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Mahmood Aliofkhazraei
Editor

Comprehensive Guide for Mesoporous Materials

Properties and Development

NOVA

MATERIALS SCIENCE AND TECHNOLOGIES

COMPREHENSIVE GUIDE FOR MESOPOROUS MATERIALS

VOLUME 3

PROPERTIES AND DEVELOPMENT

MAHMOOD ALIOFKHAZRAEI
EDITOR

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PREFACE

This is the third volume of the four volume set of Comprehensive Guide for Mesoporous Materials, mainly discussing different properties and the development of mesoporous materials. Many applications for these materials have been recognized. Ultra precision methods also developed for commercialization of these materials. Like many nanostructured materials, mesoporous materials are also found in abundance in nature, such as in cell walls that are made of mesoporous membranes although they are much more complicated. During past decades in the oil industry, natural mesoporous materials known as zeolites are widely used. However, most of them are now produced artificially.

Chapter 1 - Ordered mesoporous silicates have been recently proposed as drug carriers because of their peculiar characteristics which enable them to host drugs inside their ordered mesopores and then to release them. Many different applications have been proposed such as drug controlled release, targeted delivery and poorly water-soluble drug dissolution rate improvement. Poor solubility of a drug is one of the most serious problems in the development of a pharmaceutical product and ordered mesoporous silicates have been proposed as agents to decrease/solve this problem. Among them, MCM-41 and SBA-15 are the most studied. This chapter reviews the research work in this area and presents results on different drug loading procedures, the influence of pore size and drug physical stability. A comparison with other porous inorganic matrices is discussed as well.

Chapter 2 - The development of bioceramics designed for bone tissue regeneration has experienced an important boost with the appearance of a new generation of materials: mesoporous bioactive glasses (MBG). MBGs are commonly prepared in the systems SiO_2-CaO-P_2O_5 or SiO_2-CaO, similarly to bioglasses prepared by conventional sol-gel processes. The incorporation of a structure directing agent to the synthesis results in sol-gel bioglasses with highly ordered mesoporous structures and much higher surface area. The consequence is that MBGs exhibit much higher solubility, better bioactive behavior and the capability of hosting and releasing drugs aimed to improve the regenerative healing process. In this chapter, the preparation methods, drug delivery applications and the development of scaffolds for in situ bone regeneration are reviewed and commented.

Chapter 3 - The substitution of various main group metals such as Al, Ga, In, Zn and Cd, transition metals such as Ti, V, Fe, Cu, Nb, Mo and Zr and rare earth elements like La and Ce into the frame-work of MCM-41 has received much attention to develop more efficient and stable materials for application in adsorption, catalysis, photocatalysis, separation and chemical sensing. The metal ions can be incorporated via ion-exchange, impregnation, co-

condensation and solid state vaporization. The incorporation of a metal into the frame-work of MCM-41 seems to be easy but the retention of mesoscopic order is often difficult and the stability depends on the amount of dopant material. In case of tetravalent metals viz. Ti, Zr, Ge and Sn the grafting could be done by isomorphous substitution of tetravalent Si, into the walls of MCM-41 during in-situ or Liquid Crystal Templating (LCT) mechanism where the charge on the walls is balanced and neutral. But the incorporation of trivalent metals (Al, B, Ga and Fe) introduces a negative charge and generates a cation exchange or Bronsted acid site on the surface of MCM-41. MCM-41 have been used to custom synthesize catalysts because of the controllable properties, such as pore size, active phase incorporation, crystal size, and morphology, among others. The materials prepared by hydrothermal methods provides a very high surface area and narrow uniform pore distribution in the mesopore region, and are highly thermally stable whereby the ions are not leached out after high temperature annealing, catalyst in electrochemical devices. The incorporation of platinum, ruthenium, and palladium onto Al-MCM-41 mesoporous silica by direct inclusion of various precursors indicate that the Al-MCM-41 mesoporous-ordered structure was not affected by metallic particle incorporation. Metallic nanoparticles dispersion on Al-MCM-41 was homogeneous, platinum and palladium samples have round shape particles and ruthenium sample exhibit a rod shape. In addition to this, the bimetal modified MCM-41 materials are equally important in various redox reactions. The incorporation of two different metals might create materials with different or new redox and acid properties. Supported bimetallic catalysts are very interesting materials in general terms since one metal can fine tune or modify the structural and electronic properties of the other. The bimetal systems like Cu/Zn, Cu/Ni, Co/(V, Nb, La), Ru/(Cr, Ni, Cu) modified MCM-41 can be used in some industrially important reactions such as oxidation, hydrogenation, hydro dehalogenation, H_2 production etc.

Chapter 4 - Mesoporous catalysts, such as silica (PMOs, MCM-41, SBA-15) and activated carbons, have been used in heterogeneous catalysis, due to a combination of high surface areas and controlled pore sizes. These mesoporous materials have been used as catalyst in a wide range of chemical reactions. Due to environmental pressure and a decrease in fossil fuel sources, alternative fuel sources, such as biomass or renewable feedstock sources, have become increasingly popular. Traditionally, the biomass conversion is carried out over homogeneous catalysts. However, homogeneous catalysts have some disadvantages, such as difficulty in separations and the production of toxic waste. Solid catalysts can replace the homogeneous ones in order to make the processes simpler and more environmentally benign. Heterogeneous catalysts have been used in different reactions biomass conversion. In this work, the use of mesoporous acid catalysts (silica and activated carbons) for the biomass conversion into chemicals and fuel will be reviewed.

Chapter 5 - Structuring of titania on a nanometer scale has attracted considerable attention in the past few years, since nanostructured titania shows outstanding properties and has widespread application potentials: e.g., in photovoltaics, photocatalysis, and gas sensing. Increasing attention has recently been focused on the simultaneous achievement of high bulk crystallinity and the formation of ordered mesoporous TiO_2 frameworks with high thermal stability. Mesoporous TiO_2 have continued to be highly active in photovoltaics and photocatalytic applications because it is beneficial for promoting the diffusion of reactants and products, enhancing photovoltaics and photocatalytic efficiency by facilitating access to the reactive sites on the surface of mesoporous TiO_2 films. This steady progress has demonstrated that mesoporous TiO_2 nanoparticles are playing and will continue to achieve an important role in the protections of the environment and in developing progress of dye-sensitized solar cells (DSSC). This chapter focuses on the preparation and characterisation of mesoporous titania as efficient photocatalysts and solar cells.

Chapter 6 - In the present chapter, the authors pay attention both to technical and physico-chemical aspects of porous silicon (PS) sensors operation. The transducers and sensors of resistivity, capacitance, Schottky barrier, MIS, FET, EIS, ISFET, LAPS and optical sensors with PS are considered. The set of gas sensor`s parameters for detection of humidity, CO, NO_2, different volatile organic compounds, alcohols, H_2S, H_2 and other gases is described.

Chapter 7 - Zeolites are crystalline aluminosilicates widely used in catalysis as well as in separation and purification fields. The unique combination of properties, such as, high surface area, well-defined microporosity, high thermal stability and intrinsic acidity underlie the successful performance of these materials for a great number of applications. However, when bulky reaction intermediate species are involved the purely microporous character of zeolites is a drawback, because it often imposes diffusion limitations due to restricted access to the active sites. This is the case of some applications in the petroleum, petrochemical and fine chemical industries.

This chapter aims to provide a comprehensive examination of the different approaches that can be adopted to enhance the accessibility and molecular transport in the zeolite framework, illustrated with examples from the literature.

Dealumination and, more recently, desilication are post-synthesis treatments that have been extensively used over numerous structures with academic and industrial interest. These treatments lead to Si/Al ratio changes and, simultaneously, hierarchical structures combining micro and mesopores are commonly obtained. As a consequence of the treatments, alterations of some important properties, such as, hydrothermal resistance and acidity are also observed. The catalytic performance is enhanced and generally the structures become less sensitive to deactivation due to coke deposition. There are also several examples pointing out the great advantage of consecutive treatments (e.g., dealumination by acid treatment followed by desilication, or vice-versa) to tune the samples catalytic properties.

In recent years, template based preparation strategies have been increasingly explored to obtain hierarchical structures with two or even three levels of porosity. This will result in a great increase in the accessibility and mass transport of the guest molecules towards the active sites within the zeolite framework.

In spite of the well documented benefits of hierarchical network for catalytic applications, the main industrial application is the steamed dealuminated Y zeolite in fluid catalytic cracking. The production of hierarchical porous materials, through the several methods before mentioned, are still at an exploratory phase, although some attempts to scale-up and supply them to industrial units were recently reported, which can be the start to a new era of hierarchical zeolites in industrial catalysis.

Chapter 8 - Since the discovery of the environmental issues associated to the use of fosil-fuel based energy, special attention has been paid to the development of electrochemical energy storage devices.In this context, lithium ion batteries and supercapacitors have been proposed for satisfying the future energy demands. However, the current state of the art for both devices indicates that advanced materials are required to a truly implantation of both technologies for stationary and mobile applications. Mesoporous materials can play an important role in these advances. They mainly show unique textural and morphological properties that can facilitate the electrochemical reactions involved in a lithium ion battery or can improve the necessary electrolyte/electrode surface interaction in a supercapacitor. After an introduction exposing the different mechanism of energy storage for lithium ion batteries and supercapacitors, the authors will focus on how the interesting properties of the mesoporous materials can influence the performance of themost common electrode materials. Finally, the authors will show their more recent research in the field, namely mesoporous $LiFePO_4$ and template mesoporous carbons for lithium ion battery and supercapacitor electrodes, respectively.

Chapter 9 - Mesoporous silicon owns a large range of refractive indices and is a material which offers many advantages for integrated photonic circuits. The light propagation will be presented for waveguides manufactured from porous silicon or oxidized porous silicon layers. Optical properties of these materials will also be discussed as a function of the oxidation degree, different functionalization steps of these porous layers. Some different types of waveguides will be described. Surface and volume scattering losses of these mesoporous materials will be modeled and discussed in order to determine the principal contributions to optical losses.

Chapter 10 - Mesoporous silica material, MCM-41 was synthesized and characterized by various physico-chemical techniques such as FT-IR, X-ray diffraction, N_2 adsorption-desorption, SEM and TEM. Cysteine was selected as a pro-drug molecule and the potential of MCM-41 as a drug delivery system was explored. The study on release profile was also carried out for cysteine loaded sample in stimulated body fluid (SBF) at room temperature. It was found that MCM-41 was able to release cysteine in a controlled manner and exhibit better effect than N-acetylcysteine in solution. 100% Cysteine release was observed in 12h.

Chapter 11 - Multivalent first row transition metal oxides (V, Cr, Mn, Fe, and Co) can form various oxide structures with unique catalytic properties. The catalytic performance of a mesoporous, high surface area TM oxide is known to be better than its nonporous counterpart. However, the direct synthesis of multivalent mesoporous TM oxide materials with desired crystal structure and structural properties is still a challenge to date. The multivalent nature, lack of proper sources, weak inorganic-organic interactions, and poor control of reaction rates are problems for the direct synthesis of mesoporous multivalent TM oxides. The authors summarize here some recent results of synthesized mesoporous hybrid materials with these TMs and their catalytic performances.

Chapter 12 - "Host-guest chemistry" is a potential subject, attracting a great deal of attention from various research areas, including large-molecule catalysis, separation techniques, adsorption procedures and drug delivery. Mesoporous materials with huge specific surface area, large pore volume and uniform pore size distribution could act as a kind of "micro-reactor" for synthesis of functional nanoparticles. The interaction of host species-mesoporous materials and guest nanoparitcles as well as the restriction effect of framework of host species endow the nanocomposites embedded by mesoporous materials unique and enhanced properties that facilitate future applications. Undoubtedly, the combination of various functional species and mesoporous matrices would open a realm of new possibilities for exploring of novel materials with unexpected functions.

Chapter 13 - There exist a great variety of phenomena taking place in porous solids that are strongly affected by the morphological and topological characteristics of these media, among these processes the authors can mention: (a) the immiscible displacement of a given fluid by another, (b) imbibition and drying processes, (c) separation of fluid mixtures, (d) heterogeneous catalysis, and (e) catalytic deactivation, etc. The characterization of mesoporous and macroporous materials, especially the issue regarding the determination of the pore size distribution of these substrates from experimental data, is a subject of great practical importance that involves the development of both theoretical and experimental methods. Some of the experimental techniques, as for instance NMR, SAXS, and SANS, require sophisticated instruments while some others such as Hg porosimetry and sorption of vapors require simple devices that are available to many laboratories. In order to understand the textural results provided by these methods, a crucial issue consists in the development of a theory that can appraise the topological properties of these media.

The present chapter thoroughly describes the computational techniques developed as well as the preliminary results that have been obtained for the simulation of porous networks subjected to geometrical restrictions. Also, the structure characterization of the constructed pore networks is updated within the framework of the fractal and percolation theory, something missing in previous publications. The chapter is organized as follows. Section 2 presents the theoretical background of the DSBM approach. Section 3 describes the incorporation of geometrical restrictions into the DSBM. Section 4 covers the topological characterization of pore networks. Section 5 accounts for the algorithms for the *in silico* construction of pore networks. Section 6 describes the parallel computational techniques for implementing the previous algorithms. Section 7 displays the simulated pore networks and the results obtained therefrom. Finally, in Section 8 the perspectives and the conclusion of this chapter are stated.

CONTENTS

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Chapter 1

ORDERED MESOPOROUS SILICATES MCM-41 AND SBA-15 AS MATRICES FOR IMPROVING DISSOLUTION RATE OF POORLY WATER SOLUBLE DRUGS

Valeria Ambrogi*
Dipartimento di Scienze Farmaceutiche,
Università degli Studi di Perugia, Perugia, Italy

ABSTRACT

Ordered mesoporous silicates have been recently proposed as drug carriers because of their peculiar characteristics which enable them to host drugs inside their ordered mesopores and then to release them. Many different applications have been proposed such as drug controlled release, targeted delivery and poorly water-soluble drug dissolution rate improvement. Poor solubility of a drug is one of the most serious problems in the development of a pharmaceutical product and ordered mesoporous silicates have been proposed as agents to decrease/solve this problem. Among them, MCM-41 and SBA-15 are the most studied. This chapter reviews the research work in this area and presents results on different drug loading procedures, the influence of pore size and drug physical stability. A comparison with other porous inorganic matrices is discussed as well.

* Tel/fax +39 0755855125, e-mail: valeria.ambrogi@unipg.it.

INTRODUCTION

Main statements	References
Bioavailability problems connected to poorly soluble drugs	[1], [2], [5]
Biopharmaceutics Classification System (BCS)	[3], [4]
Main features of mesoporous silicates MCM-41 and SBA-15	[6], [7], [8]
MCM-41 and SBA-15 as drug carriers for controlled drug release	[8], [9]
Mesoporous silicates as matrices for improving dissolution rate	[10], [11], [12]

Recently the ordered mesoporous silicates have been extensively studied for their application in pharmaceutical field and in particular as agents to improve dissolution rate of poorly water soluble drugs.

The poor water solubility is one of the most frequent cause of a new entity development failure and of reduction of marketed drug performance [1, 2]. In fact more than one third of the drugs listed in the US Pharmacopoeia and half of the new chemical entities or new active ingredients are poorly water soluble or insoluble. These negative characteristics obstacle drug development starting from the first steps such as in vitro studies which always required drug solubilisation, and then in clinical trials. Also when a drug is approved for market commercialization, poorly water solubility is a parameter that influences drug effectiveness and safety. In fact the first step for a solid dosage form administered through oral route is the drug dissolution and successively its absorption through the gastrointestinal mucosa until it reaches systemic circulation. Thus drug solubility and mucosa permeability are two relevant characteristics which determinate the drug bioavailability and consequently its efficacy and safety. A drug with poor water solubility often has an erratic or incomplete absorption, which can be strongly affected also by the presence of food, variability of gastric pH and gastrointestinal transit rate. In order to obtain the required efficacy it may be necessary to increase the dose but this often causes increased side-effects.

The importance of drug solubility is proved by the Biopharmaceutics Classification System (BCS) proposed by Amidon in 1995 [3] and provided by FDA [4] which classified drugs in four different classes according to their water solubility and permeability. BCS classified drug substances in:

Class I: high permeability, high solubility
Class II: high permeability, low solubility
Class III: low permeability, high solubility
Class IV: low permeability, low solubility

All poorly water soluble drugs are classified as BCS II or IV class. Whereas class I drugs do not present problems of formulation and bioavailability, class II and IV drugs present a big challenge for the formulator and are good candidates for reformulation using the new different technologies available for solving solubility problems. These new strategies offer both the opportunity to rescue promising developmental compounds which were abandoned because of solubility problems, and to improve marketed drug performance. In particular for well absorbed drugs (class II), the step limiting the bioavailability is the drug dissolution rate which according to the Noyes-Whitney equation is proportional to drug solubility. Thus poorly soluble drugs have a slow dissolution rate with the consequence of low absorption and low bioavailability and an increase of their dissolution rate could improve their performance [5].

Recently among the range of technologies currently available for improving dissolution rate of poorly water soluble chemical compounds, the use of mesoporous ordered silicates has been proposed.

The mesoporous silicates are inorganic materials synthesized in the presence of surfactants which act as templates for polycondensation of silicic species, a source of silica, a solvent and a catalyst. [6]. When a cationic surfactant, such as alkylamonium salt, is present as a template, the M41S materials are obtained [7]. The most famous representative of this group is MCM-41 which has a honeycomb structure that is the result of hexagonal packing of unidimensional hexagonal mesopores with pore size and wall thickness do not go beyond 4.0 and 2.0 nm respectively. When a non ionic surfactant such as Pluronic P123, a triblock copolymer of poly(ethylene glycol)-poly(propylene glycol)-poly(ethylene glycol), in acidic medium is used, materials called SBA (Santa Barbara University) are obtained. The most representative SBA material is SBA-15. It is characterized by hexagonal, unidirectional pores such as MCM-41, with thicken pore walls, larger pore size and interconnected micropores. Whereas SBA-15 material has a pore diameter of 6-8 nm and pore volume > 1.0 cm^3/g, MCM-41 has a pore diameter of 2-3 nm and a pore volume > 0.7 cm^3/g. Both materials have high surface area (more than 900 m^2) and the presence of superficial silanol groups (single, hydrogen bonded and geminal) which can interact with molecules that can be hosted inside the pores (Figure 1).

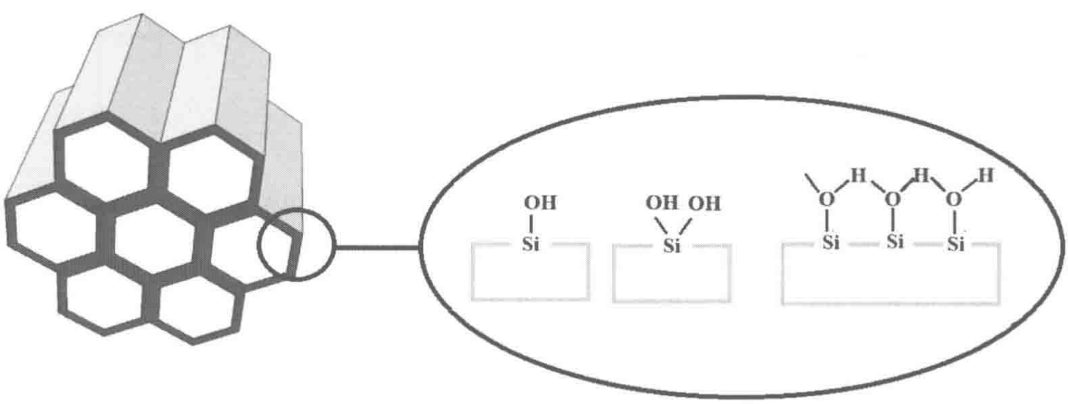

Figure 1. Schematic representation of MCM-41 and of the different kinds of superficial silanol groups (single, geminal and hydrogen bonded).

Originally the focus of mesoporous silica materials was on the development of slow release formulations after their compression in disks with the aim of obtaining bioactive biomaterials for drug controlled release [8, 9]. Then the attention of researchers was turned towards the possible use of these materials for obtaining fast drug release. First Charnay [10] evaluated the release property of MCM-41 as a powder and ibuprofen was selected as a model molecule since it is a well documented and used anti-inflammatory drug. Furthermore, it has a lipophilic character and its molecular size is suitable for inclusion within the mesopores of MCM-41. After this paper publication, the effects of mesoporous silicate materials such as MCM-41 and SBA-15 on dissolution rate of poorly water soluble drugs has been largely evaluated.

Ordered mesoporous silicates such as MCM-41 and SBA-15 result proper materials for improving drug dissolution rate because (i) their high surface area allows a wide contact between solid particles and biological fluids and this favors dissolution rate according to Noyes-Whitney equation, (ii) the unidirectional and size uniform pores shun any tortuosity and narrowing that could slow the diffusion of the adsorbed drug, (iii) the light interactions between silicate silanols and the adsorbed molecules break easily in the presence of water with consequent rapid guest release in molecular form, (iv) once adsorbed, the drug molecules are not organized in crystalline form as they are confined in the pore space which is only a few times larger than the drug molecule and thus the physicochemical properties differ dramatically from those of the corresponding bulk material; the lack of an ordered form facilitates the drug dissolution especially when there is a high lattice energy, v) the improvement of wettability properties favors the contact between the fluid and the powder surface [11,12].

Figure 2 illustrates the release of adsorbed drug molecules from MCM-41 or SBA-15 in the presence of water.

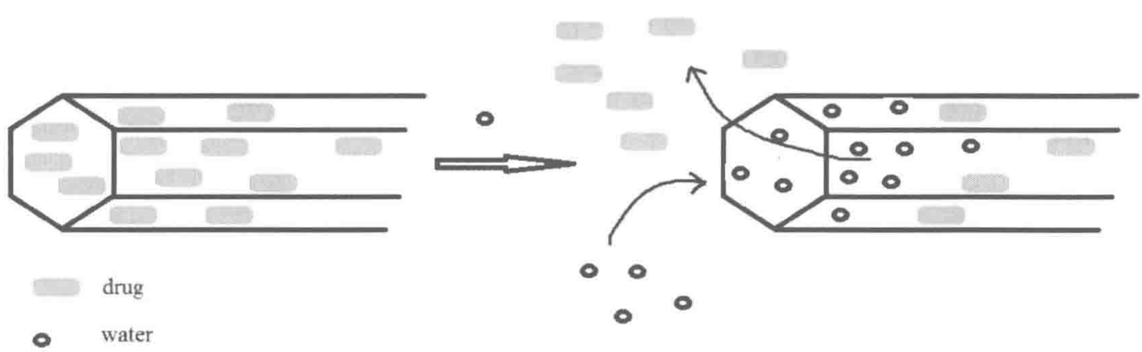

Figure 2. Schematic representation of the release of loaded drug molecules from the mesoporous silicates (MCM-41 or SBA-15) in the presence of water.

The drug loading procedure can influence the dissolution rate as it plays an important role in determining the physical state of the drug inside the pores. The most common drug loading procedures in mesoporous silicates are achieved by: (i) adsorption from an almost saturated drug solution in an organic solvent, usually ethanol but also others such as hexane, dichloromethane and dimethylsulfoxide. After equilibration the loaded silicate is recovered by filtration [10, 11, 13]; (ii) the melt method in which the physical blend of drug and matrix is heated until drug melts and enters into the pores [14, 15]; (ii) the incipient wetness impregnation method in which a controlled amount of concentrated drug solution, generally in an organic solvent, is added to the inorganic particles, giving a moist powder, and allowed to diffuse by capillarity into the pores, followed by solvent evaporation [10, 16]; (iv) the solvent evaporation method in which the silicate is dispersed in a drug solution (e.g., ethanol, dichloromethane, etc.), sometimes sonicated and finally dried, upon solvent removal, by evaporation [14, 17]; (v) co-spray drying [18]; and (vi) near-critical (liquid) [19] and supercritical [20, 21] CO_2 methods which avoid the use of organic solvents and the steps for their elimination.