

## Nanoporous TiO<sub>2</sub>: an effective carrier for the development of innovative drug delivery systems

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In the drug delivery formulation the choice of the carrier and of the procedure adopted for its synthesis is a determinant step. The investigations reported in literature deal with either polymeric materials [1] and/or inorganic oxides, such as nanoporous alumina, porous silica, nanostructured ceramics [2] and many synthetic approaches are available, among which: template method [3] and sol-gel [4]. Increasing attention has been recently devoted to titanium-based drug delivery systems (DDS) [5, 6]. Titanium, titanium based alloys and TiO<sub>2</sub> systems are among the most common implant materials (such as cardiovascular stents, joint replacements and dental implants) used in the human body because of their desirable mechanical strength, low density, excellent resistance to corrosion and lack of cytotoxic effects. Moreover, titania features can be opportunely modulated by the wise selection of the synthetic approach. The addition of controlled drug delivery properties to the well known features of titanium-based materials could expand its potential applications in the biomedical field, and this represents a very attractive research outcome. The goal of this work was the development of a reliable procedure for the synthesis of nanostructured titania materials and its application in the design of titania-based drug delivery systems. A series of titanium oxides was prepared by a surfactant template method (STM) and used as carrier to sustain the release of ibuprofen, chosen as model drug. The STM procedure provides an efficient method to prepare TiO<sub>2</sub> matrices with both high surface area (if compared with that obtained with the traditional synthetic approach) and a controlled nanoporous texture. Some parameters of the synthetic procedure were varied: pH, surfactant, ageing and calcination temperature. In particular, nanoporous matrices have been synthesized by using traditional surfactant [7] as: co-polymer (P-123) or ionic surfactant (hexadecyltrimethylammonium bromide) or biocompatibles and biodegradables oligomers of natural origin, such as chitosan. In this last way it is possible to improve the final performance of DDS, or to increase their biocompatibility and/or biodegradability, to adjust the hydrophilicity and to introduce specific surfaces functionalities. The physico-chemical nature and the structure of the carriers has been investigated by means of N<sub>2</sub> physisorption measurements, thermal analyses (TG/DTA), FT-IR analyses, transmission electron microscopy measurements (TEM), X-ray diffraction analysis; the drug delivery behaviour was tested in vitro in four different physiological solutions (simulating the gastro-intestinal tract) in order to analyze the behaviour of the TiO<sub>2</sub>-based systems if formulated as oral DDS. The synthetic parameters and in particular the nature of surfactant play a central role in directing the features of the TiO<sub>2</sub> matrix and in the performance of the final DDS. The optimized approach turns out to be a good alternative to the classical methods employed to prepare efficient TiO<sub>2</sub>-based drug delivery systems.

**References.** [1] Efentakis M., Politis S. (2006): *Europ. Polym J.*, **42**, 1183-119; [2] Arcos D., Vallet-Regí M. (2010): *Acta Biomater.*, **6**, 2874-2888; [3] Izquierdo-Barba I., Martinez A., Doadrio A. L., Perez-Pariente J., Vallet-Regí M. (2005): *Eur. J. Pharm. Sci.*, **26**, 365-373; [4] Contessotto L., Ghedini E., Pinna F., Signoretto M., Cerrato G., Crocellà V., (2009): *Chem. Eur. J.*, **15**, 12043-12049; [5] Uddin M.J., Mondal D., Morris C. A., Lopez T., Diebold U., Gonzalez R. D. (2011): *Appl. Surf. Sci.*, **257**, 7920-7927; [6] M. Signoretto, E. Ghedini, V. Nichele, F. Pinna, V. Crocellà, G. Cerrato (2011): *Micropor. Mesopor. Mater.*, **139**, 189-196 [7] Ghedini E., Nichele V., Signoretto M., Cerrato G. (2012): *Chem. Eur. J.*, **18**, 10653-10660.