Vol. 106 Nº2 ISSN 2545-8655

ANALES DE LA ASOCIACIÓN QUÍMICA ARGENTINA

Julio-Diciembre 2019

Volumen Especial DJPQ-AQA

Anales de la Asociación Química Argentina

Volumen Especial: Materiales Porosos

Editada desde 1913

Registro de Propiedad Intelectual Nº 164.756

Asociación Química Argentina
Sánchez de Bustamante 1749
1425 Buenos Aires, Argentina
TE/FAX: 54-11-4822-4886
http://www.aqa.org.ar

División de Jóvenes Profesionales
FB @djpq.aqa – TW @jovenes_AQA

Contenido

Vol. 106 Nº2, Julio-Diciembre de 2019 - Materiales Porosos

Mini-Reviews

Anales de la Asociación Química Argentina

División Jóvenes Profesionales

Mini-Review

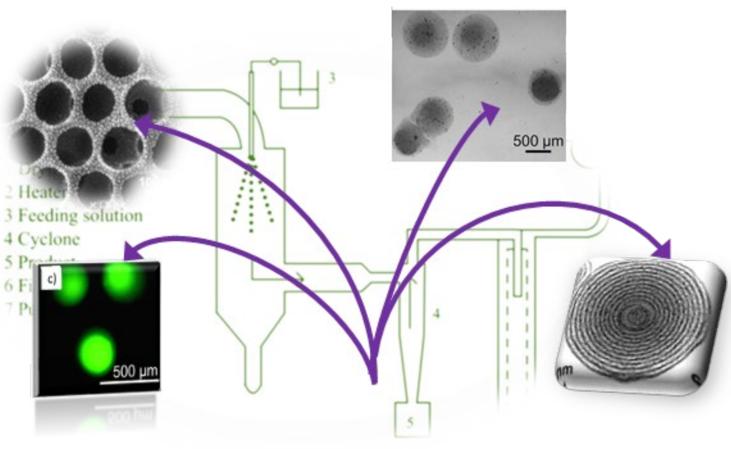
TEMPLATED MESOPOROUS NANOMATERIALS BY AEROSOL ROUTE: HISTORY AND NEW INSIGHTS OF GREEN CHEMISTRY APPROACHES

M. Verónica Lombardo[1,2*], Andrés Zelcer[2,3], Esteban A. Franceschini[4]

1. Gerencia Química, CAC, CNEA, CONICET. Av. Gral Paz 1499 (B1650KNA) San Martín, Buenos Aires, Argentina.
2. ECyT-UNSAM, 25 de Mayo y Francia, (B1650KNA) San Martín, Buenos Aires, Argentina.
3. CIBION, CONICET, Godoy Cruz 2390 (C1425FQD), CABA, Argentina
4. INFIQC-CONICET, Dto. de Fisicoquímica – Facultad de Ciencias Químicas, UNC, Ciudad Universitaria, 5000, Córdoba, Argentina

**Autor Corresponsal: marialombardo@cnea.gov.ar*

Graphical abstract



Resumen

La combinación de la síntesis por aerosol (o secado por pulverización) con la química Sol-Gel se ha trasformado en las últimas décadas en la más promisoria ruta para la obtención de materiales mesoporosos a escala industrial con variadas aplicaciones como energía, catálisis, purificación de agua, etc.

En el método de secado por pulverización, se atomiza una solución precursora para formar gotas mediante nebulización ultrasónica. Cada gota se puede considerar como un microrreactor individual. Estas gotas resultantes luego son impulsadas mediante un gas portador y pasan a través de un tubo caliente, donde el solvente se evapora rápidamente y las especies precursoras disueltas se ensamblan para generar los productos.

Este método permite la producción continua de una amplia variedad de materiales, minimizando el uso de precursores y reduciendo considerablemente los residuos generados durante la síntesis. También permite obtener partículas con alta pureza, de una manera simple, económica y continua; posibilitando la obtención de partículas esféricas, no aglomeradas y con un tamaño monodisperso.

En este mini-review, presentamos los principios básicos de la síntesis de nanomateriales utilizando el método de secado por pulverización y discutimos la posibilidad de adaptar estos procesos a los principios de la química verde.

Abstract

The combination of aerosol (spray drying process) with sol–gel chemistry has become in, the lasts decades one, of the most promising synthesis routes for the synthesis of industrially scalable mesoporous materials for various applications such as energy, catalysis, water purification, etc.

In the spray drying method a precursor solution is atomized to form droplets by ultrasonic nebulization. Each drop can be considered as an individual microreactor. The resulting droplets are then driven by a carrier gas and pass through a hot tube where the solvent is rapidly evaporated and the dissolved precursor species are assembled to generate the products.

This method allows the continuous production of a wide variety of materials minimizing the use of precursors and considerably reducing the waste generated during the synthesis. The spray drying method permits to obtain particles with a high-purity in a simple, economical and continuous way. This method allows to produce spherical shaped particles that are agglomeration free and have a relatively monodisperse size, which is very useful for material processing.

In this mini-review, we present the basic principles of nanomaterials synthesis using aerosol methods and we discuss the possibility to adapt these processes to the principles of green chemistry.

Palabras Clave: *secado por pulverización, materiales mesoporosos, síntesis de fácil escalado, química verde*

Keywords: *spray drying process, mesoporous materials, easy scalable synthesis, green chemistry.*

1. Introduction

An aerosol, system belonging to the family of colloids, consists of a relatively stable suspension of solid or liquid droplets in a gas or vapour. The term 'aerosol' originates in military research during the First World War.[1, 2] In the 19th century, aerosol particles represented the smallest known division of matter and the fundamental properties of aerosols have been studied for more than 100 years.

Aerosol technology is of great interest in numerous applications. Its use is well established in the food industry[3-11], chemical industry[12, 13], pharmaceutics production[14-18], energy applications [19], just to name a few of its many applications.

The size of the particles is of enormous interest in the establishment of the behavior of the aerosols. The sizes can vary from structures of about 0.001 microns to fog droplets and dust up to 100 microns, which significantly affects the behavior of suspended particles. That is why there are several types of aerosols that are classified according to the physical form and the generation method. The terms commonly used are:[20]

- *Dust:* a solid particle formed by the mechanical disintegration of a material.
- *Fume:* solids produced by physicochemical reactions such as combustion, sublimation or distillation.
- *Smoke:* a visible aerosol produced by the disintegration of the liquid or the condensation of the vapor.

1.1. Drying spray devices

In this review we will focus on the aerosols produced by spray drying techniques. Spray drying is a simple, rapid, reproducible and scalable drying technology,[21] which allows mild temperature conditions suitable for biopharmaceuticals sensitive to heat. Compared to other drying technologies used in drug delivery applications, spray drying is a continuous process for directly transforming various liquids (e.g., solutions, emulsions, dispersions, slurries, pastes or even melts) into solid particles with adjustable size, distribution, shape, porosity density and chemical composition.

A wide variety of instruments for the production of aerosols have been described in the literature[22-24] and the techniques used are basically similar to the mechanisms of formation of natural aerosols.

The steps of the spray drying process are basically: (1) heating the drying gas, (2) generating droplets, (3) drying the droplets and (4) collecting the particles.

Figure 1 illustrates a principle flow diagram of a spray dryer. First, the liquid feed is atomized in a nozzle. The reduction in the size of the drop leads to a large increase in the surface area. In the drying chamber, the solvent in the sprayed drops is quickly removed by the continuous flow of a hot drying gas. The dried particles are formed, separated from the gas stream and collected in a collection vessel.

A great deal of time and effort has been devoted to the research and development of aerosol generation devices. This research is usually carried out with the objective of having control of the particle size distributions. Spray drying equipment is commercially available and the production cost is generally lower compared to other drying technologies.[4, 6, 25]

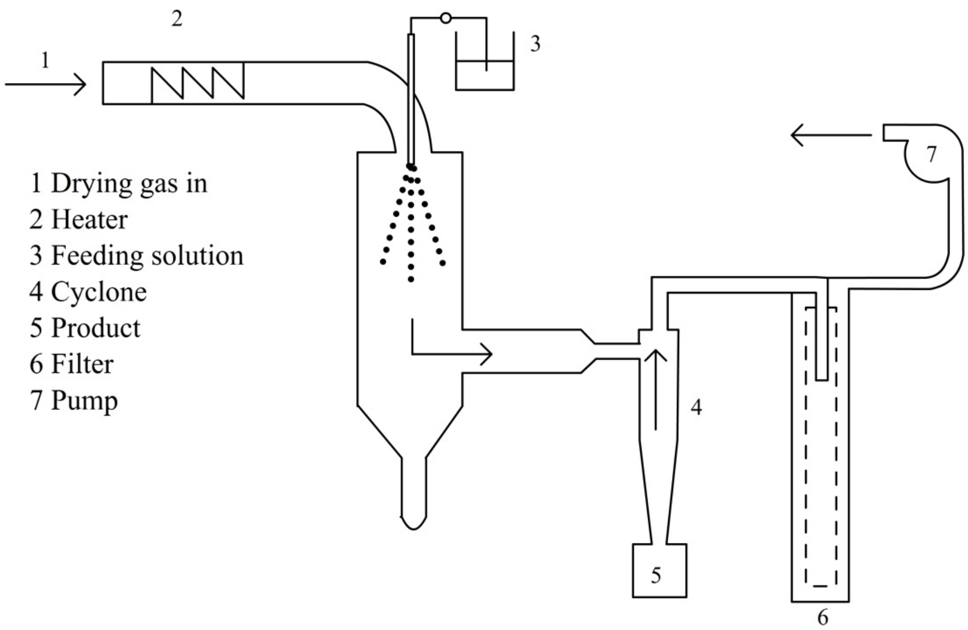


Figure 1. Principle flow diagram of a traditional spray dryer**.**

Polydispersed aerosols have many industrial applications (for example, agricultural spraying), making the applications cheaper because most of the environmental sprays are polydispersed.

Aerosols of very narrow (monodisperse) distributions have many applications in aerosol engineering, for example, for size measurement, equipment calibration, filtration efficiency tests, lung inhalation studies and, ultimately, in the production of ceramic powders. To achieve practical monodispersity, the standard geometric deviation must be less than 1.2.

Atomization generally produces a broad distribution of relatively thick droplets, with the minimum particle size determined by an equilibrium between surface tension forces that resist droplet formation at pressure or other forces that attempt to disrupt the fluid surface. Common methods used to mechanically disperse liquids to form aerosols include air nebulizers,[26,27] rotating discs,[28, 29] ultrasonic nebulizers,[30-32] and vibrating orifice generators.[33] The last three techniques are not strictly based on atomization and are capable of producing monodisperse aerosols.[24, 34]

Another important factor to consider is the concentration of the precursors. The high initial concentrations result in rapid agglomeration and a highly polydispersed aerosols. In addition, smaller primary particles are produced when the temperature increases,[35] although the same increase can cause the decomposition of aerosol precursors.

The aerosol particles generated by the direct sol-gel feeding spray dry method are quite monodisperse for particles in the submicron range,[36-39] although in the case of core-shell particles, dispersion often depends on the initial size of the nuclei core.

Japuntich et al.[40] found that monodispersity depends on a balance between free and forced convection in the condenser tube. Furthermore, they found that the most successful condensates are those with low diffusion coefficients. Thus, a linear correlation between the Reynolds number (Re) or the flux in the capacitor and the Rayleigh number was found. Therefore, for a chosen Re, the Rayleigh number can be found and for a chosen temperature, parameters of the tube radius can be calculated.

2. Synthesis methods

The combination of spray drying with the sol-gel technique allows to obtain porous particles in a simple, fast and cheap way, with the possibility of industrial scaling; although the obtaining of mesoporous spherical particles ordered and monodispersed pores is not trivial. The process is usually optimized to produce particles with the desired size, although in general the size distribution is relatively broad. The properties of the sol (concentration and rheology) are important, as are the operating conditions of the dryer (rotor speed, nozzle characteristics, temperature, humidity, etc.).

Most commonly used methods for obtaining porous particles are:

a) Using a surfactant or a block copolymer as template agent. In general, the synthesis involves Evaporation Induced Self-Assembly (EISA)[41], this method consist in solvent evaporation, allowing templated agent to reach the critical micellar concentration (c.m.c.), which induces the formation of the desired mesoporous structure.
b) Using a polymeric hard template agent. In this case the templates are polymeric nanoparticles which are eliminated after synthesis.[42]
c) Using previously synthesized nanoparticles as precursors. These particles can be well dispersed or aggregated.[43]

Lu and co-workers[44] reported a method of spherical silica mesoporous particles synthesis. They started from an acid solution of silica in ethanol/water, where the different surfactants (CTAB, Brij-58, Brij-56 or P123) were far below their c.m.c. By incorporating metal complexes or organic dyes they were also able to obtain nanostructured hybrid mesoporous particles. Although the obtained particles were spherical, they did not achieve monodisperse sizes (see Figure 2). Alonso and co-workers[45] also used EISA and spray-drying to obtain mesoporous silica particles. They used iPrOH as solvent in most cases, but they also tested the use of water. A Büchi Mini-Spray 190 apparatus was employed and cetyl-trimethyl-ammonium bromide (CTAB) was the mesoporous template. They varied the composition of the sols (solvent and siloxane oligomers) but did not varied operating conditions. When the solvent used was iPrOH, some degree of pore order was obtained, but not for the case where the solvent was water. The shape of the particles obtained was spherical in most of the samples with iPrOH as solvent, in case of water they obtained particles inside particles with a broad size distribution.

In addition to silica, there are also reported syntheses of other porous particles such as TiO_2[46-48], ZrO_2[48], CeO_2[48] and Al_2O_3[49].

The most common hard templated agent are polystyrene latex (PSL) colloidal suspensions. Precursor of matrix particles can be either nanoparticles[42, 50, 51] or molecular precursors.[52] Then, the polymers are removed by calcination, obtaining structures similar to the ones presented in Figure 3. As expected, the pore sizes increased with PSL particle size. Interestingly, with this approach it is possible to obtain macropores, something that is difficult when the pore size is determined by the size of the micelles, as discussed earlier.

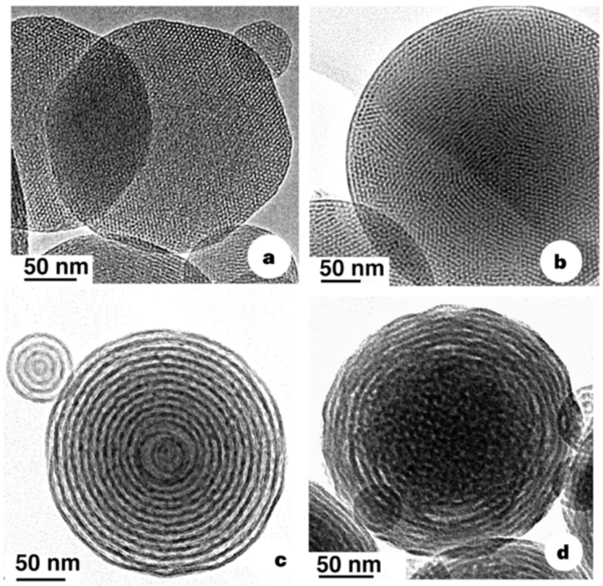


Figure 2 (a) Faceted calcined particles with a hexagonal mesophase (d_{100} = 32.5 Å). The sol was prepared using 5 wt% CTAB as template. **(b)** Calcined particles showing cubic mesostructure. The sol was prepared using 4.2 wt% Brij-58 as template. **(c)** Calcined particles showing a vesicular mesophase (d_{100} = 92 Å). The sol was prepared using 5% P123 as the triblock copolymer template. **(d)** Uncalcined silica particles showing 'growth' of ordered vesicular domains from the liquid–vapour interface. The sol was prepared using 2.5% Brij-56 as the template. Reprinted with permission of Springer Nature from reference 44.

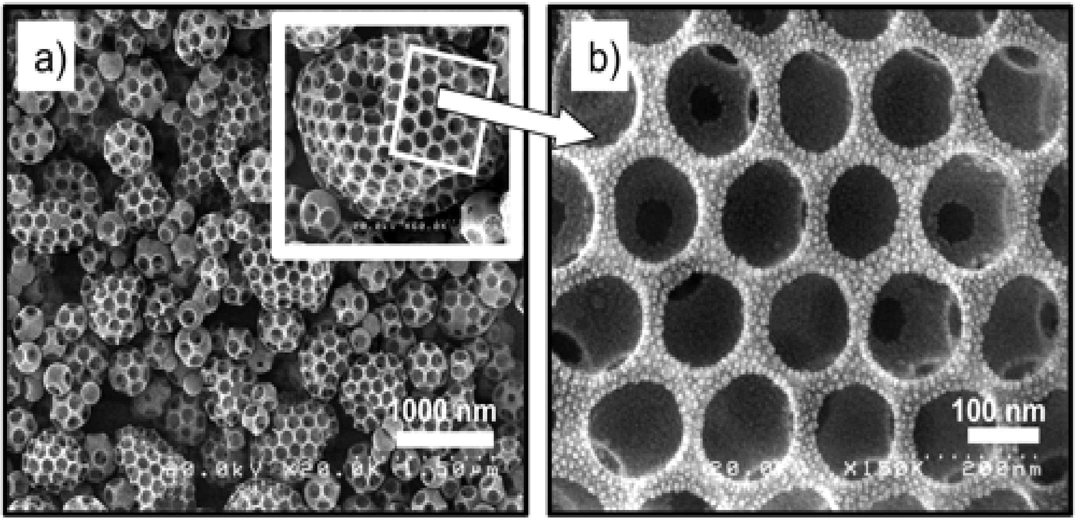


Figure 3. SEM images of silica powders prepared using 5 nm of silica particle size and 178 nm PSL particle size: (a) low magnification and (b) high magnification of surface particles. Reprinted with permission from Nano Letters 2002, 2, 4, 389-392. Copyright 2002 American Chemical Society.

The third mentioned synthesis method consists in the coalescence of previously synthesized nanoparticles that can be well dispersed or forming small aggregates. These particles coalesce when the drop dries, giving rise to new particles bigger than the ones used as precursors and leaving small cavities between them that form to the porosity.[42, 50, 51]

Another interesting application involves the formation of core-shell films that can be produced by the condensation of vapours in already existing cores (heterogeneous condensation) or in higher supersaturations, by instantaneous formation of vapour particles, which are grouped and converted into particles when their size exceeds a critical value (homogeneous condensation). Heterogeneous condensation is typically used. In such generators four processes, not necessarily separated, are common: (1) Production of cores, (2) steam generation, (3) mixing of steam cores and (4) condensation through controlled cooling of the carrier gas. Even though, there is great interest in the development of core-shell particles obtained by processing by spray drying in a single step.[53]

The spray drying method has also been adapted to produce thin fibbers (approximately 10 microns). High-viscosity sols and low viscoelastic characteristics are required for this purpose.

Gel particles were also formed using emulsion drying techniques; here droplets of aqueous sol are formed in a partially miscible solvent (for example, trichlorethylene). The water is progressively removed from the sol by transfer to the organic phase, and eventually rigid gel particles are formed. The size of the emulsion droplets can be controlled by adding an appropriate surfactant to the sol and by controlling the stirring conditions used to disperse the aqueous phase in the organic solvent. This method generally produces highly uniform particles that can have a size in the range > 1 μm to about 30 μm. In the two previous methods, narrower size distributions can be achieved by a subsequent centrifugal classification.

3. Applications

3.1. Pharmaceutical applications

By spray-drying encapsulation, various particle designs can be prepared depending on the required functionality. In the case of pharmaceutical applications, core-shell particles, multi-wall particles, and multi-core or composite particles are commonly used (Figure 4). Spray drying allows the generation of smaller particle sizes than conventional aerosol synthesis methods, which improves the bioavailability and the release of bioactive components and drugs, because they have a higher surface to volume ratio, a higher penetration rate in the cells, stability, and possibility of directed release through the decoration of the surface.[54] Also, a change of crystalline drugs to more amorphous structures provides a faster drug release kinetics. Micro and nanonization is used to change the morphology of the particles from a coarse grain to a very fine powder. This improves the solubility of the final pharmacological product due to the higher surface-to-volume ratio of nanoparticles and due to the more amorphous structures, in which the solvent (e.g., water) can penetrate more efficiently.

Practical applications include, for example, polymeric wall materials, such as gum arabic, serum protein, polyvinyl alcohol, modified starch or maltodextrin[55, 56]. Typical examples are drugs with poor water solubility[57, 58] and salts.[59]

In nanoencapsulation, typically a liquid product is embedded within a solid matrix. The encapsulated oil-in-water nanoemulsion is a common example, in which the oil droplets serve as a reservoir for a lipophilic pharmacological product.

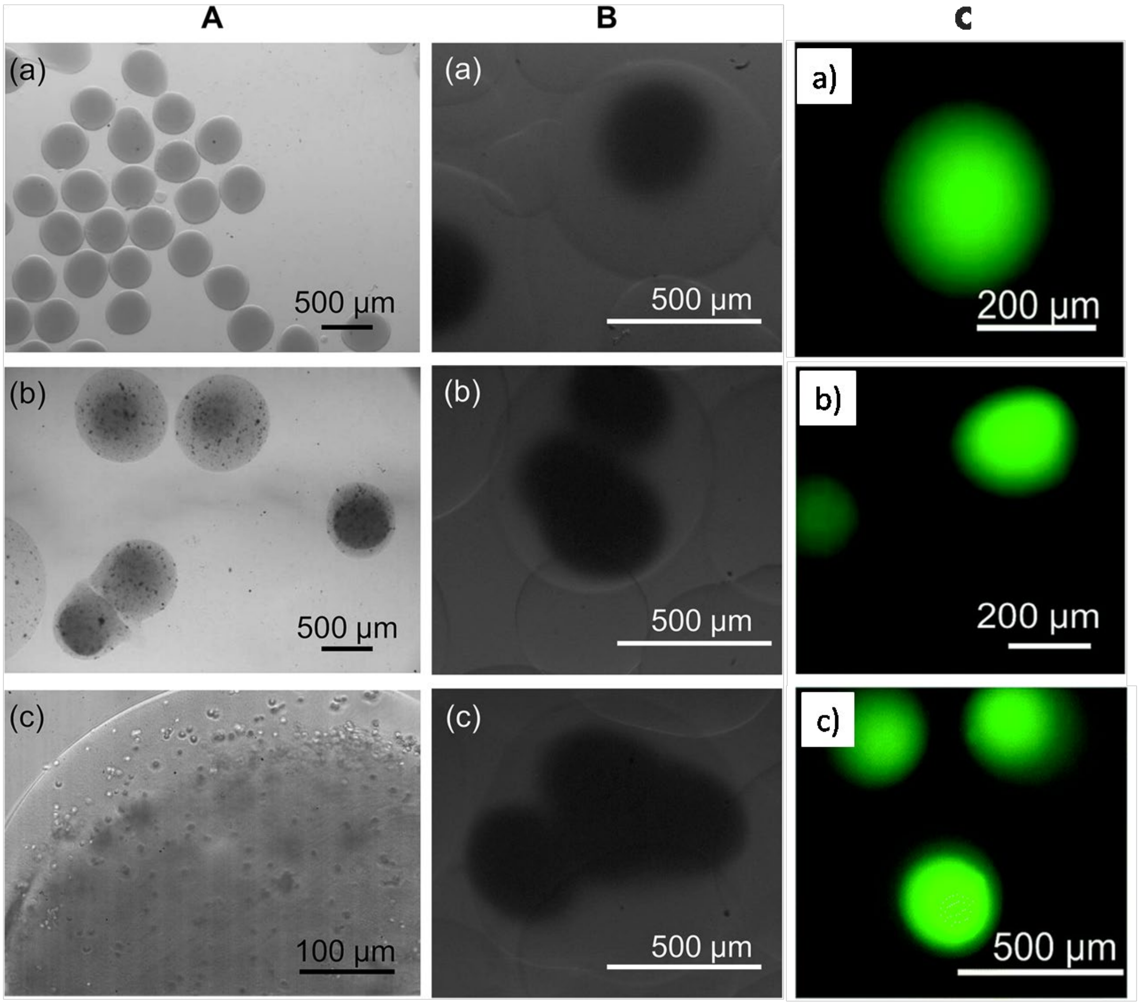


Figure 4 (A) Optical images of C/C hydrogel microspheres: (a) CMC-based microgels, (b) C/C core–shell hydrogel microspheres, and (c) a magnified view of the edge of a C/C microsphere. (B) Optical images of the C/A hydrogel microspheres, containing (a) one, (b) two and (c) three CMC-based microgel cores. (C) (a-c) fluorescence images of A/A microspheres encapsulating CdTe QDs.W. Lai, A. S. Susha, A. L. Rogach, G. Wang, M. Huang, W. Hu and W. Wong, RSC Adv., 2017, 7, 44482 - Published by The Royal Society of Chemistry.

Depending on the application, there is an optimized set of process parameters. The optimization of process parameters is usually done by trial and error. However, experimental design studies (DOE) help to optimize the nano spray drying process, as shown by several authors.[14, 25, 55, 60-67] The DOE studies allow determining the optimal conditions of the process with fewer experiments, which reduces the cost of the experiments and the materials use, which constitute determining factors for pharmaceutical applications.

3.2. Energy applications

The large-scale development and generalized use of materials for energy applications, such as catalysts for water electrolysis, nanomaterials for hydrogen storage or electrodes for lithium batteries, is significantly hampered by the high cost of materials and the low reproducibility. Thus, it is highly desirable to develop cost effective but efficient alternative materials for different energy applications.[68-70]

The implementation of mesoporous materials in electrocatalysis has allowed in recent years to considerably increase the real surface area of the used materials and, therefore, its effective activity.[71, 72]. In particular, mesoporous TiO_2 materials are of great interest for different energy applications, due to their intrinsic properties and because these materials can be obtained in the form of mesoporous particles by methods that allow the continuous particles synthesis.[73]

Additionally, the spray dry technique allows the encapsulation of nanomaterials. This core-shell type of structures can be advantageous due to the individual properties of each component material as well as the synergetic properties generated when the used layers are rationally chosen. For example, the use of a mesoporous Co_3O_4 core with a mesoporous TiO_2 shell forming an hybrid electrode with nickel (or nickel alloys) can increase the activity due to the modification of the Fermi level of Ni while the TiO_2 can protect the Co_3O_4 from the corrosive environment found in a conventional alkaline electrolyzer.[74]

3.3. Environmental applications

Heavy metals are especially toxic to humans because they can be bioaccumulated. There are also law regulations on other pollutants such as pesticides and other organic molecules that come from wastewater from a variety of industries. In this context, mesoporous materials and nanotechnology represent one of the areas of greatest development of the last twenty years and with excellent environmental application perspectives.[75-77] Combination of this kind of materials with synthesis by spray drying makes these materials have better perspectives for their use at industrial scale. In fact, spray drying has been developed for many industrial applications due to its capacity to produce high volumes of particles.[78]

There is a wide variety of materials synthesized for environmental applications such as modified carrageenan microparticles for adsorption of pharmaceutical compounds[79], magnetic chitosan microparticles grafted with methyl acrylate and tetraethylenepentamine for Cd (II) removal[80], lanthanum oxide functionalised silica microspheres for phosphate adsorption[81], graphene-Fe_3O_4 hollow hybrid microspheres for heterogeneous Fenton and electro-Fenton reaction[82] (Fenton reaction has been widely used to treat wastewater containing dyes, herbicides, antibiotics, etc), and many other materials.[47, 83, 84]

Previously, these of kind materials for environmental applications were obtained by other synthesis routes; nowadays they can be produced by aerosol, significantly reducing the costs and production times.

4. Perspectives and Green chemistry approaches

As shown throughout this work, there are a variety of methods for the production of materials by spray drying. For example, mesoporous powders spray drying production methods using EISA procedure have been recently patented. These methods use volatile and flammable solvents in high proportion which makes their synthesis more expensive, because closed circuits must be used to avoid the ignition of solvents at high drying temperatures. In summary, these synthesis methods have the following limitations:

a) high concentration of volatile organic compounds represent environmental risk,

b) flammable components present risk of ignition and

c) to control the hydrolysis-condensation processes of the inorganic precursors mineral acids in high concentration (pH < 0) are used, which also represent an environmental risk and require special materials for their processing.

These limitations make necessary the development of new synthesis methods to obtain mesoporous materials by spray drying.

In this direction, our working groups have developed and patented a synthesis method for obtaining spherical particles of mesoporous metal oxides having composition, surface area, porosity and size controlled.[85] In this method, the solvent can have a low proportion of organic solvents (less than 25% by mass) or can even be pure water. Thus, risk of ignition is eliminated. This allows to work under an air atmosphere, resulting in a safe and low cost method. The amount of volatile organic compounds is low, which reduces the environmental risk and the precursor solutions are less acidic than in other reported methods.[86]

This new method, friendly to the environment, generates high expectations for obtaining and using large-scale mesoporous materials obtained by spray drying, which have a wide spectrum of applications, some of which were described in this review, but are not only limited to them.

5. Conclusions

In this review we have covered some of the basic principles in the synthesis of aerosols, particularly nanostructured aerosols in different ways, including both hard template, and different types of soft template and sol-gel method. We have also explored some of the many facets of the multifunctionality of these materials, considering the possibility of using both organic and inorganic precursors. These materials present an enormous potential for industrial applications due to the fact that the aerosol synthesis methods are easily scalable, in comparison with other nanomaterials synthesis methods. Finally, there is a great interest in developing methods for the synthesis of nanostructured aerosols using environmentally friendly methods that allow the synthesis of multifunctional nanomaterials with a minimum impact on the environment. In this sense, nanostructured aerosols appear as highly promising materials for many applications.

Acknowledgments:

The authors thank financial support from Agencia Nacional de Promoción Científica y Tecnológica and CONICET. M.V.L., A.Z. and E.A.F. are permanent research fellows of CONICET. The authors thank Dr. Galo J.A .A .Soler-Illia for his technical support.

References

(1) Schmauss, A., The chemistry of fog, clouds and rain. Umschau, Munich, **1920**, 24, 61-63.
(2) Whytlaw-Gray, R.; Speakman, J. B.; Campbell, J. H. P., Smokes: Part I - a study of their behaviour and a method of determining the number of particles they contain. Proc. R. Soc. A **1923**, 102, 600-615.
(3) Anandharamakrishnan, C., Drying Techniques for Nanoencapsulation. In Techniques for Nanoencapsulation of Food Ingredients, Springer New York: New York, NY, **2014**; pp 51-60.
(4) Celli, G. B.; Ghanem, A.; Brooks, M. S.-L., Bioactive Encapsulated Powders for Functional Foods—a Review of Methods and Current Limitations. Food and Bioprocess Technology **2015**, 8 (9), 1825-1837.
(5) Esfanjani, A. F.; Jafari, S. M.; Assadpoor, E.; Mohammadi, A., Nano-encapsulation of saffron extract through double-layered multiple emulsions of pectin and whey protein concentrate. Journal of Food Engineering **2015**, 165, 149-155.
(6) Gharsallaoui, A.; Roudaut, G.; Chambin, O.; Voilley, A.; Saurel, R., Applications of spray-drying in microencapsulation of food ingredients: An overview. Food Research International **2007**, 40 (9), 1107-1121.
(7) Jafari, S. M.; Assadpoor, E.; He, Y.; Bhandari, B., Encapsulation Efficiency of Food Flavours and Oils during Spray Drying. Drying Technology **2008**, 26 (7), 816-835.
(8) Jafari, S. M.; He, Y.; Bhandari, B., Encapsulation of Nanoparticles of d-Limonene by Spray Drying: Role of Emulsifiers and Emulsifying Techniques. Drying Technology **2007**, 25 (6), 1069-1079.
(9) Mahdavi, S. A.; Jafari, S. M.; Ghorbani, M.; Assadpoor, E., Spray-Drying Microencapsulation of Anthocyanins by Natural Biopolymers: A Review. Drying Technology **2014**, 32 (5), 509-518.
(10) Murugesan, R.; Orsat, V., Spray Drying for the Production of Nutraceutical Ingredients—A Review. Food and Bioprocess Technology **2012**, 5 (1), 3-14.
(11) Rajabi, H.; Ghorbani, M.; Jafari, S. M.; Sadeghi Mahoonak, A.; Rajabzadeh, G., Retention of saffron bioactive components by spray drying encapsulation using maltodextrin, gum Arabic and gelatin as wall materials. Food Hydrocolloids **2015**, 51, 327-337.
(12) Masters, K., Spray Drying Handbook. Fifth Edition. Longman Scientific & Technical: Harlow, USA., 1991.
(13) Okuyama, K.; Wuled Lenggoro, I., Preparation of nanoparticles via spray route. Chemical Engineering Science **2003**, 58 (3), 537-547.
(14) Bürki, K.; Jeon, I.; Arpagaus, C.; Betz, G., New insights into respirable protein powder preparation using a nano spray dryer. International Journal of Pharmaceutics **2011**, 408 (1), 248-256.
(15) Cal, K.; Sollohub, K., Spray Drying Technique. I: Hardware and Process Parameters. Journal of Pharmaceutical Sciences **2010**, 99 (2), 575-586.
(16) Vehring, R., Pharmaceutical Particle Engineering via Spray Drying. Pharmaceutical Research **2008**, 25 (5), 999-1022.
(17) Wang, B.; Zhang, W.; Zhang, W.; Mujumdar, A. S.; Huang, L., Progress in Drying Technology for Nanomaterials. Drying Technology **2005**, 23 (1-2), 7-32.
(18) Wendel, S. C.; Celik, M., Spray Drying and Pharmaceutical Applications. In Handbook of pharmaceutical granulation technology, CRC Press: **2005**; pp 129-157.
(19) Franceschini, E. A.; Gomez, M. J.; Lacconi, G. I., One step synthesis of high efficiency nickel/mesoporous TiO2 hybrid catalyst for hydrogen evolution reaction. Journal of Energy Chemistry **2019**, 29, 79-87.
(20) Ramsay, J. D. F.; Matijević, E.; Jones, A. G.; G. Clydesdale, K. J. R. a. R. D.; Colbeck, I.; Lubetkin, S. D.; Dickinson, E.; Geddes, K. R.; Luckham, P. F.; Wedlock, D. J.; Peng, R. A. W. a. S. J., Controlled Particle, Droplet and Bubble Formation. Butterworth-Heinemann: Oxford, **1994**; p 1-388.
(21) Arpagaus, C.; Schwartzbach, H., Scale-up from the Büchi Mini Spray Dryer B-290 to the Niro MOBILE MINOR. In best@buchi Information Bulletin, **2008**.
(22) Mitchell, J. P., Aerosol generation for instrument calibration. HMSO, London, **1986**.

(23) Raabe, O. G., The Generation of Aerosols of Fine Particles**Prepared under U. S. Energy Research and Development Administration Contract E(29-2)-1013. In Fine Particles, Liu, B. Y. H., Ed. Academic Press: **1976**; pp 57-110.
(24) K., W., Generation of Aerosols and Facilities for Exposure Experiments. Ann Arbor Science Publishers **1980**.
(25) Arpagaus, C.; John, P.; Collenberg, A.; Rütti, D., 10 - Nanocapsules formation by nano spray drying. In Nanoencapsulation Technologies for the Food and Nutraceutical Industries, Jafari, S. M., Ed. Academic Press: **2017**; pp 346-401.
(26) Kerker, M., Laboratory generation of aerosols. Advances in Colloid and Interface Science 1975, 5 (2), 105-172.
(27) May, K. R., The collison nebulizer: Description, performance and application. Journal of Aerosol Science **1973**, 4 (3), 235-243.
(28) May, K. R., Spinning top homogeneous aerosol generator with shock proof mounting. J. Sci. Instrum **1966**, 43, 841-842.
(29) Whitby, K. T.; Lundgren, D. A.; Peterson, C. M., Homogeneous aerosol generators. Int. J. Water. Poll 1965, 9.
(30) Lang, R. J., Ultrasonic Atomization of Liquids. The Journal of the Acoustical Society of America **1962**, 34 (1), 6-8.
(31) Denton, M. B.; Swartz, D. B., An improved ultrasonic nebulizer system for the generation of high density aerosol dispersions. Review of Scientific Instruments **1974**, 45 (1), 81-83.
(32) Homma, K.; Serita, F.; Takaya, M., Aerosol generation from particle suspensions by ultrasonic nebulizer. In Aerosols: Science, Industry, Health and Environment, Masuda, S.; Takahashi, K., Eds. Pergamon Press: Oxford, **1990**; pp 231-234.
(33) Berglund, R. N.; Liu, B. Y. H., Generation of monodisperse aerosol standards. Environmental Science & Technology **1973**, 7 (2), 147-153.
(34) Hidy, G. M., Aerosols: An Industrial and Environmental Science. Academic Press: Orlando, FL, 1984.
(35) Wegrzyn, J. E., An investigation of an exploding wire aerosol, In Fine Particles, Liu, B. Y. H., Ed. Academic Press: **1976**; pp 253-273.
(36) Sinclair, D.; La Mer, V. K., Light Scattering as a Measure of Particle Size in Aerosols. The Production of Monodisperse Aerosols. Chemical Reviews **1949**, 44 (2), 245-267.
(37) Rapaport, E.; Weinstock, S. E., A generator for homogeneous aerosols. Experientia 1955, 11 (9), 363-364.
(38) Liu, B. Y. H.; Lee, K. W., An aerosol generator of high stability. American Industrial Hygiene Association Journal **1975**, 36 (12), 861-865.
(39) Tu, K.-W., A condensation aerosol generator system for monodisperse aerosols of different physicochemical properties. Journal of Aerosol Science **1982**, 13 (5), 363-371.
(40) Japuntich, D. A.; Stenhouse, J. I. T.; Liu, B. Y. H., Conditions for monodispersity of heterogeneous condensation aerosols using dimensionless groups. Journal of Colloid and Interface Science **1990**, 136 (2), 393-400.
(41) Grosso, D.; Cagnol, F.; Soler-Illia, G. J. d. A. A.; Crepaldi, E. L.; Amenitsch, H.; Brunet-Bruneau, A.; Bourgeois, A.; Sanchez, C., Fundamentals of Mesostructuring Through Evaporation-Induced Self-Assembly. Advanced Functional Materials **2004**, 14 (4), 309-322.
(42) Chang, H.; Okuyama, K., Optical properties of dense and porous spheroids consisting of primary silica nanoparticles. Journal of Aerosol Science **2002**, 33 (12), 1701-1720.
(43) Jang, H. D.; Kil, D. S.; Chang, H.; Cho, K.; Kim, S. K.; Oh, K. J.; Choi, J. H., Preparation of Nanoporous SiO2 Particles and Their Application in Drug Release Control. Journal of Nanoscience and Nanotechnology **2011**, 11 (5), 4169-4173.
(44) Lu, Y.; Fan, H.; Stump, A.; Ward, T. L.; Rieker, T.; Brinker, C. J., Aerosol-assisted self-assembly of mesostructured spherical nanoparticles. Nature **1999**, 398, 223.
(45) Alonso, B.; Véron, E.; Durand, D.; Massiot, D.; Clinard, C., New insights into the formation of textures through spray-drying and self-assembly. Microporous and Mesoporous Materials **2007**, 106 (1), 76-94.
(46) Pal, M.; Wan, L.; Zhu, Y.; Liu, Y.; Liu, Y.; Gao, W.; Li, Y.; Zheng, G.; Elzatahry, A. A.; Alghamdi, A.; Deng, Y.; Zhao, D., Scalable synthesis of mesoporous titania microspheres via spray-drying method. Journal of Colloid and Interface Science **2016**, 479, 150-159.
(47) Araujo, P. Z.; Luca, V.; Bozzano, P. B.; Bianchi, H. L.; Soler-Illia, G. J.; Blesa, M. A., Aerosol-assisted production of mesoporous titania microspheres with enhanced photocatalytic activity: the basis of an improved process. ACS Appl Mater Interfaces **2010**, 2 (6), 1663-73.
(48) Grosso, D.; de A.A. Soler-Illia, G. J.; Crepaldi, E. L.; Charleux, B.; Sanchez, C., Nanocrystalline Transition-Metal Oxide Spheres with Controlled Multi-Scale Porosity. Advanced Functional Materials **2003**, 13 (1), 37-42.
(49) Kim, J. H.; Jung, K. Y.; Park, K. Y.; Cho, S. B., Characterization of mesoporous alumina particles prepared by spray pyrolysis of Al(NO3)2·9H2O precursor: Effect of CTAB and urea. Microporous and Mesoporous Materials **2010**, 128 (1), 85-90.
(50) Iskandar, F.; Nandiyanto, A. B. D.; Yun, K. M.; Hogan Jr., C. J.; Okuyama, K.; Biswas, P., Enhanced Photocatalytic Performance of Brookite TiO2 Macroporous Particles Prepared by Spray Drying with Colloidal Templating. Advanced Materials **2007**, 19 (10), 1408-1412.
(51) Iskandar, F.; Mikrajuddin; Okuyama, K., Controllability of Pore Size and Porosity on Self-Organized Porous Silica Particles. Nano Letters **2002**, 2 (4), 389-392.

(52) Abdullah, M.; Iskandar, F.; Shibamoto, S.; Ogi, T.; Okuyama, K., Preparation of oxide particles with ordered macropores by colloidal templating and spray pyrolysis. Acta Materialia **2004**, 52 (17), 5151-5156.
(53) Arpagaus, C.; Collenberg, A.; Rütti, D.; Assadpour, E.; Jafari, S. M., Nano spray drying for encapsulation of pharmaceuticals. International Journal of Pharmaceutics **2018**, 546 (1), 194-214.
(54) Lee, S. H.; Heng, D.; Ng, W. K.; Chan, H.-K.; Tan, R. B. H., Nano spray drying: A novel method for preparing protein nanoparticles for protein therapy. International Journal of Pharmaceutics **2011**, 403 (1), 192-200.
(55) Li, X.; Anton, N.; Arpagaus, C.; Belleteix, F.; Vandamme, T. F., Nanoparticles by spray drying using innovative new technology: The Büchi Nano Spray Dryer B-90. Journal of Controlled Release **2010**, 147 (2), 304-310.
(56) Li, X.; Anton, N.; Vandamme, T., Spray-Drying of Nanoand Microcapsules of Nutraceuticals. In Functional Food Ingredients and Neutraceuticals - Processing Technologies, Shi, J., Ed. CRC Press, Taylor & Francis Group: Boca Raton, **2015**; pp 455-478.
(57) Martena, V.; Censi, R.; Hoti, E.; Malaj, L.; Di Martino, P., A new nanospray drying method for the preparation of nicergoline pure nanoparticles. Journal of Nanoparticle Research **2012**, 14 (6), 934.
(58) Schmid, K.; Arpagaus, C.; Friess, W., Evaluation of the Nano Spray Dryer B-90 for pharmaceutical applications. Pharmaceutical Development and Technology **2011**, 16 (4), 287-294.
(59) Moncada, M.; Astete, C.; Sabliov, C.; Olson, D.; Boeneke, C.; Aryana, K. J., Nano spray-dried sodium chloride and its effects on the microbiological and sensory characteristics of surface-salted cheese crackers. Journal of Dairy Science **2015**, 98 (9), 5946-5954.
(60) Draheim, C.; de Crécy, F.; Hansen, S.; Collnot, E.-M.; Lehr, C.-M., A Design of Experiment Study of Nanoprecipitation and Nano Spray Drying as Processes to Prepare PLGA Nano- and Microparticles with Defined Sizes and Size Distributions. Pharmaceutical Research **2015**, 32 (8), 2609-2624.
(61) Durli, T. L.; Dimer, F. A.; Fontana, M. C.; Pohlmann, A. R.; Beck, R. C. R.; Guterres, S. S., Innovative approach to produce submicron drug particles by vibrational atomization spray drying: influence of the type of solvent and surfactant. Drug Development and Industrial Pharmacy **2014**, 40 (8), 1011-1020.
(62) Gu, B.; Linehan, B.; Tseng, Y.-C., Optimization of the Büchi B-90 spray drying process using central composite design for preparation of solid dispersions. International Journal of Pharmaceutics **2015**, 491 (1), 208-217.
(63) Harsha, S.; Al-dhubiab, B. E.; Nair, A. B.; Attimarad, M.; Venugopala, K. N.; SA, K., Pharmacokinetics and tissue distribution of microspheres prepared by spray drying technique: targeted drug delivery. Biomedical Research **2017**, 28 (8), 3387-3396.
(64) Harsha, S.; Attimard, M.; Khan, T. A.; Nair, A. B.; Aldhubiab, B. E.; Sangi, S.; Shariff, A., Design and formulation of mucoadhesive microspheres of sitagliptin. Journal of Microencapsulation 2013, 30 (3), 257-264.
(65) Littringer, E. M.; Zellnitz, S.; Hammernik, K.; Adamer, V.; Friedl, H.; Urbanetz, N. A., Spray Drying of Aqueous Salbutamol Sulfate Solutions Using the Nano Spray Dryer B-90—The Impact of Process Parameters on Particle Size. Drying Technology **2013**, 31 (12), 1346-1353.
(66) Schafroth, N.; Arpagaus, C.; Jadhav, U. Y.; Makne, S.; Douroumis, D., Nano and microparticle engineering of water insoluble drugs using a novel spray-drying process. Colloids and Surfaces B: Biointerfaces **2012**, 90, 8-15.
(67) Schoubben, A.; Giovagnoli, S.; Tiralti, M. C.; Blasi, P.; Ricci, M., Capreomycin inhalable powders prepared with an innovative spray-drying technique. International Journal of Pharmaceutics 2014, 469 (1), 132-139.
(68) Faber, M. S.; Jin, S., Earth-abundant inorganic electrocatalysts and their nanostructures for energy conversion applications. Energy & Environmental Science **2014**, 7 (11), 3519-3542.
(69) 69. Halck, N. B.; Petrykin, V.; Krtil, P.; Rossmeisl, J., Beyond the volcano limitations in electrocatalysis – oxygen evolution reaction. Physical Chemistry Chemical Physics 2014, 16 (27), 13682-13688.
(70) Zheng, J.; Sheng, W.; Zhuang, Z.; Xu, B.; Yan, Y., Universal dependence of hydrogen oxidation and evolution reaction activity of platinum-group metals on pH and hydrogen binding energy. Science Advances **2016**, 2 (3), e1501602.
(71) Franceschini, E. A.; Bruno, M. M.; Williams, F. J.; Viva, F. A.; Corti, H. R., High-Activity Mesoporous Pt/Ru Catalysts for Methanol Oxidation. ACS Applied Materials & Interfaces **2013**, 5 (21), 10437-10444.
(72) Mahoney, L.; Rasalingam, S.; Koodali, R. T., Dye-Sensitized and Doped TiO₂ Mesoporous Materials for Visible Light-Induced Photocatalytic Hydrogen Evolution. In Photoinduced Processes at Surfaces and in Nanomaterials, American Chemical Society: **2015**; Vol. 1196, pp 81-101.
(73) Franceschini, E.; Lombardo, M. V.; Soler-Illia, G. J. A. A.; Zelcer, A. Un procedimiento para la obtención de partículas esféricas de óxidos metálicos mesoporosos de composición, área superficial, porosidad y tamaños controlados. (N° 20150104299). **2015**.
(74) Zakaria, M. B.; Elmorsi, M. A.; Ebeid, E.-Z. M., Nanostructured TiO2 Coated Stainless Steel for Corrosion Protection. Journal of Nanoscience and Nanotechnology **2016**, 16 (9), 9215-9222.
(75) Nanoporous materials: science and engineering. Imperial College Press Covent Garden, London, United Kingdom **2004** Vol. 4.
(76) Walcarius, A.; Mercier, L., Mesoporous organosilica adsorbents: nanoengineered materials for removal of organic and inorganic pollutants. Journal of Materials Chemistry **2010**, 20 (22), 4478-4511.

(77) Gibson, L. T., Mesosilica materials and organic pollutant adsorption: part B removal from aqueous solution. Chemical Society Reviews **2014**, 43 (15), 5173-5182.
(78) López-Juárez, R.; Reyes-López, S. Y.; Ortiz-Landeros, J.; González-García, F., Spray drying: The synthesis of advanced ceramics. In Sprays: Types, Technology and Modeling, Vella, M. C., Ed. Nova Science Publishers, Inc.: **2011**; pp 181-207.
(79) Nanaki, S. G.; Kyzas, G. Z.; Tzereme, A.; Papageorgiou, M.; Kostoglou, M.; Bikiaris, D. N.; Lambropoulou, D. A., Synthesis and characterization of modified carrageenan microparticles for the removal of pharmaceuticals from aqueous solutions. Colloids and Surfaces B: Biointerfaces **2015**, 127, 256-265.
(80) Zhang, H.; Dang, Q.; Liu, C.; Yu, D.; Wang, Y.; Pu, X.; Liu, Y.; Liang, Y.; Cha, D., Fabrication of methyl acrylate and tetraethylenepentamine grafted magnetic chitosan microparticles for capture of Cd(II) from aqueous solutions. Journal of Hazardous Materials **2019**, 366, 346-357.
(81) Emmanuelawati, I.; Yang, J.; Zhang, J.; Zhang, H.; Zhou, L.; Yu, C., Low-cost and large-scale synthesis of functional porous materials for phosphate removal with high performance. Nanoscale **2013**, 5 (13), 6173-6180.
(82) Shen, J.; Li, Y.; Zhu, Y.; Hu, Y.; Li, C., Aerosol synthesis of Graphene-Fe3O4 hollow hybrid microspheres for heterogeneous Fenton and electro-Fenton reaction. Journal of Environmental Chemical Engineering **2016**, 4 (2), 2469-2476.
(83) Debecker, D. P.; Le Bras, S.; Boissière, C.; Chaumonnot, A.; Sanchez, C., Aerosol processing: a wind of innovation in the field of advanced heterogeneous catalysts. Chemical Society Reviews **2018**, 47 (11), 4112-4155.
(84) Liu, B.-X.; Wang, J.-S.; Li, H.-Y.; Wu, J.-S.; Li, Z.-F., Hollow mesoporous WO3 spheres: Preparation and photocatalytic activity. Chinese Journal of Inorganic Chemistry **2012**, 28 (3), 465-470.
(85) Soler-Illia, G. J. D. A. A.; Lombardo, M. V.; Zelcer, A.; Franceschini, E. Method for producing spherical particles of mesoporous metal oxides having a controlled composition, surface area, porosity and size. **2017**.
(86) Kodas, T. T.; Hampden-Smith, M. J., Aerosol Processing of Materials. Wiley-VCH: **1999**.

MaríaVerónica Lombardo, **PhD.**

She is Licenciate (MSs) in Chemistry (FCEN-UBA, 2007). She worked for 3 years (2006-2009) at Boehringer Ingelheim Argentina in R&D. Then, she obtained a PhD in Science and Technology, Chemistry Mention (3iA, UNSAM, 2013). She made a postdoc (2014-2016) with CONICET scholarship in the Chemistry of Nanomaterials Group. After, she carried out another postdoc (2016-2018) with a CNEA scholarship. Nowadays, she is Assistant Researcher of CONICET in the Chemistry of Nanomaterials Group (CAC-CNEA) and Professor of General Chemistry (ECyT – UNSAM). Her work is about synthesis of mesoporous and mesoporous hybrid materials by spray drying with nuclear and environmental applications. (www.qnano.com.ar).

Andrés Zelzer, PhD.

2002: Chemistry degree, Faculty of Exact and Natural Sciences (FCEN), University of Buenos Aires (UBA)

2007: PhD in Chemistry, Inorganic, analitical and Physical Cehmistry Department (DQIAQF)-UBA/INQUIMAE-CONICET. Directors: Dr Fabio D. Cukiernik (FCEN/INQUIMAE), Dr Daniel Guillon (GMO-IPCMS) and Dr Bertrand Donnio (GMO-IPCMS).

2007-2010: Postdoc at the nanoMaterials Chemistry Group, GQ-CAC-CNEA. Supervisors: Dr Galo Soler-Illia and Dr Alejandro Wolosiuk

2011-2014: Researcher at Nanomaterials Chemistry Group, GQ-CAC-CNEA.

Since 2015: Researcher at CIBION. Head of the Hybrid and Structured nanoMaterials Group.

Esteban Franceschini, PhD.

Dr. Esteban Franceschini has a degree in chemistry from the National University of Cordoba and a PhD from the University of Buenos Aires. He worked at the National Atomic Energy Commission (Constituyentes Atomic Center) in the development of nanomaterials for fuel cells and currently is a CONICET associate researcher at Research Institute in Physical Chemistry of Cordoba developing materials for hydrogen generation in alkaline medium