Silicon Based Materials for Drug Delivery Devices and Implants

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Received: June 20, 2007; Accepted: August 13, 2007; Revised: August 22, 2007

Abstract: This patent review focuses on silicon based materials for drug delivery systems and implant devices devoted to medical applications. The article describes some representative examples of the most depictive silicon based compounds associated with drug release formulations and tissue engineering biomaterials. Ranging from inorganic to organic and hybrid inorganic-organic silicon compounds, the paper referrers to patents describing inventions which make use of the best properties of silicon dioxide, silica aerogel and xerogel, silicon bioactive materials, silicones and ormosils, pointing out the usefulness of each kind of compound within the invention embodiment.

Keywords: Biomaterials, silicon devices, drug delivery devices, silicon based implants.

INTRODUCTION

Silicon is one of the most abundant chemical elements in earth: mainly in the form of silicates in the crust, is the second behind oxygen. It is essential in plants and animals in which the role of silicon structures is central. Si presence in plant tissues enhances their strength and rigidity, improving host resistance to plant diseases by stimulating defense reaction mechanisms [1, 2]. Many sponges and unicellular algae have their shells made of silicon [3]. The finding of carbon-silicon hybrid compounds in living colony of diatoms could lead to a variety of beneficial applications such us therapeutic treatments for osteoporosis [4]. Recently, it was found that sponges have "silicateins": biosilica forming enzymes that mediate the catalytic formation of biosilica from monomeric silicon compounds [5]. The kinetic steps in this biosynthesis are fast and low energy consuming, like the majority of the biosynthesis that keep awake to the biochemists in their efforts to imitate them. These observations reinforce the conviction that biomimetic chemistry is the discipline which will help to find better mechanisms to obtain low-cost synthesis of high-performance materials [4, 6].

The present article focuses on the description of the different types of silicon based materials which lead to the building of drug delivery devices and implants. The silica chemistry developed during the fifthties with Roy's pioneer works in the understanding of the sol-gel methodology allowed the obtaining of novel ceramic materials [7-8]. In the same period Iler's works led to the first commercial development of colloidal silica powders [9]. Here below follows the description of some representative patented drug delivery devices and implants where silicon derivatives play a relevant role in the formulation properties. There is an attempt of classification dividing the biomaterials and medical devices in groups according to its use: silicon particles, silica aerogel and xerogel, bone repairing materials and so on. Moreover, this classification intends to keep a kind of order from inorganic to organic and finally inorganic-organic hybrid compounds. The reader shall understand the unavoidable mixing arising from many examples which belong to two or even more groups within this text order.

SILICON PARTICLES

An extensive use of inorganic silicon particles is the applicability of silicon dioxide as excipient in pharmaceutical formulations. There are several commercial forms varying in particle size, porosity and polarity. An exceptionally pure form of silicon dioxide is the so-called fumed silica, with particle size ranging from 7 to 50 nanometers. The submicron particles are able to move easily between larger particles forming a layer which acts like ball bearings or lubricant, aiding flow. The hydrophilic nature of the fumed silica absorbs water off from particle's surface, preventing caking. There are many registered trademarks of fumed silica for use as pharmaceutical excipient, some of them offering also hydrophobic silica, which can be used helping drug dissolution.

Silicon dioxide particles combined with polysaccharide excipients yield blends with improved compressibility properties. For example, Badwan and Al-Remawi found that coprecipitation of chitosan with silicone allows manufacturing a sustained release formulation with a substantially improved compressibility in comparison to normal commercially available high-density grades of chitosan. The optimal composition contains silicon dioxide in the range of 1-75% w/w, and the most preferable concentration is 50% w/w [10]. Marrodan's patent is another example using silica powder for improving the efficiency of pharmaceutical formulations [11]. He used silica powder as dispersing agent and filler with antifungal drugs for the treatment of fungal infection of the skin. In his invention pointed out that most drugs currently available for the treatment of mycoses have limited efficacy because they are used in low concentration owing to their high toxicity. Their beneficial effects, therefore, depends on the vehicle used. The novelty of the present invention is a silica powder with acidic properties which is by itself inhospitable for fungus.

High purity silicon dioxide processed to a micronized free flowing powder with high absorptive capacity allows the invention patented by Chauveau and *et al.*. [12]. They obtained fast disintegrating tablets, which are claimed to disintegrate in the mouth in less than one minute. The object of the invention is to provide not only a fast disintegration in the mouth but also a pleasant palatability and optimum bioavailability of the active principle together with satisfactory hardness. The micronized silica act as permeabilizing agent, which also, through its properties as a flow promoter, favours the rearrangements of the particles during compression, making possible on the one hand to reduce the amount of hydrophobic lubricant needed to ensure optimum manufacturing conditions, and on the other hand to reduce the intensity of the compression force needed to produce a tablet.

With the evolution of the sol-gel synthesis technology, inorganic silicon particles emerged as a suitable material for controlled release formulations. For example, Barbe and Bartlett described in their patent and parent article the obtaining of monodispersed controlled release ceramic particles [13, 14] able to encapsulate and release an active drug in a controlled manner. An advanced concept of drug delivery materials are the so-called smart

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1872-2105/07 $100.00+.00

injectable particulate, referred to carriers able to bring a sustained and controlled bioavailability of the active therapeutic molecules and preferential targeting to diseased tissue. For this purpose some laboratories focused on the use of derivatized silicon-based microparticles with nanoporosities [15-19]. Cohen *et al.* [15] report in their article a method for obtaining the porous silicon particles and patents 16 to 19 describe the derivatization steps giving place to the building of very specialized surface-modified silica particles. When solvent is dried away from afore mentioned silica particles the porous structure obtained is named xerogel, a topic covered in next section.

SILICA AEROGEL AND XEROGEL

The first silicon aerogel was created by Steven Kistler in 1931, as a result of a bet with a colleague of Stanford University over who could replace the liquid inside a jam (jelly) jar with gas without causing shrinkage [20, 21]. A typical aerogel is 99.8% air and 0.2% matter and is the lightest known material weighing about 3 milligrams per cubic centimeter and one of the best known thermal insulators. Aerogel is sometimes called "solid smoke" because of its extraordinarily low density and the bluish cast it takes when light shines on it. Silicon dioxide aerogels consist of bonded silicon and oxygen atoms joined into long strands and then into beads randomly linked together with pockets of air between them. Although some companies took an interest in Kistler and his aerogels in the 1930s and 1940s, for a time using the substance as an additive in cosmetics and toothpaste, interest dwindled and little other activity ensued. Aerogel research was generally abandoned for many years, due to the troublesome synthesis process.

A "silica xerogel" is a silica gel from which the liquid medium has been removed and replaced by a gas without hindering shrinkage, the structure being compressed by the surface tension forces as the liquid is removed. This shrinkage causes a significant reduction in the porosity, often as much as 90 to 95 percent depending on the system and pore sizes.

In the last years some reports pointed out aerogel usefulness. Smirnova *et al*. studied the feasibility of hydrophilic silica aerogels as drug carriers for poorly water-soluble drugs [22, 23]. Hydrophilic silica aerogels of different densities were loaded with model drugs by adsorption from its solutions in supercritical CO_2. The authors reported that the release rate of the drug-aerogel formulations was much faster than that of the corresponding crystalline drugs (rate increases in 400-500%). The reasons for the release enhancement are the enlarged specific surface area of drugs adsorption on aerogels compared to their crystalline form and the immediate collapse of aerogel network in aqueous media. Although the conclusion drawn by the authors is that dissolution rate of poor water soluble drugs can be significantly enhanced by adsorption on silica aerogels, the cumbersome procedure for aerogel synthesis makes this method unsuitable at industrial scale.

In spite of synthesis difficulties, some targeted devices make use of the particular conductive and/or insulating properties of aerogels. Verness designed an electrical medical leads taking advantage of conductive aerogels. This medical device is intended for chronic implantation in the body (heart or nearby) for applying electrical stimulation and/or sensing electrical activity, particularly related to cardiac diseases [24]. Along years the term aerogel found in the literature shows a slightly different concept regarding the essential material properties defined originally by Kistler in 1931. This change is clarified in the description of Yoldas's patents about synthesis methods allowing to obtain porous silica materials under subcritical conditions. Yoldas affirms that "porosity of the resulting silica aerogel is high, ordinarily at least 68 percent by volume, which represents only a small shrinkage of the gel. The remaining few percent is a continuous silica skeleton". He claims that, "although the process is more nearly akin to that for producing silica xerogels than the supercritical method traditionally used for producing silica aerogels, the properties of the product are more nearly characteristic of the silica aerogels than the silica xerogels. For this reason the products are referred to herein and in the claims as silica aerogels" [25, 26]. Nowadays the term aerogel is regularly used in the case of highly porous silica materials. In their patent "Smart aerogels" Daitch and *et al.*. show silica aerogels with encapsulated bio-affinity molecules and/or receptors designed to catch bioaerosols in its porous structures. In this patent aerogels are described having have two major properties of interest: a complex pore structure with micro- and meso-pores ranging from 2 nm to 100 nm, as well as a macro structure of over 100 nm, and a large internal surface area (about 1500 m.sup.2 /g) that can be coated with reactant compounds [27]. Ogorka and *et al*. have also used silica aerogel in their invention. They designed a tablet which matrix contains silicon aerogel as lubricant and also fumed silica in the coating and in the matrix core. The invention allows a controlled release of active agents in a time-controlled manner [28].

On the other hand, the use of silica xerogel in pharmaceutical and medical devices is also much extended, as carrier for active agents [29, 30] or even carrier for chromophoric coloring components in a dental binder [31]. Fig. (**1**) shows the schematic synthesis of aerogel and xerogel doped porous matrices and a picture of the kind of materials obtained. The reader will find applications and descriptions of silica xerogel materials in other sections within this article.

BONE REPAIRING MATERIALS. BIOACTIVE GLASSES AND SCAFFOLDS

"With the invention of bioactive glasses in 1969, Professor Larry Hench helped to shift the paradigm that was the cornerstone of developing biomaterials for implantation in the human body; namely that materials should be as inert as possible to minimize reactions with the body. The demonstration that a synthetic material could not only be biocompatible, but could form a tenacious bond with living tissue was a critical milestone in the field" [32].

Bioactive glasses are any glass capable of forming hydroxy-apatite after exposure to simulated body fluid. Bioactive scaffolds are temporary platforms combining physical support with biological activity. The role of silicon on this repairing material is clear: its presence increases bone ingrowth and bone/implant coverage: "Biochemistry studies suggest that specific genes are activated by soluble silicon species": this sentence starts an excellent discussion drawn by Hench, where the author reviewed his own findings and the most relevant studies in the literature [33, 34]. Fig. (**2**) shows a scheme depicting bioactive glass formation. For interested readers, many other relevant articles discuss about the putative mechanisms by which a bioactive material and a target tissue interact [35-38]. Here below some patents proposing improved silicon-containing bioactive materials are described.

In 2001, Hench and co-workers presented a patent which consists in injectable suspensions of bioactive glass and dextran or a dextran derivative, especially able to repair soft tissue or even hard bone in mammals, particularly humans. Bioactive glass composition contains SiO_2, Na_2O, CaO, P_2O_5, CaF_2 and B_2O_3. Dextran derivatives include free radical groups which can be polymerized following injection into a patient. The invention can be used to treat vocal cords, periurethral tissue, periureteral tissue, ear, tooth root canal, vertebral spaces, subcutaneous and intradermal soft tissues, among others. The inventors claim three additional important properties of this biomaterial: 1-the material form strong adherent bonds comprising a thin layer of collagen at a glass/soft tissue interface upon injection in the animal; 2- do not contribute to the formation of excess scar tissue, giant cells or acute inflammatory cells; and 3- do not cause long lasting foreign body reactions [39].

Silicon bioactive glasses find also application in dentistry: Litkowski and co-workers [40] found a method for preventing tooth

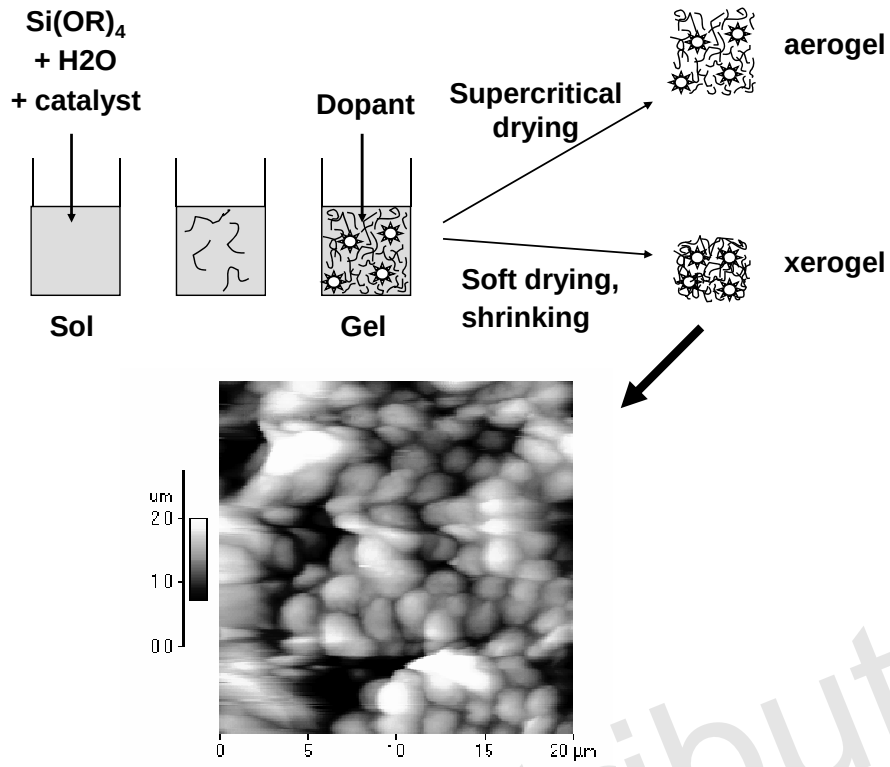

Fig. (1). Scheme depicting aerogel and xerogel synthesis. The dopant can be a pharmaceutical drug, a protein, or a template devoted to improve mechanical properties. The microscopy shows this last example of a silica xerogel doped with Tween surfactant. The atomic force microscopy (contact mode) shows particle sizes in the order of few micrometers. Adsorption nitrogen studies reveals nanopores in the order of 1-10 nm.

decay comprising a particulate bioactive and biocompatible glass. The material is a silica based bioactive glass composition that can be delivered by an agent such as a toothpaste, and will form a rapid and continuous reaction with body fluids due to the immediate and long term ionic release of calcium and phosphorus from the core silica particles to produce a stable crystalline hydroxy carbonate apatite layer deposited onto and into the dentin tubules. This allows tooth surface remineralization and long term reduction of dentin hypersensitivity.

Ahola and coworkers patented a method for obtaining controllably dissolvable silica-xerogels prepared via sol-gel process for its use as delivery device into which structure a biologically active agent is incorporated. This material has potential application for orthopedic and surgical purposes, providing a method of administering a biologically active agent to a human or animal body, which comprises implanting, injecting, or transmucosally attaching the xerogel matrix to a human or animal body [41]. The porous nature of xerogel plays a crucial role in this application as bioactive scaffold. In similar manner, Gerger patented a inorganic resorbable bone substitute material, an hydroxyl apatite/silica granular material of defined morphology, comprising a crystalline calcium phosphate embedded silica xerogel matrix, which is characterized by a variable mechanical strength and by a high resorbability *in vivo* [42]. The porosity of xerogels allows the resorption of the biomaterial and improves the bioactivity which is obviously produced by the calcium phosphate components by body-inherent proteins from the blood of the patient attaching themselves to the high internal surface. Consequently, the cells do not classify the biomaterial as foreign to the body [42, 43].

Hybrid silicon components can be found in bone repairing materials in the invention patented by Wiegand and Hu [44]. This material consists in organic silicon compounds derived from tetraloweralkylorthosilicates, silicon tetracarboxylates, and silicon-containing reaction products with carbohydrates such as glucose, sucrose, and ascorbic acid. The field of inorganic-organic hybrid silicon compounds is better described in another section.

SILICON AND SILICONE COATINGS

The coating may impart a number of characteristics to the material such as altering its surface properties, its rate of dissolution, or its rate of diffusion and/or release of an active encapsulated component. Reviewing silicon derivatives, we can find both inorganic and organic options for biomaterials coatings.

One example of inorganic coatings is fumed silica. This type of silica has chain-like particle morphology. In liquids, the chains bond together via weak hydrogen bonds forming a three dimensional network, trapping liquid and effectively increasing the viscosity. These properties allow fumed silica to be used for biocompatible coatings. Its controlled evaporation helps to prevent fat edges caused by surface tension effects when fast evaporation arises near the edges. Besides, when allowed to stand for long enough, coatings become sag resistant.

Santamaría and co-workers applied a porous silicon coating (mesoporous silica and titanosilicates) to cover medical devices like intravascular stents for inhibiting the onset of angioplastic restenosis, encapsulating furthermore the suitable pharmaceutical formulation [45]. The invention also takes advantages on the controllable drug release kinetics modulated by the coating porous size and film thickness.

It is often found the use of silicon hybrid inorganic-organic coatings on medical devices. For example, Briquet and Lord patented a biocompatible coating consisting on a mixture of polysiloxane and acetoxysilane as crosslinking agent, reinforcing filler (fumed silica) and a metal catalyst. The composition of the mixture is applied to the medical device by dip coating, spray

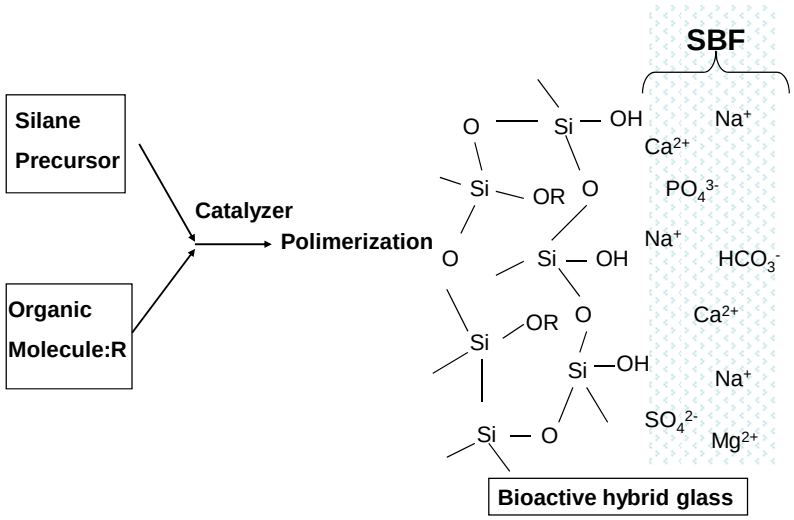

Fig. (2). Schematic drawing of the structure of a bioactive inorganic–organic hybrid. The organic molecule improves the mechanical properties of the material increasing flexibility.
SBF: Simulated body fluid

coating or flow coating. Thickness of the coating can be varied between 0.1 and 10 micrometers [46]. Talton focused on the coating of particulate materials with ultrafine silicone films (among other polymers) by vapor deposition using pulsed laser ablation deposition [47]. Although difficult to apply on a large scale synthesis, the technique offers the advantage of producing very thin and uniform coatings.

A different application of coating is the invention patented by Tan and *et al.*. [48]. This patent depicts a method for preparing functionalized nanoparticles where the silica coating is derivatized with one or more functional groups to yield particles particularly suited for specific applications like for example, the identification of cells expressing a preselected molecule. This method consists in providing silica nanoparticles coated with a functional group that binds to the selected molecule, such as an antibody. When particles are mixed with a cell suspension they will specifically bind the cells expressing the preselected molecule; then the suspension can be analyzed to find the bound nanoparticles. In addition particles can be fluorescently stained, allowing microscopy analysis as well.

This is an example of silicon based materials applications in nanotechnology for medical diagnosis, which also includes systems based on quantum dots. Quantum dots are metal nanocrystals having a characteristic spectral emission, which is tuneable to a desired wavelength by controlling the size of the nanocrystal. However, quantum dots have poor solubility in water and therefore results non compatible with biological aqueous environments. In this regard, silica appears as a good choice as coating material since it prevents the coated nanocrystals from coagulation in aqueous dispersion. Additionally, silica nanoparticles can also be labelled with biofunctional groups linked to the surface [49-51]. Quantum dots are powerful in highly sensitive fluorescent biological assays**,** fluorescence labelling of living cells and detection of antigens. Some patented examples are quantum dots fabrication using cast or moulded silicones [52] and silica nanoparticles as hosts [53].

Jordan and *et al.* [54] elaborated a method for encapsulating therapeutic substances in cells. The invention relates the use of nanoparticles as carriers for therapeutically active substances and to target them to cells by means of a particular coating. The particles are chemically formed in such a way to enable a high absorption into the cells. The procedure enables an increased efficiency of the encapsulated substance with a simultaneously low systemic toxicity and reduction of side effects.

For its biocompatibility and good mechanical properties, silicone is a much found material in medical devices design. McGhee and co-workers [55] patented an inventive coating designed to deliver a pharmaceutical agent to a selected body area within the insertion or application of a medical device made of silicone. The coating is a hybrid of urethane and silicone which can incorporate additives such as anti-microbial, anti-fungal and other organic compounds. The release rate is adjusted by utilizing different salt forms of the additive and adjusting the relative concentrations of urethane and silicone.

SILICONE IMPLANTS

Silicone rubber is a unique synthetic elastomer made from a cross-linked polymer which is reinforced with silica to improve tensile strength. Its characteristics are such that it provides the perfect balance of mechanical and chemical properties required by the most demanding applications. Have also the advantages of high and low temperature stability, chemical resistance and can be molded in a variety of shapes and sizes with different hardness's from very soft to hard materials.

Silicone has been in use as a medical implant material in various forms since the 1960s. Nowadays, silicone elastomers are widely used and accepted materials throughout the medical field. This allows creating devices to be applied in quiet different body environment, as will be accounted in the examples below. For the interested reader, a detailed silicone chemistry description and history review can be found in reference [56] (and references therein). Here below we describe some of the last applications in implantable devices.

In 2006, McClay patented an intravaginal drug delivery device for the administration at a constant release rate of oestradiol precursors during three weeks [57]. The implantable device is a biocompatible hydrophobic elastomeric polymer matrix forming a hollow annulus having a sheath surrounding the matrix. A similar device was previously developed to be used in the treatment of uterine myoma [58], consisting in a multiple layered silicone implant encapsulating the drug to be delivered during several weeks. Greenberg patented an implantable drug delivery device able to deliver drug to the retina. The device minimizes stress by

virtue of its softness and smooth shape. This is possible because of the particular mechanical properties of silicone materials. The released drugs delivered by osmosis stimulate the retina to enable vision in blind patients [59].

An interesting application taken advantage of silicone elasticity is the one patented by Lee and *et al.*. [60]. They invented a silicone hollow tube able to deliver drugs intravesically by having a reservoir containing the drug. The device is configured for minimally invasive insertion into a body cavity, such as the bladder. The hollow tube is elastomeric to permit the device to be elastically deformed from its initial shape into an elongated shape for passage through a catheter, where following such passage the device can return to its initial shape to facilitate its retention in the body cavity.

Implants like a mitral heart valve [61], materials for surgical reconstruction of tendons and ligaments [62], shunt implants for treating glaucoma [63], diffractive lenses for vision correction [64] and even a flexible finger [65] can be built using the versatile biocompatible silicone materials.

INORGANIC-ORGANIC HYBRID BIOMATERIALS

The chemistry of covalent inorganic-organic silicon compounds is in permanent development. Some authors called these materials IPN's (inorganic organic interpenetrating networks). But a most specific name given to this kind of silicon hybrids in the late eighties is ormosils (organically modified silanes) [66, 67]. Outside medical field, ormosils have found a wide variety of applications such as coatings, corrosion protective for metal surfaces, photochromic glass surfaces and color decorative for glasses and plastics. These materials can be produced in the form of nanoparticles, aerogels, bulk, nanocomposites and fibers. Some publications reviewing synthesis processes and applications can be mentioned: Shimojima and Kuroda report recent progress in the synthesis of nanostructured siloxane-organic hybrids; in another field Saliterman reviewed the role of ormosils in MEMS medical devices and Tripathi *et al*. reviewed the use of ormosils for building biosensors [68-70]. There are hundreds of patents related to ormosils in different technological areas. Herein only few medical applications are mentioned with the aim to illustrate the advantages of hybrid materials.

Bone repairing therapies always need the finding of new materials improving reconstructive surgeries. Giordano and Wu patented a re-inforced anatomically accurate bioactive protheses [71] that is a good example of hybrid material. This invention embodies implants comprising a porous surface layer and a tough inner core of interpenetrating phase composite. The porous surface layer enhances the biocompatibility and tissue ingrowth, while the tough inner core improves the mechanical properties of the implant. The internal regions are one or more interpenetrating phases. Many FDA-approved polymers can be utilized for the filling material, e.g. polyethylene glycol, waxes, hydrogels, acrylic latexes, and other water-soluble or water-dispersible materials. The embodiment of the invention comprises inorganic-precursors dispersed in polymer/ monomer combinations. Examples of inorganic precursors include but are not limited to alkoxides (metal alkoxides, silicon alkoxides, non-silicate tetravalent metal alkoxides, sol-gel organic-inorganic hybrids, and other organic-inorganic hybrids which can lead to in situ crystallization or formation of an interpenetrating phase of organic-inorganic hybrid.

Diaz and *et al.*. patented prosthesis for total or partial replacement of an articulating skeletal joint having two opposed bearing surfaces made of a ceramic and a metal, respectively. The ceramic material is a silicon nitride or silicon carbide and the metal is preferably nitrogen alloyed chromium stainless steel. The inventors claimed that this hybrid material has improved surface smoothness and wear resistance to reduce osteolysis [72]. Prasad and co-workers deve-loped poynucleotide-amino functionalized ormosil complexes that can be used for delivery of the polynucleotides to cells [73]. For example, these complexes can be used as a non-viral gene transfection vehicle. The amino functionalized ormosil particles provide a mechanism to insert genes into host tissue efficiently without the side effects associated with viral and chemical methodologies.

A last issue to be mentioned within the frame of hybrid inorganic-organic silicon materials is their application in the growing area of MEMS (microelectromechanical systems) devices. Some articles and patent examples can be mentioned as a guide. Grayson *et al*. reviewed "Electronic MEMS for triggered delivery" [74, 75], two articles devoted to biosensing and drug delivery devices and materials at the microscale. In these articles they reviewed electronic devices such as pacemakers and neural implants used for electrical stimulation. The usage of microfabrication techniques allowed the achievement of pulsatile drug delivery devices. A repertoire of structures, including microreservoirs, micropumps, valves, and sensors are described. Two years before, Edell and Farrel patent regards microelectronic components, integrated circuits, and implantable electrodes used extensively in implantable devices such as cardiac pacemakers, cochlear prosthesis devices and neuroprostheses [76]. As the device size and conductor size decrease to below approximately 10 micrometers, the hybrid substrate must be micro-machined using photolithographic techniques to pattern and put down the conductor traces. Devices need to be encased with an encapsulant such as silicone chemically bonded to the substrate. Other methods of hybrid microfluidic and integrated chip construction are described by McCaskill and co-workers [77]. McCaskill described the design of a silicon–polydimethylsiloxane -based construction of electronic microfluidic devices devoted to the development of an online programmable microfluidic bioprocessing unit (BioModule) for rapid pipelined selection and transfer of deoxyribonucleic acid (DNA) molecules and other charged biopolymers.

The invention patented by Ouellet and Antaki [78] regards the fabrication of advanced silicon-based MEMS devices consisting in a modular approach fabricated on a common substrate by depositing and patterning at least one layer of amorphous silicon, allowing producing intelligent microsystems with application in biomedical and medicine biochips, lab-on-a-chip and such. A similar application related to an implantable microfabricated sensor device consisting in a wireless MEMS capacitive sensor for physiologic parameter measurement was patented by Rich and co-workers [79].

In the drug delivery area, Voskerician *et al*. have developed a silicon-based implantable drug delivery system that uses elemental gold membranes to seal individual drug-filled reservoirs [80]. The goal of this MEMS delivery device is to release specific therapeutic agents in complex dosing patterns. The device can be used for the release of hormones, chemotherapeutic agents, analgesics, anesthetics, and other bioactive agents. Its biocompatibility and biostability properties as well as its resistance to the impact of the surrounding tissue on its function (biofouling) were successfully tested.

SUMMARY

In this paper, we have revisited some applications of silicon derivatives in medicine and pharmaceutics. Silicon compounds can be clearly divided into organic (silicones) and inorganic compounds. Each type has particular characteristics:

Silicones have unique properties because it's mechanical flexibility, allowing easy micromachining. The physical and chemical characteristics of the polymer can be modulated by the ratio between precursor and curing agent. The nature of the crosslinking agent can also modulate the natural hydrophobic character of the rubber. Silicones have excellent biocompatibility; however, degradability is very slow and occurs only in some conditions not found in living organisms. All the mentioned

properties make these compounds useful as constitutive materials for the design of long life devices and implants.

The inorganic branch of silicon compounds such as silicon dioxide, silica particles, etc; have, as counterpart, excellent resorbability, making them very adequate for tissue repairing. They are hydrophilic and degrade fast, being easily metabolized and eliminated in urine as silicic acid. Silica particles are good lubricants and improve compressibility in tablets, but superlattice silicon structures are fragile and need the addition of organic templates to avoid cracking.

In summary, hybrid forms can fulfill many of the requirements for a biomaterial devoted to built implants and drug delivery devices.

CURRENT & FUTURE DEVELOPMENTS

The synthesis of silicon based drug delivery devices and implants at industrial scale requires the achievement of carefully supervised reactions sequences. This necessarily implies the knowledge of every synthesis step at the nanoscale level, which constitutes the heart behind the obtaining the final porous structure.

Complementary properties of inorganic and organic compounds make both of them to be desirable in some extent into a biomaterial, and this is a tendency we can see in the evolution of the inorganic-organic hybrids devices patented in the last years. The addition of foreign biocompatible and biodegradable polymers into silicon structures can help to surmount some of the usual lacks found when encapsulating active drugs. Solubility problems and difficulties in controlling the kinetics of drug release and matrix degradation (or tissue integration) can be tailored by the mixing of organic and inorganic structures. Nanotechnology approaches to improve this integration will be a fruitful field of investigation in the next years.

ACKNOWLEDGEMENTS

Dr. D.L. Bernik is a member of the Scientific Career of the Consejo Nacional de Invetigaciones Científicas y Técnicas (CONICET). The author thanks CONICET for financial support (PIP 6382).

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