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Composite Materials Based on Ormosil for the Construction of Electrochemical Sensors and Biosensors[1]

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Abstract—Sol–gel process has gained tremendous attention in past decades for the preparation of pure and composite material for numerous applications. Organically modified sol–gel glasses (ormosils) have hybrid properties of rigid inorganic silica matrix and organic functionalities. Ormosils provide ambient environment for bio-molecules encapsulation and such systems have been used widely for biosensor applications. Biological elements including enzymes, antibodies, antigens, DNA, whole cells, tissues, proteins, biologically derived material, and biomimetic materials provide the possibility of biological recognition to the device and transducer to detect the biological signals with the help of associated electronics and software to amplify these signals into a readable form for the user. In this review we report on the formation of sol–gel based composite materials primarily on ormosil along with carbon nano tubes, metal nano particles, mediators, inorganic complexes, polymers, ionomers and biological materials and cite the electrochemical sensor/biosensor system based on it.

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INTRODUCTION

Materials quite different in their properties can combine to result in a composite material. Composite materials have been fabricated to obtain materials possessing superior and valuable properties. In this article we restrict our study on fabrication of composites from various micro-sized and sub micro-sized materials along with ormosil matrix and on their possible importance in the wide area of electrochemical sensor devices. When one of the constituents of a composite material has dimension less than 100 nanometer such a composite material is called “nanocomposite” material [1]. Generally multi-component fabrication is adopted to obtain composite materials where each component play its specific role and synergic effect of components in a composite provides an improved performance of a device based on composites.

Ormosil is a shorthand name for the organically modified silica or organically modified sol–gel glass. Ormosils have marked advantages as low temperature processing materials; chemically, photochemically, mechanically and thermally stable, physically rigid, with negligible swelling, controllable porosity, optical transparency which make them suitable for various applications and can be cast in desired shape and pattern, i. e., monoliths, thin films, fibers, and powder having controllable surface area, pore size. Their compatible nature makes them appropriate material for the stable and ambient encapsulation of biological molecules, thermally unstable molecules and compatible with many organic or inorganic reagents. A number of reviews and research articles consider the physics and chemistry of ormosil and other sol–gel processed materials, and discuss their various applications [2–37]. Non-traditional sol–gel method, non-hydrolytic sol–gel process, has also been investigated to obtain organic–inorganic hybrids which involve the reaction of a “metal” halide with an oxygen donor, leading to the formation of an inorganic oxide. Hay et al. reviewed synthesis of organic–inorganic hybrids via non-hydrolytic sol–gel chem.-istry, its scopes and limitations and potential applications [38]. Lev et al. reviewed the use of

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mediators and chromophores, metal and organometallic catalysts, preconcentration agents, ionophores, and active proteins, redox polymers, conducting polymers, carbon along with sol–gel based materials for electrochemical applications including modified electrodes, solid electrolytes, electrochromic devices, corrosion protection coatings, supercapacitors [39]. On the same track Walacarius also reviewed electrochemical application of silica-based organic-inorganic hybrid materials [40–41].

Material scientists have tried to improve the properties of transducer material to obtain better sensing devices. Tess et al. reviewed advances of materials chemistry and its impact in the sensor design, particularly optical and electrochemical sensor systems [42]. Many techniques are reported in the literature such as covalent binding, adsorption; encapsulation and entrapment of sensing agents in a polymeric matrix by using a cross-linker but ormosil immobilization platforms can be preferred to other methods due to tedious procedures, poor stability, and perturbed functions of other methods which require expensive reagents or environmentally unattractive solvents. Besides a variety of material such as metal nano particle, carbon nano tube, biological materials, polymeric material, metal complexes, organic dyes, ionomers can easily be doped within the ormosil processed inorganic rigid matrix. Hence, ormosil based composites are becoming popular and a thorough review is extremely necessary about ormosil based composites.

Ormosil Based Composite Materials

In a composite material, it is essential and important to understand the effect of each individual component of a hybrid or composite system because the hybrid material has some unique properties, some hybrid/synergistic properties of its components along with individual properties of its components. The mechanical and optical properties of ormosil depends on alkoxide precursors $RSi(OEt)_3$ used (R may be methyl, vinyl or amyltriethoxysilane, mercapto, amino, epoxy, alkyls, glycidoxypropyl etc) . Different type of precursor's molecules, additives and processing techniques are adopted to achieve new and improved properties. Properties of ormosil material can be tailored by varying the processing parameters, types of precursors, nature of additives, composition of precursors, amount of water, ratio of hydrophobic and hydrophilic precursors, and catalyst used. So we can by carefully controlling the process parameters control the properties and characteristics of final composite material, such as: hydrophobicity, hydrophilicity, porosity, optical, electrical, and thermal properties, hardness, film thickness, cracking, brittleness, toughness, flexibility, and morphology. The covalently bound organic groups decrease the mechanical tension during the drying process. Porous sol–gel materials provide the dwelling space for various dopants but these dopants can be leached out from the material with larger pores. Sometimes the material pores are very small and unsuitable for doping purpose, and such pore-free materials are suitable for coating purposes. Pauliukaite et al. used GPTMS and MTMS mixture to obtain controlled pore sized sol–gel material without external addition of alcohol. GPTMS-based sol–gel had a lot of nanopores about 50 nm in diameter whereas MTMS- based material had few and much larger pores from which enzymes can be leached out [43]. We can easily control porosity of ormosil for desired composite systems.

Bio-nanocomposite materials based on ormosil. A variety of sol–gel based bionanocomposite materials has been used for numerous technological applications including biosensors**.** In 1950 Dickey introduced silicate-based biomaterial by entrapping biological moiety in it [44]. Iqbal Gill reviewed sol–gel science and its multidisciplinary approach to provide a vast survey on the encapsulation of functional biomolecules like enzymes, antibodies, proteins, DNA, RNA, antigens as well as more complex assemblages such as cell membranes and organelles, and even living microbial, plant, and animal cells within ceramic matrices. In this way they not only retained the structural integrity of the entrapped biomolecules but also the biological functioning from molecular recognition, catalysis, and signal transduction to sustained cell metabolism and reproduction [45–46]. J.D. Brennan reviewed biocompatibility nature of sol–gel materials and their emerging applications. He discussed the entrapment of membrane protein, liposome, photoactive membrane proteins, and membrane receptors in sol–gel material [47]. Avnir et al., Sheng et al, Sakai-Kato et al. also published reviews on the preparation of biomaterials by entrapping enzyme and protein in sol–gel material [48-49]. The phenomenon of protein immobilization in the porous ormosilthymol blue composite material has been studied by our group [50]. Coradin et al. reviewed bio-nanocomposite material based on silica and biopolymers. They provide a vast survey regarding collagen/silica nanocomposites, gelatin/silica nanocomposites, cellulose/silica nanocomposites, alginate/silica nanocomposites, chitosan /silica nanocomposites, protein/silica nanocomposite, enzyme/silica nanocomposite, and biotechnological aspects of biopolymer/silica materials in terms of their field of applications, i. e., biosensors, bioreactors, and bioactive materials [51]. Mixtures of sol–gel precursors can control hydrophobic and hydrophilic properties, and porosity can be adjusted to make sol–gel composite material more compatible with the protein encapsulation. Hydrophobic silica-forming monomers repel water from its surface and have high contact angle and weaker adherence at the electrode surface whereas the hydrophilic monomer dissolves easily and has a good adhesion to the electrode surface.

Weetall discussed silane coupling for binding proteins with special emphasis on enzymes, general preparation and characterization of silane coupled [52]. Goring et al. investigated phase separation in protein-compatible nanocomposite materials which have impact on mechanical properties of the material, the optical clarity of protein-doped materials (important factor of an optical biosensors), protein performance (i.e., local environment for protein, which could influence protein stability or interfacial activation of membrane-associated proteins), and the potential for solid phase extraction of hydrophobic analytes into the film. They also focused their investigation on the effect of number and type of substituents on organically modified silane, the organosilane doping level, the processing method (separate or co-hydrolysis of silanes), and the effect of low molecular weight additive (polyethylene glycol) on the phase separation within composite materials formed by a two-step aqueous processing method [53]. Smith et al. synthesized silica–biopolymer hybrid material using silica and gelatin as biopolymer and observed hydrophilic nature of proteins to increase the wetted area of sol–gel derived material which characterized the electrochemical active area and capacitive current of the electrode [54]. Shchipunov et al. reported polysaccharide–silica monolithic bionanocomposite using various polysaccharides via sol–gel processing without the addition of an organic solvent and a catalyst. They incorporated alginate, kappa-carrageenan, iota-carrageenan, xanthan locust bean gum, hydroxyethylcellulose, cationic derivative of hydroxyethylcellulose, chitosan, polyvinyl alcohol, and polyethylene oxide and concluded that the structure and properties of composite depended on the polysaccharide type, charged degree of their macromolecule, and concentration. They observed that polysaccharides not only promote silica polymerization through acceleration and catalysis by the formation of hydrogen bonds between hydroxy groups of macromolecules and silaneols generated by the hydrolysis of precursor but also serve as a template for silica generated in situ [55].

Metal nano particle and ormosil composite materials. Nanomaterials have been implemented for a variety of technological applications such as production of large scale composite material for numerous applications as fillers, coatings material, strong lightweight material, high surface area materials, electrode materials for batteries, single electron memory electronic device, logic gate, quantum computer, spin polarized electronics, photonic crystals/device, optoelectronic devices, actuators, magnetic and electrical applications, high capacity capacitor, fuel cells, solar cells, hydrogen storage, electromechanical transducers, nanostructuring templates, AFM-Tips, SPM molecular tweezers, electrochemistry, gas adsorbents, catalysts, nanoreactors, biosensors and many more [56]. Nanomaterials can be classified as carbon-based nanomaterials, metals & alloys, biological nanomaterials, nano-polymers, nano-glasses, nano-ceramics, and nano composites. Nanocomposites possess a variety of size-dependent interesting magnetic, electric and catalytic properties.

The composition, size, shape, alignment, and distribution of the nano particles within a nanocomposite can be major factors of the control of the material properties. Sandra K. Young presents a report on different types of silica-based organic-inorganic nanomaterials [57]. Different techniques has been adopted to prepare nanoparticles of noble metals which include wet chemical synthesis, solvent exchange, electrochemical, thermal decomposition, in various polymers and sol–gel glasses [58–63]. The incorporation of nano particles of gold, silver, platinum, zinc, palladium, etc. in a sol–gel material not only shows a well-defined voltammetric response but also provides a high stability and reproducibility for continuous measurement. Daniel et al. reviewed various aspects of gold nanoparticles including its quantum size effect and single-electron transitions, synthesis and assembly and its application for formation of composites [64]. Piccaluga et al. reviewed nanocomposite materials based on metal-silica and metal oxide-silica [65]. Reisfeld et al. prepared and characterized composite material based on silver nano particles and ormosil materials [66]. Grain size dependence of physico-optical properties of nanometallic silver in silica aerogel matrix has been studied by Balkis et al. [60]. Du et al. provides direct evidence of gold nanoparticle binding with thiol groups within the sol–gel structures and potential of the 3-mercaptopropyl trimethoxy-silane for biosensor development on the basis of electrochemical and spectroscopic studies [67–68]. Mesoporous gold-silica nanocomposite materials obtained via sol–gel process with nonsurfactant (dibenzoyl tartaric acid) templates has been reported by Cheng et al. for the detection of Cr(VI) ion. [69]. Jia et al. reported a third-generation horseradish peroxidase based hydrogen peroxide biosensor by self-assembled gold nanoparticles to prepare three-dimensional sol–gel network [70]. Ferrara et al. reported homogeneous nanocomposite silica films which have uniform doping of selected size gold nano particles [71]. Sampath et. al reported graphite, palladium, and ormosil based composite material for amperometric detection of glucose biosensor [72]. Pandey et al. have reported palladium-linked ormosil material [73] and fabricated dopamine sensor by additional doping of ferrocene within the same matrix [74]. They also reported a glucose sensor based on the same material [75]. Kielbasa et al. reported nano-composites material by embedding Ag nanowires in a sol–gel host, and it was morphologically and optically investigated [76]. Zhao et al. reported deposition of hemoglobin and colloidal silver nanoparticles entrapped in a titania sol–gel matrix by vapor deposition method on a glassy carbon electrode (GCE) for the catalytic action of hemoglobin on the reduction of NO_2^- [77]. Ravishankaran et al. reported (3-mercaptopropyl) trimethoxysilane, silver, and graphite modified electrode for the detection of hydrogen peroxide, where graphite provides conductivity, silver particles act as catalyst, and cross-linked silica provides a rigid network [78]. On the same track they also fabricated copper-dispersed ceramic-graphite composite electrode for hydrogen peroxide detection [79]. Copper-dispersed sol–gel derived ceramic-graphite composite material has been used by the same group for the fabrication of glucose biosensor [80].

An Au- and Pt-doped inorganic-organic hybrid silica sol was deposited on glass substrates by a two-layer coating methodology by Pal et al. where interlayer diffusion results in porous bimetallic Au-Pt nanoparticles in SiO_2 film matrix [81]. Kang et al. reported a glucose biosensor based on multi-walled carbon nanotubes, Pt nanoparticles and chitosan/silica organic-inorganic hybrid composite. [82]. Di et al. reported one-step method to immobilize superoxide dismutase and gold nanoparticles in silica film for the detection of superoxide [83]. Jena et al. reported highly sensitive electrochemical biosensor for NADH based on dehydrogenase enzymes, gold nanoparticles, and thiol-terminated silicate network. They also detected amperometrically lactate and ethanol [84]. Lei et al. also used gold nano particles as mediator for the fabrication of hydrogen peroxide sensor based on horseradish peroxidase (HRP). [85]. Iridium powder has been introduced in the sol–gel process to prepare iridium-ceramic composite by Tian et al. for the detection of glucose. [86].

Carbon nano tubes and ormosil composite materials. Carbon ceramic composites are well studied by many workers including graphite, carbon black, carbon nano tubes (CNTs), acetylene black, and fullerene. Rabinovich et al. reviewed the composition, physical, electrochemical characteristics of carbon ceramic composite materials, and surveyed its sensor, biosensor, energy storage applications [87].

Importance of CNTs in sensor technology for various technological applications is well reported [88–90]. The incorporation of CNTs greatly influences properties of composite materials. Electrochemical investigations reveal that CNTs act as conductive part of the composite which facilitate fast electron transfer rates. We have reviewed the fabrication, the importance of composite materials based on CNTs and polymers, and their application for sensing devices [91]. Gavalas et al. developed CNTs/silicate composite material and demonstrated its application for biosensors by incorporating L-aminoacidoxidase to detect amino acids [92]. Gong et al. reported ceramic-CNTs nanocomposite electrodes which exhibit a tunable dimension ranging from conventional electrode to nanoelectrode ensemble. Such nanoelectrode ensemble is demonstrated to possess good electro-catalytic activity toward the oxidation of ascorbic acid (AA), glutathione [93]. Cho et al. reviewed the composite material based on ceramics and CNTs. They have described processing route, electrical and thermal properties, and multifunctional applications of ceramics-CNT system [94]. Yang et al. applied platinum nanoparticle-doped sol–gel solution as binding material for multi-walled carbon nanotubes (MWCNTs) and fabricated electrochemical sensor for glucose [95]. Chen et al. reported ceramic-carbon nanotube nanocomposite film for hydrogen peroxide sensor by doping HRP and MWCNTs into a silicate gel matrix which showed direct electron transfer at glassy carbon electrode [96]. Gavalas et al. used three different silane precursors, methyltrimethoxysilane, ethyltrimethoxysilane, and propyltrimethoxysilane for the preparation of the sol–gel/CNTs composite [97]. Wang reported a new third-generation biosensor based on sol–gel material/CNTs modified electrode [98].

Many workers have incorporated mediator with CNTs/silica composite due to synergetic effect of mediator and CNTs. Water-soluble dyes, such as methylene blue, phenazine methosulfate, and other dye derivatives, have been used as efficient electron transfer and low cost mediators [99, 100]. Recently many research groups have reported ormosil/CNTs/mediator/enzyme composites using different mediator molecules, such as nile blue [101], methylene green [102], cresyl blue [103], potassium ferricyanide [104], ferrocene derivative [105-107], Celestine blue [108]. Upadhaya et al. reported the incorporation of MWCNTs and Nile blue along with ormosil matrix using 3-aminopropyltrimethoxysilane and 2-(3,4-epoxycyclohexyl)ethyltrimethoxysilane for the development of an amperometric hydrogen peroxide biosensor[101]. They also immobilized methylene green along with MWCNTs in ormosil matrix for peroxide detection [102]. Cationic quinine imide dye brilliant cresyl blue, horseradish peroxidase, and MWCNTs-modified ormosil nanocomposite film for the detection of hydrogen peroxide have been reported by Peng et al. [103]. In our laboratory we have incorporated MWCNTs along with potassium ferricyanide and HRP for hydrogen peroxide sensor using 3APTMS, 3 GPTMS, and TEOS as precursors [104]. Qiu et al. entrapped glucose oxidase in a chitosan composite doped with ferrocene monocarboxylic acid-aminated silica nanoparticles conjugate MWCNTs for glucose detection [105]. They also reported glucose biosensor based on nanocomposite through covalent adsorption of ferrocenecarboxaldehyde on MWCNTs for electrical communication between glucoseoxidase and electrode, using chitosan as matrix [106]. In the similar way Tripathi et al. reported a nano composite material using bovine serum albumin, MWCNTs, ferrocenemonocarboxylic acid within ormosil for glucose sensing [107]. Noorbakhsh et al. fabricated glucose sensor by using celestine blue, MWCNTs, and sol–gel composite material [108]. Arvinte et al. have reported MB-SWNTs-sol–gel nanocomposite for the detection of NADH and its application for developing lactate sensor [109].

Polymeric materials have also been incorporated along with carbon nano tubes where carbon nano tube povides conductivity and polymeric material prevents cracking of the composite. Kang et al. used chitosan along with sol gel and MWCNTs for immobilization of HRP for the H_2O_2 detection [110].

Inorganic oxides and complex salts incorporated in composite materials. Inorganic oxides such as titanium oxide, zinc oxide, zirconium oxide, iron oxide, nickel oxide have also been incorporated within ormosil. These metal oxides impart very interesting physical, optical and magnetic properties. Samantaray et al. have reviewed the effect of anions in titania-silica samples and structural, physicochemical properties have been compared [111]. Fe–Si mixed oxide nanocomposite materials in which the iron(III) oxide is the major component was synthesized using $FeCl_3 \cdot 6H_2O$ as iron oxide precursor, and it was mixed with tetramethyl- or tetraethylorthosilicate in ethanol and gelled using an organic epoxide; it could be implemented for environmental applications, catalysis, and as magnetic material [112]. Bao-Ling et al. prepared composite film of ZnO and ormosil which shows high transmittance and low surface roughness at different temperatures [113]. TiO_2-ormosil, ZrO_2-ormosil, SiO_2-ormosils hybrid system are also reported in the literature [114–116]. Nanocomposites containing nickel nanoparticles in silica has been reported by Trimmel et al. [117].

Mediators incorporated composites. It is well known that because of deep embedding of electrochemical prosthetic groups in protein structure, absorptive denaturation and unfavourable orientation of proteins occur at electrode and exhibit a rather slow rate of heterogeneous electron transfer [118]. Mediators are molecules which can facilitate electron-transfer reaction as well as reduce the detection overpotential.

Many metal hexacyanoferrates, metallocenes, other coordinate metal complexes have been used along with ormosil material as redox mediators. Salimi et. al fabricated a carbon–ceramic composite along with ruthenium complex for the amperometric detection of sulfide and sulfur oxoanion [119]. This group has also reported insulin sensor based on carbon-ceramic, nickel powder, and potassium octacyanomolybdate based composite [120] and carbon ceramic composite electrodes modified with electrocatalytic detection of hydrazine, hydroxylamine based on nickel hexacyanoferrate [121]. Khalil reported ceramic-carbon composite electrode by mixing methyl trimethoxysilane sol–gel precursor and carbon powder with thionine hexacyanoferrate (HCF)–Th(IV) ion pair for the electrocatalytic oxidation of ascorbic acid and dopamine [122]. Sheng et al. reported terbium hexacyanoferrate mechanically attached to the surface of carbon ceramic electrodes which exhibited excellent electrocatalytic oxidation of AA [123]. Copper hexacyanoferrate along with poly(neutral red), were deposited onto the carbon-film electrodes for detection of glucose [124].

Methylene blue-intercalated α-zirconium phosphate micro particles supported on graphite powder have been dispersed into methyltrimethoxysilane-derived gels to yield a conductive composite in which α-zirconium phosphate acts as a solid host for MB. Graphite powder ensured conductivity by percolation, the methyl groups of silica endowed a limited wetting section of the modified electrode due to its hydrophobicity [125]. Pandey et al. reported nine different composite materials based on ormosil by using potassium ferricyanide and ferrocene monocarboxylic acid, and combination of different alkoxy monomers [126]. Yang et al. reported covalent immobilization of glucoseoxidase with amine functionalized composite formed by graphite powder, ferrocene, methyltrimethoxysilane, and 3-aminopropyltrimethoxysilane [127]. Thenmozhi et al. also reported graphite ceramic composite for amperometric detection of hydrogen peroxide. Toluidine blue was covalently immobilized via glutaraldehyde crosslinking with an organically modified silane, namely 3-aminopropyltrimethoxysilane which provided a site for the immobilization. Methyltrimethoxysilane was used to controls the hydrophobicity of the electrode surface, thus limiting the wettabilility [128]. Tian et al. reported microelectrode biosensors for the detection of ATP and hypoxanthine using Ruthenium Purple based composite material. [129]. Prussian blue incorporated within silica matrix was reported by Pandey et al. [130].

Many organic compounds have also been used along with ormosil material as one of the constituent of composite to improve electron transfer kinetics such as methylene green, Nile blue, Thymol blue, Toluidine blue, neutral red, methylene blue, meldola blue, methyl viologen, anthraqinone-2-carboxylic acid[131]. Nanocomposite of methylene blue (MB) and silicon oxide was synthesized by Yao et al. [132].

Polymer-incorporated composite materials. Importance of conducting and non conducting polymers in the composite formation and biosensor application has been vastly studied [133–136]. The incorporation of polymeric compounds not only effectively prevents cracking and brittleness of ormosil film but also acts as modifier which provides extra qualities to ormosil materials since conducting polymers can act as nano wires and as redox mediator within inorganic material and can provide biocompatible microenvironment. The polymerization along with sol–gel synthesis is a simple way for preparation of hybrid systems. Various types of organic polymeric materials including conducting polymers, non-conducting polymers, ionomeric compounds, natural and artificial membranous material has been reported to develop composite material with inorganic silica matrix. Polymer–inorganic nanocomposite materials have been reviwed by Pomogailo [137]. Kickelbick reviewed some most common principal concepts used to incorporate inorganic systems in the submicron range (up to a few hundreds of nanometers) into an organic polymeric matrix, and the resulting properties of such materials. He extensively studied sol–gel process in the presence of preformed polymer, polymerization in sol–gel networks, simultaneous formation of interpenetrating networks, dual network precursors, incorporation of metals and metal complexes in polymers by coordination interactions [138].

Kabulov et al. reported functionalized nanocomposite sorbtional material based on chitosan and polyethoxysilane oligomer. [139]. Wang et al used chitosan/sol–gel film for hydrogen peroxide detection [140]. Tan et al used chitosan/MWCNTs/sol gel/cholesterol oxidase composite material for cholesterol detection [141] and chitosan/Prussian blue/glucose oxidase/silica matrix for glucose sensing [142]. Chen et al. also constructed glucose biosensor using organically modified silicate and chitosan composite [143]. Zhang et al. have prepared chemiluminescence biosensor by immobilizing ECL reagent Ru(bpy)3(2+) and alcohol dehydrogenase in sol–gel/chitosan/poly (sodium 4-styrenesulfonate) organically modified composite material [144].

Nafion is well studied polymeric ion-exchange material (perfluorosulfonated ionomer) containing negatively charged sulfonate groups used to prevent the cracking and brittleness of ormosil films. Selectivity of the biosensor can be improved because it can prevent access of certain negatively charged interfering species from partitioning into an electrode surface [145]. Uppadhya et al also used nafion to prevent cracking of ormosil/nile blue MWCNT composite film [99]. Wang et al. used methylene green/nafion with sol–gel material for hydrogen peroxide detection [145]. Choi et al. reported nanoporous composite films of sol–gel-derived metal oxide (titania and silica) and Nafion, on a platinized glassy carbon electrode for glucose monitoring [146].

In situ polymerization of an alkoxide within a polymer matrix is very simple and easily produces hybrid materials. Polyacrylamide–silica nanocomposite material in aqueous solution has been reported by Jang et al. [147]. Other polymers, having hydroxy functional groups to form hydrogen bonds, include poly(methyl methacrylate), poly(vinyl acetate), poly (acrylic acid), poly(vinylpyrrolidone) which have been successfully used to prepare hybrid materials [148–151]. Polysiloxane–PVA–glutaraldehyde hybrid composite have been implemented for immunosensor by Lima et al. [152]. Wang et al. attempted to immobilize horseradish peroxidase in sol–gel/PVA composite [153]. Polyvinyl alcohol-modified composite for the urea detection has been reported by Tsai et al. [154]. Wang et al. reported glucose sensor based on sol–gel material having grafted copolymer of poly(vinyl alcohol) with 4-vinylpyridine which prevents the cracking and eliminates the swelling of the hydrogel, and tetrathiafulvalene has been used as a mediator [155]. Cox et al. investigated stability of lactateoxidase within a conventional sol–gel material and with silica sol–gels-poly(ethyleneimine) to establish its analytical importance [156]. Polyacrylate-silica nanocomposite has been reported by Ma et al. [157]. Santos et al. constructed valproate-selective electrodes based on sol–gel composite membrane made up of manganese(III) tetraphenylporphyrin [Mn(III)TPP–Cl] (as ionomers), poly(vinyl chloride), and methyltrimethoxysilane membrane[158]. Pauliukaite et al. reported poly(neutral red)-modified carbon film electrodes coated with oxysilane sol–gels for glucose detection [124]. Ghica et al. reported biosensor for amperometrically detecting acetaldehyde using a bienzymatic strategy (FMN-dependent NADH oxidase and NAD+-dependent aldehyde dehydrogenase) at carbon film-based electrodes using poly(neutral red) as redox mediator. [159] Poly(neutral red)-mediated glucose sensor was also reported by Paquim et al. [160]. Park et al. detected hydrogen peroxide by immobilizing horseradish peroxidase and an osmium redox polymer as mediator [161]. They also reported determination of lactate by immobilizing lactate-oxidase and an osmium redox polymer on the surface of a glassy carbon electrode, followed by coating with a sol–gel film derived from methyltriethoxysilane [162].

Silica sol–gels are not an intrinsic conductor. To overcome this problem Ita et al. tried *in situ* polymerization of aniline with sol–gel process. They found polyaniline appeared as an aggregate in conducting polymer-silica hybrid composite [163]. The electrochemical properties of polypyrrole formed in the sol–gel were studied by Verghese et al. [164]. Chen et al. used alumina and co-immobilized bovine serum albumin with glucose oxidase. Electropolymerized phenol film has been used to minimize interferences [165]. Chaubey et al. fabricated lactate sensor based on electro-entrapped polyaniline within sol–gel composite [166]. Wei et al. reported composite material based on TEOS, poly[methylmethacrylate-co-3(trimethoxysilyl)propylmethacrylate], camphorsulfonic acid-doped polyaniline which showed excellent adhesion to inorganic substrates and high conductivity [167] . Widera et al. doped various ratios of aniline into sols of TEOS, 3-aminophenyl-[3-triethoxylsilyl)-propyl and urea. Polyaniline was covalently anchored to the sol–gel matrix [168]. Yao et al. reported glucose biosensor based on composite membrane of sol–gel enzyme film and electrochemically generated poly-(1,2-diaminobenzene) film to improve the selectivity of enzyme sensors [169].

Synthesis of NO-releasing materials has led to significant progress in the development of intravascular sensor system. NO improved biocompatibility of *in vivo* sensors because its effect will be local, not systemic. Sol–gel-derived NO-releasing materials have been reported where amine-functionalized silicon alkoxides (aminosilanes) were bound to a sol–gel backbone [170]. Sol–gel/polyurethane composite, which can release NO, used for the fabrication of in-vitro glucose biosensor has been reported by Shin et al. [171]. Roohangiz et al. reported organic-inorganic hybrids from 3-glycidoxypropyl-trimethoxysilane and bisphenol A via the sol–gel process. In fact, in hybrid systems organic groups that are dispersed throughout the film apparently serve to increase the hydrophobicity of the coatings, repelling water, and enhancing the corrosion protection properties [172].

CONCLUSIONS

The commercialization of biosensors is rather slow due to some technological difficulties such as biosensor contamination (which is a major issue), incompatibility of biomolecules with transducer matrix materials, and activity loss of bioreceptors after a certain period of time. Concerned biologists have concentrated on biological investigations to identify new bioreceptors molecules and biomarkers. They are also looking for stable immobilization of bio-receptors to maintain long-term catalytic activity as a result of which a variety of analytes can be efficiently and consistently analyzed by biosensor. On the other hand, material scientists have explored plethora of new materials as hosts for enzymes and other bio-receptors for better device designing. Controlled sol–gel process certainly provides a better platform to prepare new nanocomposite materials which offer mild microenvironment for biomolecules. We have not considered all the work carried out by the scientists in the last couple of decades but have tried to summarize the idea of composite fabrications based on ormosil and their application for sensor/biosensor devices, and have tried to present an understanding of the importance and diversity of sol–gel based composite materials and their broad applications. Generally pure materials may not have all the desired characteristics, so the fabrication of a composite material is a right move to enjoy desired properties for a specific application. Ormosil-based composites are greatly affected by the precursor used, ratio of precursor's mixture, water: precursor ratio, additives used, nature of dopants, interaction between dopants and silica network, and process parameters, so these parameters should be carefully controlled and optimized to get material of desired properties. We can conclude from the above discussion that a multi-component composite material based on ormosil is an easy way to get many new and improved properties in the material, and such materials can provide better opportunity to develop reliable biosensors.

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