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Recent Advances in Nanosponges

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ABSTRACT

The widespread need for immediately effective treatment has enhanced the requirement of Novel Drug Delivery Systems in recent times. Novel Drug delivery systems involve the various approaches and technologies for Modified, Controlled and Sustained Drug Delivery Systems. A compilation of these qualities exhibited by an integral form of Nanotechnology is Nanosponges. Nanosponges are the three-dimensional network of crosslinkers with polymers, co-polymers or stabilizers. It is admixture in solution with small molecules called cross-linkers that act like tiny grappling hooks to fasten different parts of the polymer together. The net effect is to form spherically shaped particles filled with cavities where drug molecules can be bonded. They have been studied in recent times because of their ability to covalently bind to hydrophilic, hydrophobic drugs, metals, metal oxides, pore-forming toxins, regenerated RBCs, etc. They have an average particle size of 1-100 nm of the cavity internally along the x-, y-, z-, axes. The outer dimensions of these structures lie in the range of 10-1000 nm or the micron range. The use of natural polymers like cyclodextrins, carbonates, dianhydrides and synthetic polymers such as ethylcellulose, polystyrenes, stabilizers/copolymers like poloxamers have been the key sources to form these structures. Their application in varied fields of science, the chemistry of molecules such as catalysis, electrocatalysis, in reactions such as Heck's coupling and in the regeneration of Hydrogen molecules to form renewable energy sources In this article nanosponge applications to help the mankind have been highlighted.

INTRODUCTION

Aim: Recent Advances in the field of Nanosponges.

Review of literature: The word nano lies in the range between 1-100nm i.e below the submicron range 100-1000nm but above the quantum range less than 1nm called as pico range. Nanosponges (NS) are porous structures having voids in the range of 1-500 nm.[1] Nanomaterials are conventionally defined materials having at least one dimension between 1-100nm.[1] Nanoparticles may have all three dimensions in the nanometer range. Nanosponges can be considered as nanoporous structures having all three external dimensions in micro or macro range and internal cavity pores or voids in the nanometer range.[1]Nanosponges can be counterintuitively be classified as nanomaterials because of the presence of nanometer-sized cavities in the bulk, despite the fact that the dimensions of a given specimen along the x-,y-,z-axes can be larger than 100 nm.[1] From this viewpoint, Nanosponges are characterized by structural features as nanoparticles but are not nanoparticles. They form a three-dimensional scaffold network forming a covalent bond with a backbone of numerous particles with their crosslinking agents.[2] NS surface morphology looks like that of interwinding locks. The interlinking forms a network to which the active forms a bond. NS have enormous utility in pharmaceutical and non-pharmaceutical areas. In changing times this nanotechnology has served as the multivariate tool for extensive applications, as nanosponges show tunable properties, high versatility, low-cost synthetic routes, high stability, and excellent absorption properties, making them ideal materials for the removal of unwanted molecules from the environment [1] or on the other hand for selective release of added value compounds as in drug delivery or in targeted and controlled release. Nanosponge can be either of organic, inorganic, natural or of synthetic origin.

Objective: The objective of this review is to determine the advances in nanosponges to enhance their applicability and to state their utility in Pharmaceutical and Non-Pharmaceutical areas,

Challenges of conventional therapy

The conventional therapy has put forward many challenges that need to be addressed, such as uncontrolled, non-sustained release, short drug dosing interval, increased frequency of administration, toxicity, etc. The feasible formulation for Biomimetic applications used for effective treatment are issues faced these times. In non-pharmaceutical areas issues of multistep reactions, continuous hydrogen-generating renewable sources, oxygen reduction reactions are some of the areas that require immediate attention. Size and shape of actives are needed to be optimized for its half-life circulation and entrance to a cell. [5] Each particle faces with two elimination systems that threaten its circulation time, including renal clearance and phagocytosis [6]. Drugs that need to enter the intracellular space to have suitable therapeutic effects are destroyed in extracellular space with enzymatic degradation, cannot be uptaken by cells or are degraded by interaction with cytosol proteins. [4] By improving nanotechnology and introduction of new drug carriers, the mentioned drawbacks have been solved.[3]To avoid former system, the particle must be larger than 10 nm, and the ones smaller than 500 nm cannot be uptaken by phagocytic system.[6]

Need of nanosponges

The importance of nano-sized particles in changing times have been a necessity. Nanotechnology has thus been an integral part of scientific advancements, they overlay the majority of the disadvantages of conventional technologies. These drawbacks have been addressed by downsizing conventional technology to Nanotechnology. Nanoparticles benefit from their high surface area because they can carry a large amount of drug and decrease the need to apply a high-dose carrier to reach the therapeutic level.[7,8] Nanosponges are a kind of nanoparticles. Nanosponges have occupied the elite position in addressing given drawbacks. The porosity of nanosponges has been an important attribute for addressing poor solubility, site-specificity, acute toxicity, etc. Due to this unique quality possessed by nanosponge, it makes them useful in various pharmaceutical and non- pharmaceutical fields. The conventional systems for pharmaceuticals addressed by nanosponges include controlled release, lowered dosing frequency and prolonged duration of dose administration. Their applications in biomedical and fields of chemistry have also been enormous such as oil absorption [18] and RBC biomimetics.

Role in drug delivery [11]

A long, linear molecule scrunched into a sphere ~10 nm in width where several surface sites are available for drug molecule attachment.

Factors influencing nanosponge formation[12]

Type of polymer used

Type of polymer employed influences the formation and performance of nanosponges. Their cross-linking ability is required to alter the porosity and density of theses nanosponges. The cavity size is required to be able to accommodate drugs of the required molecular weight.

Types of drugs

The following criteria are required for a drug molecule to be incorporated into a nanosponge.[13]

- Molecular weight between 100 and 400 daltons.
- Drug molecule consisting of less than five condensed rings.
- Solubility in water to be less than 10mg/ml.
- The melting point of the substance to be less than 250°C.

Increase in the temperature decreases the magnitude of the apparent stability constants of the Drug/Nano sponge complex, maybe due to a result of possible reduction of drug/nanosponge interaction forces, as hydrophobic forces and Van Der Waal forces causing the rise of temperature.

Disadvantages

The main disadvantage of these nanosponges is their ability to include only molecules with molecular weight less than 400 daltons.[13] Nanosponges could be either Para crystalline or in crystalline form. Degree of crystallization is an important factor in drug loading. Para crystalline nanosponges show variable loading. The nanosponges can be synthesized to be of specific size and to release drugs over time by varying the proportion of crosslinker to polymer.[13]

Mechanism of release from nanosponges

Nanosponge are open structures, the active added to the vehicle in encapsulated form, freely moves from the particles into the vehicle until equilibrium is achieved or vehicle gets saturated. The equilibrium shifts result in unsaturation of vehicle containing active ingredients.[14]Consequently, the flow of active ingredients present, occurs until the vehicle is either dried or absorbed completely. The nanosponges retained thus continuously releases active ingredient over an extended period.

Types of nanosponges and their application

1. Cyclodextrin nanosponges [10]

Cyclodextrins (CD) are low molecular weight oligosaccharide comprising of D-glucopyranose units bound via (1, 4) glycosidic linkages. They are CDs containing six, seven, eight glucopyranose units. The arrangement of D-glucopyranose monomers in chair confirmation gives cyclodextrin a specific truncated cone shape structure with a hydrophobic inner cavity and hydrophilic outer surface. The inner central cavity is lined by skeletal C-H groups and ethereal oxygen of the glucose residue imparting lipophilic property. The hydroxyl functions of sugar moieties of CDs are oriented to the exterior of the cone where the secondary hydroxyl group is located at the wider edge and the primary ones are positioned on the narrow edges, which make the outside surface hydrophilic. Cyclodextrin complexation technique is mostly used to alter the solubility of drugs. The solubility of drug drastically changes when it makes a complex with cyclodextrin. This property of CDs has been crucial for the formation of nanosponges. Cyclodextrins can include molecules of size and polarity compatible with its lipophilic inner cavity. Synthesis of cyclodextrin polymers using cross-linking agents, form cyclodextrin-based nanosponges. In Cyclodextrin-nanosponges (CD-NS) cyclodextrins come together by cross-linking with the linkers. Their inner central cavity serves as a pore of a regular sponge and can incorporate substances in it. The polymerized CD is less soluble and more stable. NS exhibits very high efficiency to accommodate poorly soluble molecules via inclusion and non-inclusion complexation. The presence of the lipophilic cavities of cyclodextrin monomers and hydrophilic channels of the porous structure of CD-NS provides the ability to incorporate a wide variety of compounds. The ratio of CD with cross-linker can be varied to obtain a polymer with wide drug loading capacity and desired release profile. Nanosponges (NS) technology arises as a CD-based host system more efficient in achieving solubilization, stabilization, enhancement of activity, permeability, and bioavailability.

Application of CD-NS

1. Graphene quantum dot (GQD)-based nanocarrier are used for theranostics in breast cancer, by modifying the GQD-NH_2 with β-CD and Herceptin the carboxyl-functionalized

GQDs with high quantum yield carboxyl groups on their surfaces, they are hypothesized as a multi-functional crosslinker for CDs, also endowing fluorescent function. Based on the hypothesis, fluorescent hyper-crosslinked β-cyclodextrin-carbon quantum dot (β-CD-CQD) hybrid nanosponges were synthesized for tumor theranostic application by facile condensation polymerization of the carboxyl-functionalized carbon quantum dots (CQDs) and β-cyclodextrin as multi-functional monomers.[15]

2. Solid-phase extraction clean-up has enabled liquid chromatography methods to detect analytes at low levels and in complex matrices. Cyclodextrin polymer materials have been used as solid-phase sorbents in solid-phase extraction methods to test toxins in food and beverage matrices. The use of cyclodextrin polyurethane polymers are used as solid-phase extraction sample clean-up to detect ochratoxin A in grape juice and wine.[16]

3. Activated Carbons [17]

Activated carbons are materials characterized by a highly porous structure with internal surface area ranging from 500 to more than 2000 m^2 /g. They display good adsorption capacities towards various substances as activated carbon, obtained from physical and chemical activation treatments. Physical achieved by direct activation using thermal treatments under inert atmosphere or to microwave radiations. Chemically, it is obtained by a previous impregnation with specific chemical agents as H_3PO_4, H_2SO_4, HNO_3, $ZnCl_2$, NaOH and KOH, etc followed by thermal treatment. Thermal treatments are normally carried out at temperatures higher than 600℃. Among carbon precursors, beta-cyclodextrin based nanosponges have been highly effective tools to obtain spherical shaped microporous carbons via pyrolysis at 800℃. The fibrous NS was used as a precursor to producing a carbon material.

4. β cyclodextrin based pH-sensitive Polyamino Nanosponges [20]

Diamines such as 1,6-diamino hexane and 1,8-diaminooctane, and two polyamines, bis-N, N-(3-aminopropyl)-methyl-amine and bis-N, N'-(3-aminopropyl)-1,2diamino-ethane are the linkers for this reaction. These structures are polyamine linkers having a difference in their length and hydrophobic character, they are intrinsically nucleophilic. The link to the βCD residues which are the electrophilic synthons of a trivial nucleophilic displacement reaction. This leads to the formation of pH-responsive nanosponges. Sequestration tests positively assess their pH-dependent adsorption abilities towards these nanosponges.

II. Carbonaceous nanosponge [18]

Carbonaceous nanosponges (CN) are a porous network of spherical nanoparticles with a broad pore size distribution. It shows no absorption of water but it adsorbs 33 times its weight of light crude. An acetylene plasma obtained under low power and low pressures led to a nanoporous material. CN show both superhydrophobicity and oleophilic. The CN can be used to selectively and efficiently adsorb hydrocarbons from water, with negligible water uptake. The material maintains its hydrophobicity for 30 min of UV exposure and gradually starts wetting afterward but keeps oil affinity. The change in wetting behavior would not affect the performance of the CN in sunlight exposed to the environment, considering that its oil sorption rate is enough for it to absorb the oil much faster than the time it takes UV irradiation to make the CN hydrophilic.

III. Calixarene nanosponges

1. Considering Copper-Catalyzed alkyne-azide cycloaddition (CuAAC)approach, by reacting a tetrakis(propargyloxy) calixarene with a diazidoalkane. This reaction results in the formation of bis(1,2,3-triazole-1-yl) alkylidene chains as the linkers between the calixarene monomer units. They were effective in sequestrating organic model pollutants, such as p-nitroaniline derivatives or dyes, from aqueous solution. [19]

2.Polyaminoazide mixtures, used for the preparation of Calixarene nanosponge (CaNS) materials with pH-tunable properties, by reacting the (5,11,17,23tetra(tert-butyl))-(25,26,27,28-tetrakis(propargyloxy)calixarene (Ca) under the CuAAC reaction conditions. The synthon is obtained by reacting the parent (5,11,17,23-tetra(tert-butyl))-(25,26,27,28-tetrahydroxy)calixarene with an excess of propargyl bromide . The pH-dependent abilities of the relevant calixarene-based polymeric materials obtained were tested for pollutant models.[21]

IV. Biomimetic nanosponges

1. Biomimetic toxin nanosponges (RBC-NS) used for absorbing and neutralizing bacterial virulence factors associated with numerous bacterial infections are Polymeric nanoparticles coated with a membrane of intact red blood cells. To induce lethality in mice, he whole secreted proteins (wSP) of methicillin-resistant Staphylococcus aureus (MRSA) are collected to. The wSP preserve the complexity of bacterial virulence profile while avoiding the

intricacy and dynamics of infections by live bacteria. RBC-NS are first quantified for their neutralization capacity against the hemolytic activity of MRSA wSP in vitro. In vivo studies were demonstrated using a mouse model, by neutralizing the hemolytic activity, RBC-NS confer significant survival benefits against wSP-induced lethality. When mice are challenged with a sublethal dosage of MRSA supernatant, RBC-NS reduce lung damages and inhibit the activation of nuclear factor kappa B in the spleen. They give a systematic evaluation of RBC-NS toward the treatment of severe MRSA infections such as MRSA bacteremia and MRSA-induced sepsis.[22]

2. Stealth agent and photolytic carrier that transports graphene quantum dots and docetaxel (GQD-D) sponge-inspired carbon composites-supported RBC membrane. These RBC-membrane hybrids are used to address the difficulties in low blood half-lives and tumor penetration which otherwise are removed from blood circulation or pile up near the tumor periphery. This enveloped nanosponge (RBC-NS) are integrated into a targeted protein that accumulates in tumor spheroids via high lateral bilayer fluidity which exhibits an 8-fold increase in accumulation compared to the nanosponges. Facilitating penetration and drug delivery deep into the tumor tissue is stimulated by near-infrared irradiation through a one-atom-thick structure by penetrative delivery of GQDs. By single irradiation, the synergism of chemotherapy and photolytic effects was delivered by the theranostic GQDs deep into tumors, which effectively damaged and inhibited the tumor in 21 days. Tumor suppression is achieved by targeted RBC-GQD-D/NS due to its enhanced tumor targeting, NIR-induced drug penetration into tumors, and thermal ablation for photolytic therapy.[23]

V. Metal Nanosponges

Porous metal oxides can combine and interact with other atoms ions and molecules. They form a porous interconnected network in nanosize range, they have enhanced physical and chemical properties compared to non-porous analogs. Due to porous structure, they have high surface area higher electron mobility and mass transfer. Other properties are semiconductive behavior, bandgap, and surface energy. Based on their pore, six porous metal oxide nanosponges are divided into microporous (less than 2 nm), mesoporous (2-50 nm) and macroporous (more than 50 nm).[1]

Metal-organic framework (MOF) of nanosponges are considered as self-assembly of metal ions that combine with organic liners. They are usually carboxylate or nitrogen-containing heterocyclic compounds that form strong organic-inorganic coordination. Synthesis of MOFs with more than one metal ion or crosslinkers is because of the flexibility of design.[1]

Metal nanosponge formation is done by using different M-BNHx nanocomposites where M = Ag, Au, Pd, Pt, and Cu. It was found that the B–H bond of the BNHx polymer being unstable in water gets hydrolyzed and produces hydrogen gas bubbles which impart porosity and the rate of B–H bond hydrolysis has a direct impact on the porosity of the final nanostructure.[24]

Metallic nanosponges are classified as Mono, Bi, Polymetallic nanosponges, Single metallic have aggregation and availability of lesser catalytic site as compared to bimetallic Pt-Cu, Fe-Pt, Ag- Au-Pd. [1]

A.Monometallic nanosponges

Nanoporous metals are nanostructures where nanoparticles are attached in such a way that the structure consists of inherent pores. Due to the presence of these voids, they possess high surface area which is quite appropriate for varied applications as catalysis, sensors, electrodes, and membranes. Metallic precursors such as silver, gold, palladium platinum copper are used for the formation of monometallic nanosponge. Porous metal has a profound effect on the catalytic activity as compared to their bulk counterparts due to their three-dimensional porous structure which offers a large number of surface-active sites for a catalytic reaction, as well as the interconnected pores, facilitate easy diffusion of the substrates. [1]

Hydrogen with a chemical energy per mass of 142 MJ kg which is at least three times as large as the liquid hydrocarbons. This is expected to be an important source of energy carrier of the future. Use of hydrogen as an energy carrier is threatened by various problems about its storage safely. Hydrogen storage has been achieved either in the form of metal hydrides and complex metal hydrides or via physisorption. Metals and alloys are important because they are capable of storing a large quantity of hydrogen reversibly. Thus, nanostructured metals have significant advantages because in the nanosize regime they exhibit improved kinetics and thermodynamics over their bulk counterparts for hydrogen storage property and Catalytic activity. [25]

In metals, only palladium shows hydrogen sorption characteristics. Upon nanostructurization, thermodynamics of hydrogen sorption improves as compared to their bulk counterparts. The catalytic activities of these nanosponges were assessed by carrying out the reduction of 4-nitrophenol using Sodium borohydride. All the metal nanosponges exhibit better catalytic activity as compared to their bulk counterparts. Palladium nanosponge showed the highest catalytic activity among all other nanosponges and retained its porous structure after a few cycles of reduction reaction.[1]

B. Metal Oxide Nanosponges

1. Molybdenum Oxide Nanosponges

Catalysis of organosulfur oxidation and sequestration of the products from reaction mixtures are carried out using, Group VI metal oxide as CrOx, MoOx, WOx, nanoparticles are embedded within hollow graphitized carbon nanofibers (GNFs), which act as nanoscale reaction vessels for oxidation reactions are used in the decontamination of fuel. When immersed in a model liquid alkane fuel contaminated with organosulfur compounds as benzothiophene, dibenzothiophene, dimethyl dibenzothiophene, it was found that MoO_2-GNF nanoreactors, consisting of molybdenum dioxide nanoparticles grown within the channel of GNFs, show superior abilities toward oxidative desulfurization (ODS). The nanotube cavity can selectively absorb and remove the ODS products namely sulfoxides and sulfones from several model fuel systems. Catalytic nanosponge namely MoO_2-GNF is yielded by an adsorptive desulfurization (ADS) mechanism, in combination with ODS .[27]

2. Lithium Oxide Nanosponges [28]

Dextrin-based nanosponges are hyper-cross-linked polymers characterized by its ability to encapsulate a great variety of substances in the liquid phase. They are nanostructured within a three-dimensional network. Amorphous modified polyetheretherketone (PWC) and nanosponges derived from cross-linking dextrin and cyclodextrins, from flat sheet membranes. PWC features are changed by the presence of nanosponges in the membrane. PWC/NS membrane displays very low oxygen permeability, good ionic conductivity and assures suitable interfacial stability with Lithium metal. The membrane is suitable to protect highly reactive Lithium metal anode from oxygen crossover, dendrite formation and from side reactions due to oxygenated Dimethylsulfoxide based electrolyte. Lithium oxide lab-scale cells are assembled with the membrane sandwiched between Li and separator soaked by electrolyte, with a continuous oxygen flow of 3 ml/min at the cathode side. Membranes determine long cell cycle life at reversible capacity and better capacity retention during cycling in full discharge/charge conditions.

C. Bimetallic nanosponges

They have a higher number of pores, higher catalytic activity, and higher stability compared to monometallic nanosponges. [1]

1. Platinum Copper alloy nanosponges [29]

They are achieved by varying the feeding molar ratio of Platinum Copper (Pt-Cu) Cu 3 : 1, 2 : 1, 1 : 1, 1 : 2, 1 : 3, the obtained products are referred to as Pt_3Cu, Pt_2Cu, Pt Cu, $PtCu_2$, and $PtCu_3$ using Pt(acac)2 and Cu(acac)2 as metal precursors and formaldehyde as a reducing agent. Pt-Cu nanosponges were comprised of interconnected small nanoparticle building blocks, the bottom-up method was successfully applied to prepare composition-tunable Pt-Cu alloy nanosponges. Due to the porous structure, structure defects, and synergetic effect of Pt and Cu, the Pt-Cu alloy nanosponges exhibit good electrocatalytic performances towards methanol oxidation.

2. Platinum Rhodium nanosponges [30]

Platinum Rhodium (Pt-Rh) NSs were obtained in a high yield of three-dimensional(3D) foam-like nanostructure with interconnected pores. The electrocatalytic performance of synthesized Pt-Rh NSs was composition-dependent, and they exhibited remarkably improved methanol oxidation activity as compared to Pt-NSs and commercial Pt/C catalyst. Pt-Rh NSs were also found to be much more stable 3D porous nanostructure. Alloy effect and clean particle surface show their superior electrochemical properties. A highly active electrocatalyst towards MOR in the acid medium was prepared with it.

3. Platinum Ruthenium nanosponges [31]

Methanol electro-oxidation reactions are used for the development of direct methanol fuel cells, which are considered to be one of the promising clean energy sources. Pt-Ru is considered as the best catalyst system to obtain both high catalytic activity and stability for methanol electrooxidation resulting from the good catalytic synergism.

4. Platinum Nickel nanosponges [32]

The incorporation of carbon dots into graphene dots, which eventually encapsulate the Platinum-Nickel (Pt-Ni) nanocrystals were prepared. The strong Pt–carbon interaction propels the formation of the G-PtNi NS with large specific surface area and good long-term stability. The Graphene Platinum-Nickel(G-PtNi) NS shows high reactivity for an oxygen reduction reaction (ORR). The graphene layers physically stabilize the Pt-Ni NS and chemically adjust the oxygen affinity of the Pt-Ni NS, which both positively contribute to the ORR performance.

D. Polymetallic nanosponges

Polymetallic nanosponges have enhanced the catalytic activity, fuel cell and water purification thus they have potential applications and have been used variedly in these areas. Their key properties responsible for these activities are large surface area and high porosity, oxidation and hydrolysis of Sodium Borohydride which forms hydrogen bubbles which lead to the formation of polymetallic nanosponges. The performance of nanosponge depend on high surface area and controlled pore size. Alloying is useful for the synthesis of these nanosponges.[33]

1. Platinum Ruthenium Nickel alloy nanosponges [34]

Formation of support-free trimetallic $Pt_{53}Ru_{39}Ni_8$ nanosponges with a clean surface was obtained by mixing the H_2PtCl_4, $RuCl_3$, $NiCl_2$ and sodium borohydride ($NaBH_4$) solutions together and thus synthesizing $Pt_{53}Ru_{39}Ni_8$ nanosponges which were nanocatalysts for the electrochemical performances of hydrogen evolution reaction (HER) and hydrazine oxidation reaction (HOR). Hydrogen plays a key role in a clean energy source. For hydrogen generation, the electrocatalytic reduction of water is done via HER, hydrazine is a carbon-free energy source with high power density, without producing poisonous CO-like species inducing the catalyst poison. Thus, direct hydrazine fuel cells are feasible through the catalytic hydrazine oxidation reaction (HOR) in power sources.

2. Palladium cyclodextrin-polyurethane nanosponge [35]

Immobilized palladium nanoparticles on a cyclodextrin-polyurethane nanosponge (Pd-CD-PU-NS) were found to be an efficient heterogeneous catalyst in the cyanation reaction of aryl halides in aqueous media.

VI. Encapsulating Hybrid nanosponges

1. Hybrid nanosponges such as alginate nanosponges are nanosponges containing several holes that carry the drug molecules and can entrap drug molecules in the aqueous core. [1]

2. Complexing hybrid nanosponges

a. The nanoparticles attract the molecules by electrostatic charges such as hydrogels combined to nanosponges. [1]

b. Using Ascorbic Acid (AA) as a reduction agent and further complexing PteAg nanosponges adsorbed with hexadecyltrimethylammonium ions (CTAþ) to the sidewalls of SDS-modified herringbone GNs via an electrostatic attraction to form non-covalent PteAg/GNs electrocatalysts.[36]

3. Conjugating hybrid nanosponges

These nanoparticles coupled to drug molecules through robust chemical bond Ag-Au (Silver-Gold) hybrid nanosponge, having controlled porosity and composition ratio they were fabricated through the cyclic electroless deposition of Ag into the porous Au-NSs. In the Ag-Au hybrid NSs, both Au and Ag components with mesoscale ligament size are continuously percolated over the entire structure. They were prepared for application in Surface-Enhanced Raman spectroscopy (SERS) detection. The cycles of Ag deposition can be controlled to tune the plasmonic properties. Plasmon peaks were attributed to Au and Ag component's blue shift with an increasing amount of Ag. Upon the increasing amount of deposited Ag,, the volume porosity is reduced. Deceasing porosity played an important role in the blue shift according to theoretical calculations. Moreover, the Ag−Au hybrid nanosponges exhibit higher SERS detection.

4. Magnetic hybrid nanosponges

These nanosponges are often magnetic ones in the presence of compounds having magnetic properties[1]

a. Cyclodextrin nanosponges and octakis (3-chloropropyl) octasilsesquioxane followed by incorporation of Palladium and magnetic nanoparticles. Sonogashira and Heck reactions were promoted in absence of any ligand and co-catalyst by the resulting composite, which was utilized as an efficient heterogeneous catalyst.[38]

b. A ternary hybrid system composed of CDNS, POSS, and Fe_3O_4 nanoparticles, is prepared through the facile procedure and applied for the immobilizing Pd nanoparticles. The resulting catalytic system, Palladium Fe_3O_4-Hybrid, was then applied as a magnetic catalyst in ligand and copper-free Sonogashira and Heck coupling reactions.[39]

c. Amine-functionalized core-shell Fe_2O_3 hollow spheres (h-Fe_2O_3-SiO_2-N) were decorated with Chlorine Functionalized cyclodextrin nanosponge, CDNS-Cl, covalently. The formed hybrid system, hFe_2O_3-SiO_2-CDNS, was then used as magnetically separable support for the immobilization of Pd(0) nanoparticles.[40]

5. Silicon hybrid nanosponges [41]

The nanosponges are fused with silicon as a core material to make a hybrid system like hybrid photovoltaics silicon nanosponges. Hybrid of silicon nanosponge- polymer silicon cells were injected into liquid precursor solution of ferrocene dissolved in dichlorobenzene into a quartz tube furnace, under a gas flow of hydrogen and argon. Chemical vapor deposition (CVD), a method is used for the growth and study of carbon nanotubes. The sponges showed a high degree of flexibility and mechanical integrity and could be twisted and handled without breaking.

6. Fluorescent dependent nanosponges [42]

Their supramolecular building blocks of cholesterol-$(K/D)_n$DEVDGC$)_3$-trimaleimide units feature a trigonal maleimide linker to which lysine $(K)_{20}$ or aspartic acid $(D)_{20}$ are linked. A consensus sequence for caspase-6 (DEVD-GC) was integrated into these structures. Caspases −3 and −6 are taken up by cells and are, therefore, suitable to cleave the consensus sequences of nanosponges that have been taken up by transport cells, thus triggering their release using apoptotic processes, which enhance the porosity of the transport cells and then dissect them into apoptotic bodies. Both, (cholesterol-$(K)_{20}$DEVDGC$)_3$-trimaleimide and mixtures of (cholesterol-$(K)_{20}$DEVDGC$)_3$-trimaleimide and (cholesterol-+$(D)_{20}$DEVDGC$)_3$-trimaleimides form stable nanosponges (short notation: DK20) the nanosponge structure is featuring aspartate- and lysine-rich regions, together with cholesterol domains and aqueous solvent filled nanoholes. Nanosponges are immediately formed upon mixing with aqueous buffers DK20. They are capable of incorporating fluorescent dyes *e.g.* carboxyfluorescein or PKH26 which can be used for fluorescence imaging and payload release studies.

VII. Graphene-based nanoporous sponges [43]

These materials possess significant elasticity and behave as nanosponges that enable the force-driven liquid-gas phase transition of molecules. Compression and free-expansion of the nanosponge exhibit cooling upon evaporation and heating upon condensation. Such a mechanism can be applied to green refrigerants such as H_2O and alcohols, cooling systems using such nanosponges can potentially achieve high coefficients of performance by decreasing Young's modulus of the nanosponge. The quasi-liquid adsorbed inside nanopores is in equilibrium with the gas phase, whose pressure is much lower than the bulk saturation pressure, and therefore, it's gas-liquid equilibrium line can be considered as shifting downwards.

VIII. Deoxyribozyme-nanosponges [44]

Deoxyribozyme nanosponge absorbs Indocyanine Green (ICG) in a sponge-like manner, they were constructed easily by assembling a cation polymer and long single-stranded DNA with repeated DNAzyme domains. The nanosponges were of an appropriate size for accumulation at the tumor via enhanced permeability and retention (EPR) effect. The multivalence of the DNAzymes that were incorporated into the nanosponge allowed the effective attenuation of the thermoresistance by silencing the HSP gene. The multivalent DNAzyme can efficiently silence the HSP70 gene to sensitize MCF-7 cells to heat, eliminating the heat shock response of cancer cells.

IX. Europium doped ZnO nanosponges [45]

Nanosponges with tuneable ZnO crystal promises in the frame of photocatalysis due to its large porosity and great surface accessibility to gases and liquids. Photoluminescence (PL) and optical absorption were assessed, such as crystallinity, crystal size, porosity as well as defect and bandgap structure. The photocatalytic performance of the highly porous ZnO nanosponges was evaluated by assessment of their capability to degrade the model organic dye rhodamine B (RhB) under UV illumination. This was attributed to the synergistic effect that heat treatment and doping has on the structural and optical properties of the synthesized ZnO photocatalysts.

X. Platinum Molybdenum Nanosponges [46]

Three-dimensional Platinum Molybdenum **(**Pt-Mo) nanosponge wrapped with graphene dots was developed for catalyzing the hydrogen evolution reaction (HER). at a low temperature in an aqueous solution. The graphene-dot wrapping takes place via the exfoliation of carbon dots during the co-reduction of Pt/Mo precursors and carbon dots. HER performance and durability in both acidic and alkaline electrolytes are an outcome of the synergistic effects of inner metallic alloy networks and outer graphene dots in the 3D PtxMo1-x-graphene.

CONCLUSION

The study here shows that nanosponges have applications in varied fields of technology. The foremost applications of nanosponges in pharmaceutical delivery has been overlaid by non-pharmaceutical uses. Nanosponges have formed a stepping stone in nanotechnology to form a base for different applications. Pharmaceutical uses include poorly soluble drugs that are entrapped within these nanostructures are made soluble due to the soluble crosslinkers and also to enhance their permeability through various membranes to increase bioavailability, solubility and site-specificity. Nonpharmaceutical uses involve the area of research such as absorption of toxins or forming hybrids to forming complexes with β cyclodextrins increasing porosity of the nanoparticles. They are extensively used in chemical and metallurgical for the generation of hydrogens as a renewable resource, for catalytic and electrocatalytic uses, etc. Nanosponges have been curating many age-old issues for which required many step-process, these processes are addressed by the formation of nanosponges.

Future endeavors

In future Nanosponges can be used for the adsorption of biological hazards to reduce the toxicity of water bodies, to clear the drainages of toxic waste. Using nanoparticles for spray nanostructures are effective from a dermatological point of view which can be considered for any application to give immediate effect on areas such as burns and warts as they tend to permeate the barriers easily due to fewer particles size. Formation of pH-responsive nanosponges through cross-linking with polyamine linkers with βcyclodextrins enhance their sensitivity and detection of different pH.[20] Carbonaceous Nanosponges can be used for surface treatment of textiles or metal meshes, producing membranes with potential applications as selective barriers for oil/water separation.[18] Electrophilic cyclodextrin synthon, the synthetic approach used to form cyclodextrin based nanosponges causes a shift in paradigm and also forms pH smart nanosponges. Compression and free-expansion of the nanosponge cause cooling upon evaporation and heating upon condensation, graphene-based nanoporous materials possess significant elasticity and behave as nanosponges that enable the force-driven liquid-gas phase transition of molecules.[43] The present mechanism has been applied to green refrigerants such as H_2O and alcohols, this can lead to decrease in use of ozone layer depleting agents and thus protect ozone depletion and control harmful effects on climate change. Nanosponges can deliver large molecules – specifically peptides and proteins – into specific subcellular locations. A targeting unit attached nanosponges can deliver drugs to the surface of tumors in the lungs, brain and spinal cord due to their smaller particle size, they can cross these biological membranes. This delivery system can be extensively used to carry the chemotherapy agents for targeted delivery to tumors. Drug-loaded magnetic nanosponges could be developed, where a localized magnetic field gradient could be applied to attract particles to the site of action and hold them in place, in the required therapeutic concentration, until therapeutic activity completes. Nanosponge technology has gained popularity due to the rationale and simplicity of approach. Nanosponge-ICG is a promising nanotherapeutic agent for Photothermal therapy due to biocompatibility and high efficiency which can be used to assist cancer therapeutics.[44] These porous systems have also been studied for drug delivery through pulmonary route, which depicted that this system has effective drug release even in the scarce of the dissolution fluid, thus colon targeted delivery may be able to expand like never before. Nanosponge particles can also be implied in cell culture media, leading to a new loom in stem cell culture, cellular regeneration in the body and cytology.

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