped TiO_2/α- or β-cyclodextrin was generally acicular, and for the corresponding complexes with doped TiO_2 this was rhomboidal. The main dimensions of the crystals were in the range of tens to hundreds nanometers.

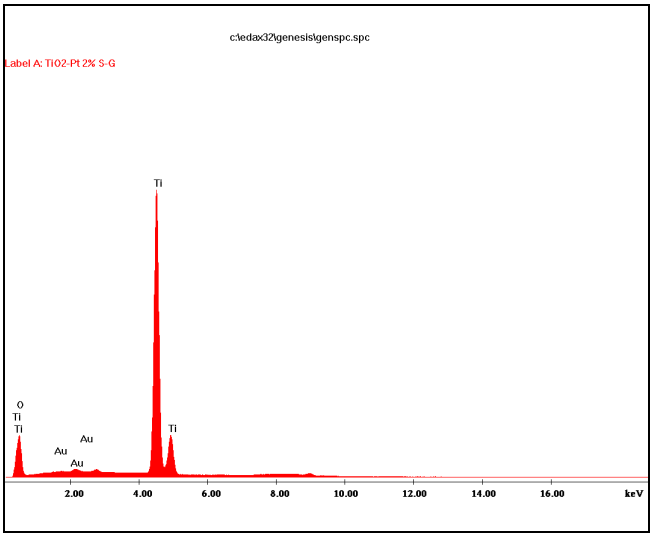
Thus, the commercial β-cyclodextrin had irregular crystals with the dimensions of tens micrometers, much higher than the undoped TiO_2/α- or β-cyclodextrin complexes, with the main dimension of hundreds of nanometers (Fig. 3).

In the case of TiO_2-Au/aCD complex the morphology of crystals was similar to the case of undoped TiO_2, but the crystals were more conglomerated. The morphology of TiO_2-Au/bCD was more different, more uniform, with lower dimensions, polyhedral shaped (figure 4). The same morphology was observed in the case of TiO_2-Ag/CD and TiO_2-Fe/CD.

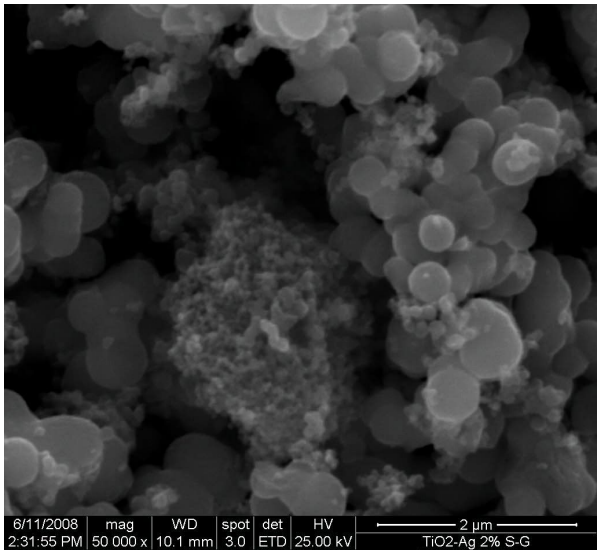
EDAX analysis revealed that the complex of cyclodextrins with undoped TiO_2 and those doped with gold has higher concentrations of Ti (and lower concentration of cyclodextrins), especially in the case of α-cyclodextrin, probably due to the higher solubility of this cyclodextrin in water (Fig. 5).



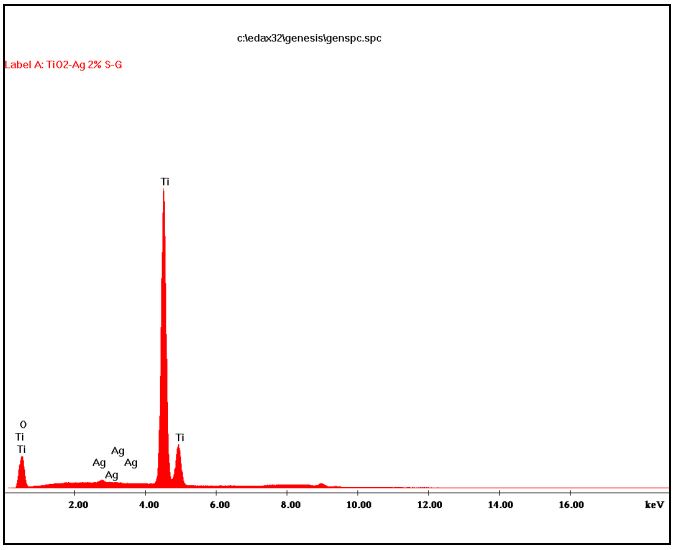
a



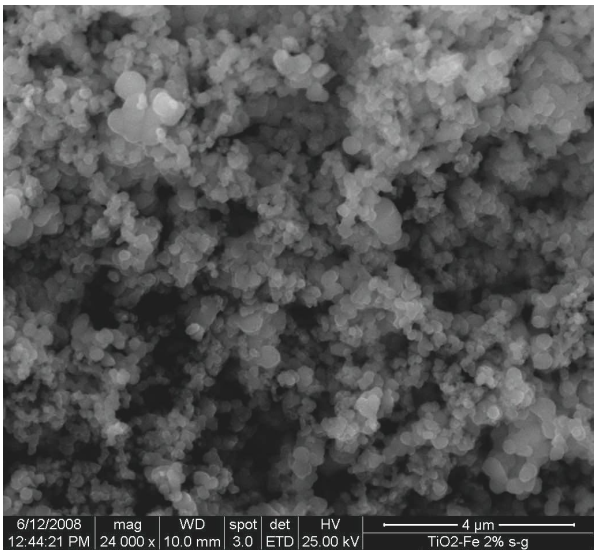
d



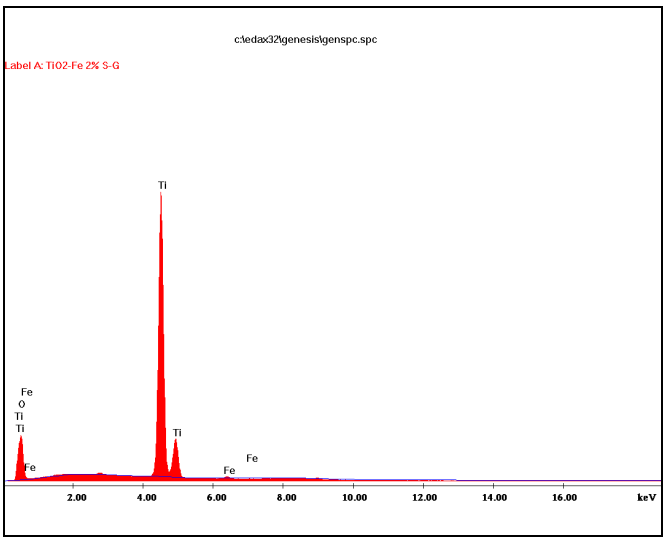
b



e

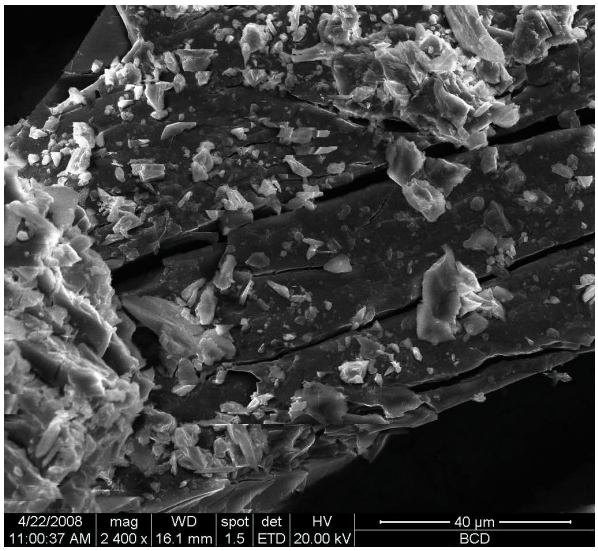


c



f

Fig. 2. SEM morphology for TiO_2-Au (a), TiO_2-Ag (b), TiO_2-Fe (c) and EDAX analysis for TiO_2-Au (d), TiO_2-Ag (e), TiO_2-Fe (f).



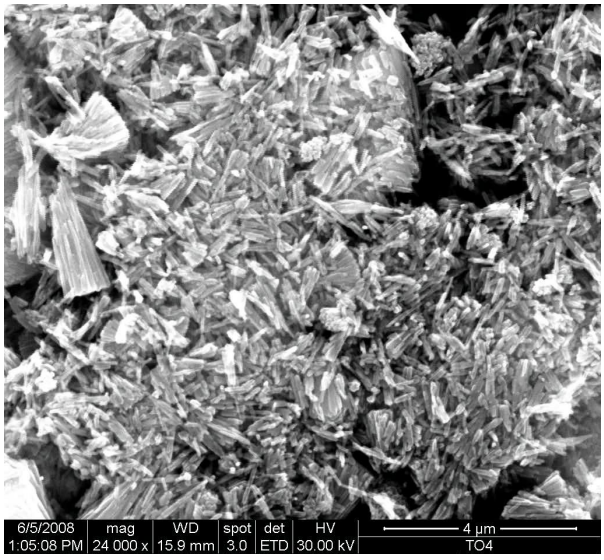
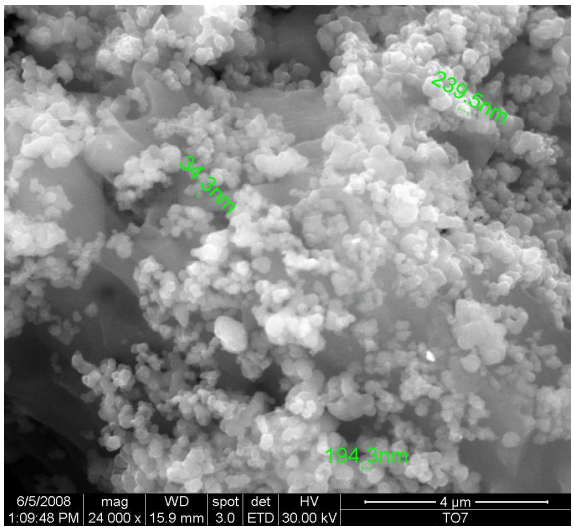


Fig. 3. SEM analysis of the commercially β-cyclodextrin (2 400× magnitude; left) and of the undoped TiO_2/bCD complex (24 000× magnitude; right)



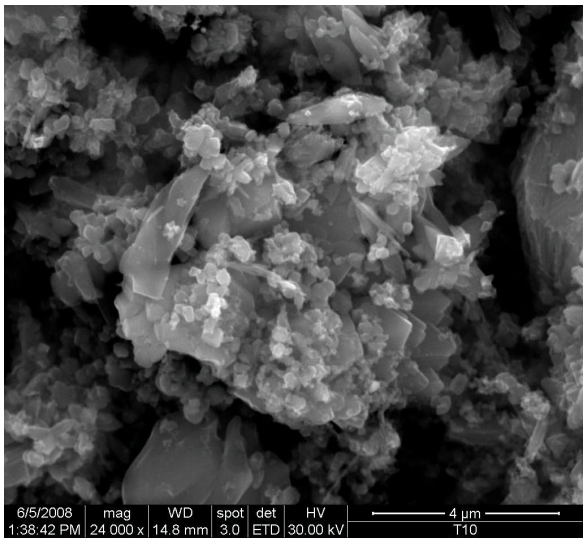


Fig. 4. SEM analysis of the TiO_2-Au/bCD complex (24 000× magnitude; left) and of the TiO_2-Ag/aCD complex (24 000× magnitude; right)

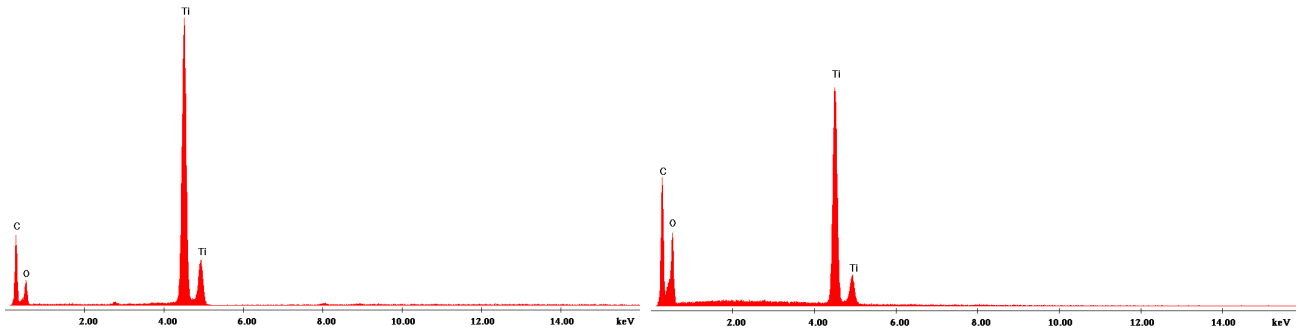
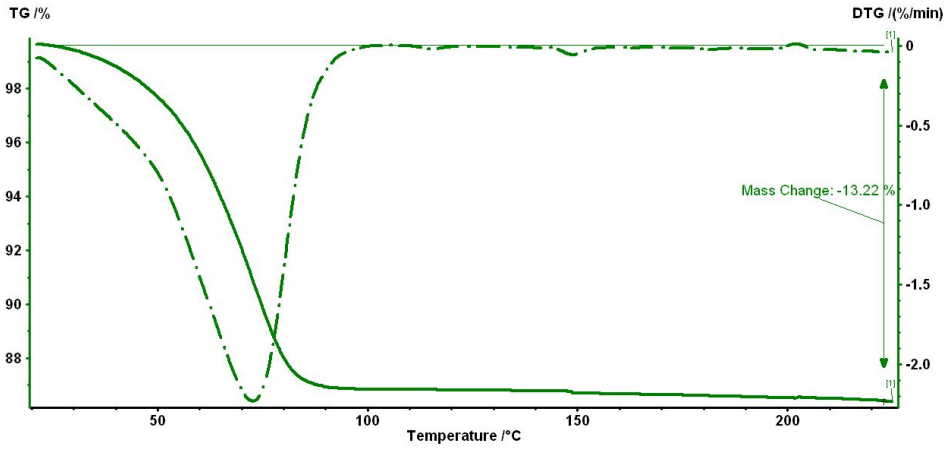
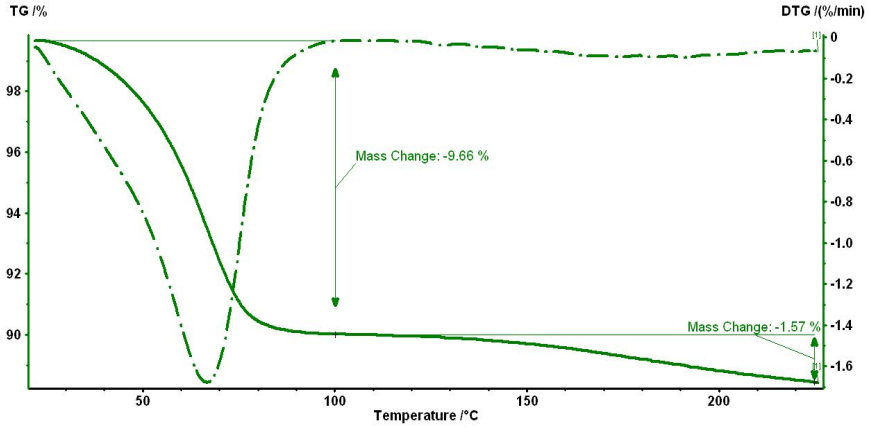


Fig. 5. EDAX analysis of the undoped TiO_2/aCD (left) and TiO_2-Au/bCD complex (right)

Thermogravimetric and FT-IR analyses of the commercially cyclodextrins and their complexes with undoped or doped TiO_2 revealed that the behavior and spectrum are similar. This can be explained by the stability of titanium dioxide and only the mass loss from the TG analysis is lower in the case of complexes (Figs. 6 and 7).

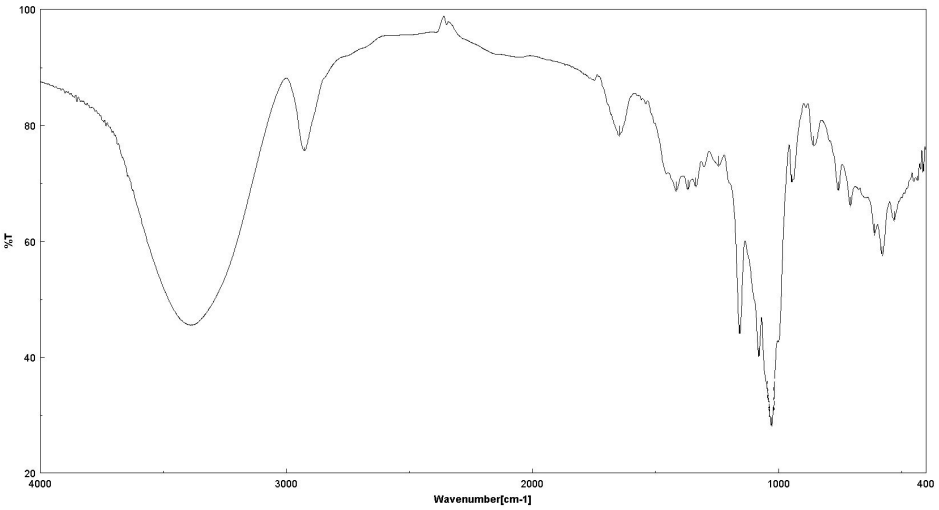


a)

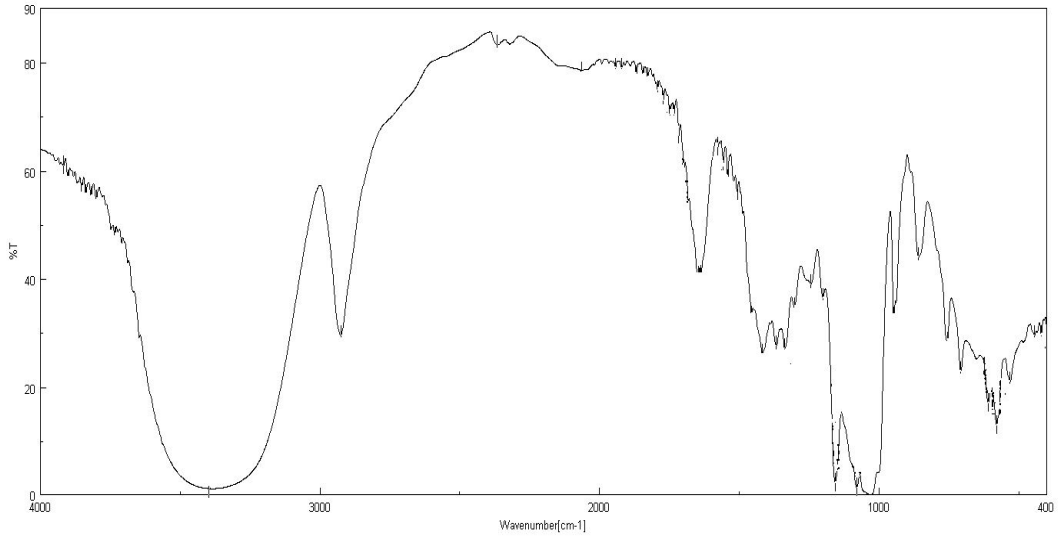


b)

Fig. 6. TG analysis of the β-cyclodextrin (a) and for the TiO_2-Au/bCD complex (20-225ºC) (b)



a



b

Fig. 7. FT-IR analysis of the β-cyclodextrin (a) and TiO_2-Au/bCD complex (b).

4. Conclusions

The undoped and doped TiO_2 nanocrystals used in this experiment, exhibit *anatase* by crystallization. The TiO_2-Au, TiO_2-Ag and TiO_2-Fe nanospheres, show dimensions in the range 10-20 nm.

The study regarding the preparation and analysis of undoped and doped titanium dioxide/α- and β-cyclodextrin complexes indicate that the morphology of the crystals are acicular in the case of gold doped titanium dioxide/cyclodextrin complexes or rhomboidal/polyhedral shaped in the case of silver or iron doped titanium dioxide/cyclodextrin complexes. The dimensions of particles/crystals are submicron (from tens to hundreds nanometers) and they can be classified as nanoparticles. The organic/inorganic mass ratio is lower in the case of undoped titanium dioxide and higher (but subunitary) in the other cases and the possibility to enhance the bioavailability of doped titanium dioxide is increased.

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