LASER SYSTEMS FOR SYNTHESIS OF NANOSTRUCTURED MATERIALS FROM LIQUID AND GASEOUS PRECURSORS FOR BIOMEDICAL APPLICATIONS

ERNEST POPOVICI1, *, ION NICOLAE MIHAILESCU1, CARMEN RISTOSCU1, GABRIELA DEMIAN2

1National Institute for Lasers, Plasma and Radiation Physics (INFLPR)
Atomistilor Str. 409, P.O. Box MG-36, cod 077125, Bucharest, Romania
2University of Craiova, Faculty of Mechanics, Calea Bucuresti Str., No 107, 200512 Craiova, Dolj, Romania

(Received April 23, 2013)

The wide interdisciplinary world of Nanotechnology and Nanoscience has experienced a fast development during the past years. One exciting subject is the possibility of using a large kind of nanoscale materials for biomedical applications due to their special characteristics. We list here some nanostructured materials, such as TiO2, iron based, SiO2, SiC, which can be synthesized by laser pyrolysis with an elaborated synthesis set-up. New developments of methods and studies undertaken allowed for the targeting of nanoparticles with characteristics that permitted an optimal use in biomedicine. TiO2 nanoparticles and nanocomposites can be used as vehicles for delivery of drug payloads, biomedical and histological imaging of nanoparticles, diagnosis, drug delivery, detection (imaging), etc. The innovation consists in the use of liquid precursors, such as TTIP, TEOS, Fe(C5H5)2, Fe(CO)5, etc., as well as gaseous SiH4. A new laboratory with adequate infrastructure became functional. We explored the possibilities to synthesize by single step laser pyrolysis technique of magnetic nanoparticles and/or composite materials and their characterization by SEM, EDS, XRD, TEM and FTIR.

Key words: Laser pyrolysis, nanoparticles, nanostructured materials, nano-biomedical applications, biomaterials.

INTRODUCTION

The energy required to process substances under different forms of aggregation by laser pyrolysis is provided by laser beam. The beam characteristics (temporal and/or spatial) are modified through an optical transport and processing system, so that the foreseen beam-matter interaction to produce the

* Corresponding author (E-mail: popovici05@yahoo.co.uk)

ROM. J. BIOCHEM., 50, 1, 53–63 (2013)
physicochemical desired effects (1-3). Laser pyrolysis fully exploits the special properties of the laser beam, such as monochromaticity, power density, directionality (4). It is thus possible to obtain high purity powders without material contacts with the reaction chamber walls. Dimensional distribution of nanopowder is controlled and it is generally accepted that dimensions in the range 0.2–100 nm can be produced. Synthesis takes place in a tightly controlled geometrical space with predetermined and continuous physical (pressure, temperature, speed, energy, power density, absorption) and chemical (aggregation state of precursors, composition) parameters. The nucleation of molecules is homogeneous and a very accurate growth control can be ensured via the residence time of nanoparticles. Pyrolysis can be applied under conditions and by adaptation of the set-up to process corrosion precursors (SF₆), pyrophoric, explosive (SiH₄, C₂H₂, C₂H₄), Toxic (Fe(CO)₅), TTIP (Titanium tetraisopropoxid), TEOS (tetraethyl orthosilicate), Fe(C₂H₅)₂, and so on. Precursors may include substances that absorb the laser beam energy under control. The influence of each parameter is important and must be coordinated with the reaction chamber configuration and with other secondary parameters (optics, Ar flow, confinement gas nature and temperature, and so on).

Laser pyrolysis was initiated in the early ‘80s, in MIT laboratories (5-7). One can indentify three generations of laser synthesis systems, and their development required the development of principles and rules in design as well as in implementation and operation phase (8, 9). In terms of applicability and economic value, the industrial scalability (10-12) of an installation or laser pyrolysis system is of great importance. Comparisons with other methods of synthesis of nanostructured powders must be also considered. Equipments targeting industrial scaling pyrolysis were designed and built. Nevertheless, the methods using liquid precursors processed by bubbling, US dispersion and aerosols were not successful, mainly because of their poor reproducibility (13). Nanostructured powders could be synthesized with a new set-up and developed principles and methods, e.g., based on Fe (mainly because of the magnetic properties), Si and Ti. The nanopowders based on iron in form of oxides (Hematite – α-Fe₂O₃, magnetite – Fe₃O₄, Maghemite – γ-Fe₂O₃) are perhaps the most important in terms of biomedical applications. The synthesis methods are different (14) and they should allow predetermination of dimensionality, morphology and composition to be harmonized with specific subsequent applications in biochemistry (8). The most important property is the superparamagnetism at normal ambient temperature (10-40° C). Biomedical applications in general, and in particular of nanostructured magnetic materials based on Fe are possible in vivo and in vitro, respectively. Among therapeutic applications, we mention hyperthermia (increase of local body temperature in conjunction with other cancer treatments) drug delivery, diagnostic applications (MRI contrast enhancement) and/or indication of circulatory status (15, 16); magnetorelaxometry, for instance, is an example of in vitro diagnostic applications.
An interesting application is the synthesis of composite nanopowders, such as Fe@SiO₂, Fe@C, etc. Composites were synthesized by bubbling of aerosol using different precursors (17-21). SiC nanopowders were synthesized starting from SiH₄ (22, 23), a pyrophoric and exothermic gas. Biomedical applications of ceramic and composite nanoparticles are increasingly studied, resulting in important applications (more than 20 nanoparticles types are clinically used in various therapies) (24, 25). Several ways of implementation of the different nanoparticles after appropriate functionalization should be highlighted. Magnetic nanoparticles for drug delivery encapsulated to ensure biocompatibility can be used in bio-ferrofluids, which are appropriate to transport proteins, antibodies, and drug substances (26-31). TiO₂ nanoparticles (32, 33) are commonly used in active and passive tumor targeting in chemotherapy, MRI imaging, optical imaging and drug delivery, due to their surface properties (34, 35).

We report herewith a new principle of laser pyrolysis synthesis using liquid precursors, such as TTIP, TEOS, Fe(CO)₅ and SiH₄. To the difference of bubbling or aerosol dispersion by ultrasound, we ensured flow control in a stable and pure liquid phase.

MATERIAL AND METHODS

Fe and Ti based NPs synthesized by laser pyrolysis from liquid precursors

The method consists in the control of the precursors mass of in liquid phase, followed by thermal processing it to bring the in gaseous phase, and introduction into the reaction chamber through an injector. To study the synthesis process, which largely depends on the evolution of temperature in the reaction zone, one supposes that it is quasi-stationary when the synthesis parameters reached stable values. The principle of liquid precursor synthesis in gas phase is different from bubbling, aerosol or U.S. dispersion. Processing methods of liquid precursors are working in gas-vapor phase. This vapor state (Fig. 1a) implies a physical process in two-phases (vapor and gas), which is difficult to control. Under the action of photon energy transferred by the laser beam, the liquid is completely vaporized at boiling temperature of the precursor in a fully isothermal process. It results a temperature increase with a high gradient (Fig. 1b). The technological difficulty was solved in the actual set-up by separating the evaporation process from the chemical synthesis. For this kind of substances, synthesis occurs in gaseous phase, which is subject to physical and chemical transformations in the gas phase materials. The developed set-up is schematically depicted in Fig. 2. The system is very tight, ensuring protection of the environment against toxic substances. The temperature of processed substances is strictly controlled. The control and monitoring systems ensure synthesis reproducibility with an accuracy of ± 5%. The process is automatically controlled and can be interrupted under command only. The evaporator was designed for liquid precursor vaporization above the boiling temperature and has the following functions: preheat of gases (carrier and
sensitizer), vaporization of liquid substances inhibiting any leak of toxic and hazardous gases, temperature measurement and control by a thermostat, thermal insulation from the environment, and electrical insulation. Control system and process temperature maintenance throughout the operating system by multipoint monitoring ensure an accuracy of ± 10°C from a preset value. It also permits the injected fluid temperature to be by default 30°C over the substance boiling temperature of the liquid component with the lowest temperature of vaporization.

Fig. 1. – (a) Phase diagram of p and t parameters of precursor, (b) temperature diagram on the synthesis zone.

Fig. 2. – Schematic representation of the installation using liquid precursor.
We used TTIP and Fe(CO)₃ as liquid precursors for the synthesis of TiO₂ and Fe₂O₃. All the initial parameters will be refined depending on the destination of the nanostructured powders, according to the acquired feedback. A major novelty is related to the configuration of the synthesis chamber, which requires proper adjustment of parameters. Experimental conditions are collected in Table 1. The ratio of Anatase/Rutile phases and evolution of nanostructured TiO₂ powders dimensionality resulted by interpretation of the XRD patterns (Table 2). The comparison between samples was performed before and after heat treatment applied to remove C (Table 3). This is an auxiliary process, which seeks to oxidize the carbon contaminants. During synthesis, carbon is attached in form of carbides and originates from the sensitizer (C₂H₄) used for the enhancing of energy transfer.

**Table 1**

**Experimental parameters used for the synthesis of TiO₂ or SiC nanoparticles**

<table>
<thead>
<tr>
<th>NO.</th>
<th>S V N T</th>
<th>PARAMETERS</th>
<th>VELOCITY</th>
<th>INJ</th>
<th>LASER BEAM</th>
<th>PR</th>
<th>t</th>
<th>d</th>
<th>(SEM)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>P</td>
<td>TTI/ SiH₄</td>
<td>Ar</td>
<td>Ar</td>
<td>Ar</td>
<td>Ar</td>
<td>C₂H₄</td>
<td>C₂H₂</td>
</tr>
<tr>
<td>1</td>
<td>Ti-II</td>
<td>10</td>
<td>270</td>
<td>0.4</td>
<td>2</td>
<td>3</td>
<td>5</td>
<td>3.6</td>
<td>18/1.5</td>
</tr>
<tr>
<td>2</td>
<td>Ti-IV</td>
<td>50</td>
<td></td>
<td>0.4</td>
<td>2</td>
<td>3</td>
<td>3</td>
<td>3</td>
<td>127/12/27</td>
</tr>
<tr>
<td>3</td>
<td>SiC-16</td>
<td>0.3</td>
<td>-</td>
<td>-</td>
<td>103.8</td>
<td>88.28</td>
<td>63/55</td>
<td>63/62</td>
<td>174.5</td>
</tr>
<tr>
<td>4</td>
<td>SiC-19</td>
<td>0.5</td>
<td>-</td>
<td>-</td>
<td>0.24</td>
<td>5</td>
<td>174.5</td>
<td>5</td>
<td>127/12/27</td>
</tr>
</tbody>
</table>

**Table 2**

Anatase/Rutile phases ration and dimensionality evolution

<table>
<thead>
<tr>
<th>Sample</th>
<th>Calc temp</th>
<th>A (%)</th>
<th>R (%)</th>
<th>Anatase</th>
<th>Rutile</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>a (Å)</td>
<td>c (Å)</td>
<td>Dₐ (nm)</td>
<td>a (Å)</td>
</tr>
<tr>
<td>Ti-II</td>
<td></td>
<td>3.77</td>
<td>9.46</td>
<td>10.9</td>
<td>4.55</td>
</tr>
<tr>
<td>Calc</td>
<td>480°C</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ti-IV</td>
<td></td>
<td>3.77</td>
<td>9.46</td>
<td>10.9</td>
<td>4.55</td>
</tr>
<tr>
<td>Calc</td>
<td>480°C</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>94.4</td>
<td>3.77</td>
<td>9.46</td>
<td>10.9</td>
<td>4.55</td>
</tr>
<tr>
<td></td>
<td>94.7</td>
<td>3.76</td>
<td>9.45</td>
<td>13.0</td>
<td>4.55</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

The ratio of Anatase/Rutile phases and evolution of nanostructured TiO₂ powders dimensionality resulted by interpretation of the XRD patterns (Table 2). The comparison between samples was performed before and after heat treatment applied to remove C (Table 3). This is an auxiliary process, which seeks to oxidize the carbon contaminants. During synthesis, carbon is attached in form of carbides and originates from the sensitizer (C₂H₄) used for the enhancing of energy transfer.
Synthesis of SiC NPs by laser pyrolysis of SiH₄

To better understand the formation of SiC nanoparticles and to appreciate the influence of various experimental parameters, a series of experiments have been conducted in order to study the influence of laser power and beam processing and transit; combustion phenomena; and precursors’ temperature, among others. We studied the initiation of silane burning process without oxygen, i.e. the chemical decomposition. This decomposition is an exothermic process which contributes to the synthesis by releasing heat given by the chemical equation:

\[2 \text{ (SiH}_4\text{) } + 1 \text{ (C}_2\text{H}_2\text{) } \rightarrow 2 \text{ (SiC) } + 5\text{(H}_2\text{)}\]

The synthesis of SiC takes place only if the ratio silane/acetylene is higher than 2.5. Acetylene is a C donor, while silane is a good absorber of infrared CO₂ laser beam. The synthesis parameters (chamber pressure, gas flow rates of various precursors, room configuration and injector) were carefully adjusted. The study of the combustion process allowed for an accurate control of powder dimensionality. By flame image processing, we obtained the relations between the laser beam power, power density, kinetic combustion and injector configuration. The results allowed to synthesize SiC by laser pyrolysis, with very well controlled and secure characteristics. This is important because the pyrophoric silane gas is highly dangerous. The pyrolysis installation used in experiments is schematically depicted in Fig. 3. This configuration permitted the focusing of the processing optical beam in the center of the reaction. The synthesis parameters and conditions, together with the results of analyses that were performed on nanoparticles dimensionality, are presented in Table 1.

Fig. 3. – Schematic representation of the installation used for the synthesis of SiC nanoparticles.
RESULTS AND DISCUSSION

Experiments have revealed that the new principle ensures an increased productivity. After a series of investigations for optimization of the synthesis process, the physicochemical characteristics of TiO₂ nanopowders were improved in respect with dimensional dispersion, and not only. As visible from Fig. 1, the two diagrams show notable differences: curve II indicates a significant increase in temperature due to the elimination of vaporization threshold at boiling temperature of the precursor. For TTIP, the boiling temperature is 239°C. When surpassing this temperature, the precursor does not contain fractions of vapor or liquid aerosols, due to vaporization at the boiling temperature and to brutal volume increase by warming during synthesis. Gas temperature is measured directly in the gas stream. The amount of energy required to convert or vaporize a liquid to vapor is heat of vaporization. During the synthesis, the heat of vaporization is provided by the evaporator designed and adapted to the specific requirements and conditions: tightness, precise measurement and control of temperature, high thermal inertia, easy connection, no local heating points, no cold spots, compactness, security and electrical safety, and possibility of mixing the precursors (Fe(CO)₅/TEOS). The powder obtained was characterized by different methods and compared to the quality of those obtained by other methods. According to Table 2, the C content was on average 4.4%. This is a good result, because the carbon content in other TiO₂ preparation methods is significantly higher. XRD analysis showed that the ratio Anatase/Rutile (Table 3) slightly increases after decarburation treatment, while the dimensional ratio Anatase/Rutile was kept.

Table 3
Mass loss during calcination

<table>
<thead>
<tr>
<th>Sample</th>
<th>Mass</th>
<th>Final mass</th>
<th>Mass loss %</th>
<th>Temp. °C</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ti-II</td>
<td>1.9057</td>
<td>1.8247</td>
<td>0.0801</td>
<td>4.25</td>
</tr>
<tr>
<td>Ti-IV</td>
<td>1.9479</td>
<td>1.8593</td>
<td>0.0886</td>
<td>4.55</td>
</tr>
</tbody>
</table>

The results of experimental synthesis of SiC are presented in Fig. 4. Parameters of 18 synthesis runs are analyzed. The data presentation was chosen for the sake of easy observation and interpretation of parameters variation influence on the dimensionality and productivity. Variations are marked of laser beam power (Pow), power density (Pd), active precursor flow rate (SiH₄/C₂H₄), gas confinement (Ar), dimensionality of SiC nanoparticles (SIZE), optics used and configuration of the injector (nozzle central diameter). An important result is the analysis of the reaction zone in terms of temperature evolution (Fig. 5). An indication is available on the efficiency of synthesis and the transfer to industrial scale.
Fig. 4. – Diagram of experimental parameters and their reciprocal influence.
CONCLUSIONS

The results valorization in biomedical applications has imposed the synthesis of nanostructures from a new perspective: required improvements to meet current and future development trends. The originality consists in the use of liquid precursors, such as TTIP, TEOS, Fe(C₅H₅)₂, Fe(CO)₅, etc., as well as gaseous SiH₄. We compared different methods of processing and precursors, highlighting advantages and disadvantages of our approach. We formulated a physical principle that proposes new rules for the synthesis of liquid precursors by laser pyrolysis and their implementing conditions. On this basis, the developed set-up can be considered for further industrial applications. The chemical synthesis is virtually limitless and the only concern is related to the product recovery system. A part of our results is under patenting (36-37). The studies pointed to the mandatory existence of TiO₂ nanoparticles in the final product, in particular for avoiding water pollution, which is a prerequisite respected in our technology.

Acknowledgments. E.P. expresses special appreciation and gratitude to the General Manager of INFLPR, Mr. Ion Morjan, whose help and direct support made it possible to obtain the results presented here. E.P., I. N. M., C. R. thanks the European Social Fund POSDRU 2007–2013 through the contract POSDRU/89/1.5/S/60746
REFERENCES