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Mesoporous Santa Barbara Amorphous For Novel Drug Delivery System

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ABSTRACT:
The Santa Barbara Amorphous (SBA) is a highly significant mesoporous silica with unique properties, including ordered and homogeneous mesopores, hydrothermal stability, thick walls, large surface area, and abundant pore volume. Researchers have suggested that SBA can be used to create a hybrid system for improving the delivery of poorly water-soluble drugs and prolonging their release, by simultaneously entrapping both drug molecules and pharmaceutical excipients within the silica matrix. In this review article, we will discuss the synthesis and characterization of mesoporous SBA, its morphology, various types of SBA, drug loading methods, the mechanisms of SBA in the formulation of novel drug delivery systems, and its applications in drug delivery.

KEYWORDS: *Characterization, Drug loading, Mesoporous, Solubility, Synthesis*

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I. INTRODUCTION:

Santa Barbara Amorphous-15 (SBA-15) is a highly stable mesoporous silica sieve that was developed by researchers at the University of California, Santa Barbara in 1992. It has emerged as a new generation of inorganic platform for biomedical applications and is different from conventional materials due to its high hydrothermal and mechanical stability[1]. Mesoporous silica contains uniform hexagonal pores with hundreds of nano-scale channels ranging from 5nm to 15nm in diameter, and its framework walls are relatively thick, ranging between 3.1nm and 6.4nm in size [2].SBA-15 has a high internal surface area, which makes it suitable for various applications, including environmental adsorption and separation, acting as a host for a variety of biological agents, and providing pathways for drug diffusion and adsorption of a larger number of molecules [3].

In 2001, MCM-41 (Mobil Crystalline Materials) was reported as the first mesoporous silica drug carrier. Since then, research on the biomedical application of mesoporous silica has increased aggressively, and a wide variety of bioactive agents, such as small molecule drugs, peptides, proteins, and Small interfering RNA (siRNA) have been successfully applied [4,5]. Mesoporous materials find wide application in catalysis, drug control delivery, biosensors, biofuel, sorption, and membrane separation [6-11]. Typical compounds of mesoporous materials include silica, alumina, carbon, and transition metal oxides [12-14]. Silica is widely employed as the main building block of mesoporous materials because it is inexpensive, thermally stable, chemically inert, and harmless [15].

Recently developed new pharmaceutical ingredients show very low water solubility, resulting in a slow dissolution rate and poor oral bioavailability [16]. Over the past few decades, the manufacture of amorphous solid dispersions containing water-insoluble drugs in appropriate materials has attracted much attention [17,18]. Hence, the unique advantages of mesoporous SBG materials make them a promising reservoir for encapsulating a large amount of therapeutic active constituents [19].

The concept of mesoporous silica as a drug delivery carrier was utilized by Vallet-Regi and colleagues in 2001[20]. Subsequently, research on its biomedical applications has increased exponentially, and it has been successfully applied to a variety of poorly water-soluble drugs to improve the rate of dissolution [21,22]. Compared

with traditional porous materials containing a heterogeneous structure, mesoporous silica exhibits a highly ordered porous interior without an interconnection between hundreds of nano-size channels. This makes it adaptable as a storage host for various therapeutic drugs and simultaneously offers pathways for drug dissolution. When poorly soluble drug molecules are confined to the inner space of mesoporous silica channels, intermolecular interactions leading to crystallization can be effectively prevented [23-25]. Therefore, the amorphous state can be maintained during the shelf-life, and subsequently, the drug dissolution rate can be increased after oral administration.

SYNTHESIS OF MESOPOROUS SBA

The synthesis process for SBA involves a cooperative self-assembly process with the use of a non-ionic triblock copolymer template, Pluronic P123, consisting of ethylene oxide and propylene oxide units (EO20,PO70,EO20), and either tetra ethoxy silane (TEOS) or tetra methoxy silane (TMOS) as silica sources. This results in the formation of a 2-D array with long 1-D channels [26,27]. The hydrophobic propylene oxide unit and the hydrophilic ethylene oxide units determine the morphology of SBA [28]. The synthesis process involves dissolving the template in an acidic solution and adding the silica source. The mixture is heated and then kept for a specific time period to form a white solid, which is then filtered, washed, and air-dried at room temperature. The sample is further dried in an oven and calcined at a high temperature to remove the template. The ratio of EO:PO affects the morphology of SBA, with a lower ratio forming hexagonal morphology and a higher ratio forming cubic mesoporous silica [29]. Different types of mesoporous SBA materials are used for drug delivery, and their characteristics are summarized in Table 1.

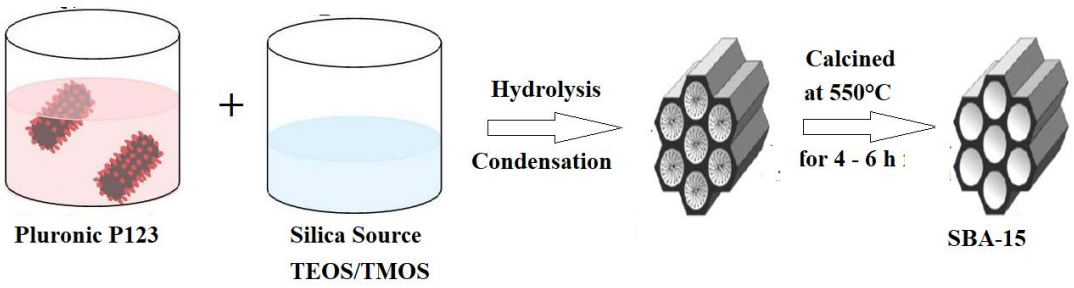

Figure 1: Synthesis route for preparation of SBA-15

Table 1. List of mesoporous Santa Barbara Amorphous (SBA) used for drug delivery

Mesoporous SBA type	Pore symmetry	Pore size (nm)	Pore volume (cm^3gm^{-1})	Reference
SBA-11	3D cubic	2.1-3.6	0.68	34
SBA-12	3D hexagonal	3.1	0.83	35
SBA-15	2D hexagonal	6	1.17	36
SBA-16	cubic	5-15	0.91	37

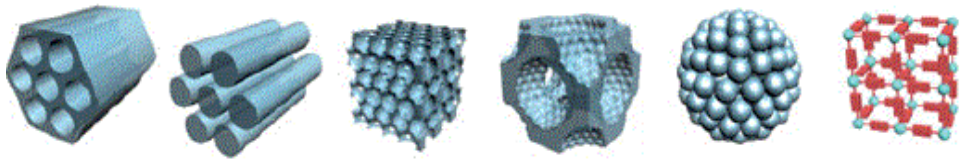

Figure 2: Different types of SBA

CHARACTERIZATION OF MESOPOROUS MATERIALS

Ordered mesoporous materials can be categorized based on their pore geometry and structural dimensions. Among them, cylindrical structures with uniform pore diameter show potential for applications such as catalysis, adsorption, and drug delivery. Cage-type mesoporous materials consist of spherical or ellipsoidal cages connected three-dimensionally by smaller windows, which can be used to control the mass transfer of active agents. Mesoporous materials, such as silica, are commonly characterized using techniques such as X-ray diffraction, N2 adsorption or desorption, scanning electron microscopy (SEM), and transmission

electron microscopy (TEM). X-ray diffraction is used to identify the crystallographic symmetry of material phases at both the nano- and meso-scale. However, phase identification for mesoporous materials using X-ray diffraction can be challenging because most of the peaks appear at low angles and may overlap due to similar short-range order. High resolution transmission electron microscopy can provide detailed analysis of pore order and symmetry at the mesoscale [31-32].

Table 2. Characterization techniques and evaluation parameter[33,34]

S.No	Characterization techniques	Evaluation parameter
1	X -ray diffraction	Pore structure topology
2	Fourier transformed Spectroscopy	Structural details especially silanol group
3	Nitrogen adsorption or desorption	Pore size, pore volume and surface area
4	Scanning electron microscopy	External structural morphology
5	Transmission electron microscopy	Interior structural morphology especially pore geometry
6	Differential scanning calorimetry	Physical changes as a function of temperature
7	Elemental analysis	Estimation organic elements especially after functionalization
8	Thermogravimetry	Evaluation of the mesopore volume and specific surface area
9	High resolution transmission electron microscopy	Phase identification for mesoporous materials

PARAMETERS CONSIDERED FOR MESOPOROUS SBA DRUG DELIVERY SYSTEM

To formulate a mesoporous SBA drug delivery system, several parameters need to be considered, including surfactants, co-surfactants, silica sources, solvents, temperature, and pH.

a. Surfactants

Surfactants play a crucial role in the formulation of mesoporous SBA dosage forms by acting as templates for the growth of mesoporous materials. The type and quality of surfactants used determine the structures of the resulting materials[35]. When surfactants are present at concentrations above their critical micelle concentration (CMC), they can change their shape from spheres to cylinders and hexagonal channels, resulting in larger pores. The use of a swelling agent, along with changing the type and quality of surfactants, can lead to the synthesis of mesoporous materials with well-defined pores[36].

The commonly used surfactants can be classified into four types. Cationic surfactants, which are positively charged, have a polar head and nonpolar tail. Examples of cationic surfactants include cetyltrimethylammonium chloride (CTAC), cetyl trimethyl ammonium bromide (CTAB), and hexadecyltrimethylammonium (HDTMA)[37,38]. Anionic surfactants, which are negatively charged, have a long hydrocarbon tail and a polar head consisting of sulfated (R-OSO3Na) and sulfonated (R-SO3Na) compounds[39]. Non-ionic surfactants are neutral surfactants that have a non-dissociable type of hydrophilic head, such as amide and phenol, and cannot ionize in an aqueous solution. Examples of non-ionic surfactants include Triton X-100, polysorbate, Pluronic F127, and Pluronic P123[40]. Zwitterionic or amphoteric surfactants have positive and negative charges on their hydrophilic ends, which cancel out each other, producing a zero-net charge. Examples of zwitterionic surfactants include phospholipids, betaines or sulfobetaines, and amino acids[41].

b. Co-surfactants

In addition to surfactants, co-surfactants such as ethanol and butanol can also have an impact on the pore size and structure of mesoporous silica materials [42]. Higher concentrations of co-surfactants can lead to the formation of amorphous particles with disordered pore sizes, and cause a loss of the characteristic spherical shape of mesoporous silica nanoparticles [43,44]. It's worth noting that some of the surfactants used in the synthesis of mesoporous silica materials can also act as co-surfactants.

c. Solvents

Solvents play a crucial role in formulating mesoporous SBA drug delivery systems, with alcohols such as ethanol, propanol, butanol, and pentanol being the most commonly used examples. These alcohols not only enhance pore formation but also alter the sizes of mesopores. However, the morphological characteristics of mesoporous materials can be slightly affected by alcohols that have low evaporation rates and high molecular weights [45]. For instance, alcohols with long chains can facilitate the transition from one phase to another. To

illustrate, Agren et al utilized hexanol to synthesize a hexagonal phase in MCM-41 and generate a new lamellar phase [46].

d. Silica sources

To form well-ordered drug delivery systems, various precursors such as sodium silicates, colloidal solutions, and organosilanes like tetramethyl orthosilicate (TMOS), tetraethyl orthosilicate (TEOS), tetramethoxy vinyl silane (TMVS), tetrapropyl orthosilicate (TPOS), and trimethoxy silane (TMS) are required [47]. Among these precursors, TMS is known to rapidly form silicate mesoporous structures compared to others, making it a preferred choice [48].

e. Temperature

Temperature plays a critical role in the formulation process, and two essential factors that need to be considered are the cloud point (CP) and critical micelle temperature (CMT). It is important to ensure that the CMT of surfactants used in the formulation is lower than the temperature applied during the process, to avoid any potential issues [49].

f. pH

Neutral conditions can be utilized to synthesize well-ordered mesoporous materials by adjusting the hydrolysis and condensation of silica precursors and incorporating fluorine as catalysts. On the other hand, under alkaline conditions with a pH range of 9.5-12.5, polymerization occurs, creating adjustable silicate species networks, utilizing silica precursors such as TEOS, colloidal solutions, and Na2SiO3. During synthesis under alkaline conditions, pH changes occur, with silica hydrolysis resulting in a decrease in pH at the beginning of the reaction, followed by a slight increase during the condensation of silica species [50].

DRUG LOADING METHODS

The optimal drug loading process should aim to minimize the amount of drug that remains adsorbed on the external surface of the particles and ensure efficient loading of a substantial quantity of the drug. The method chosen for drug loading can significantly impact various factors, such as the physicochemical properties of the loaded drug, the extent of drug entrapment, and the distribution of the drug within the carrier material [51,52].

There are several approaches to loading drugs into the pores of mesoporous SBA, which can be broadly categorized into two main methods: solvent-free and solvent-based (also known as wet methods) (as shown in Figure 3). Each method has its advantages and limitations, and the choice of method should be carefully considered based on the specific requirements of the drug delivery system [53,54].

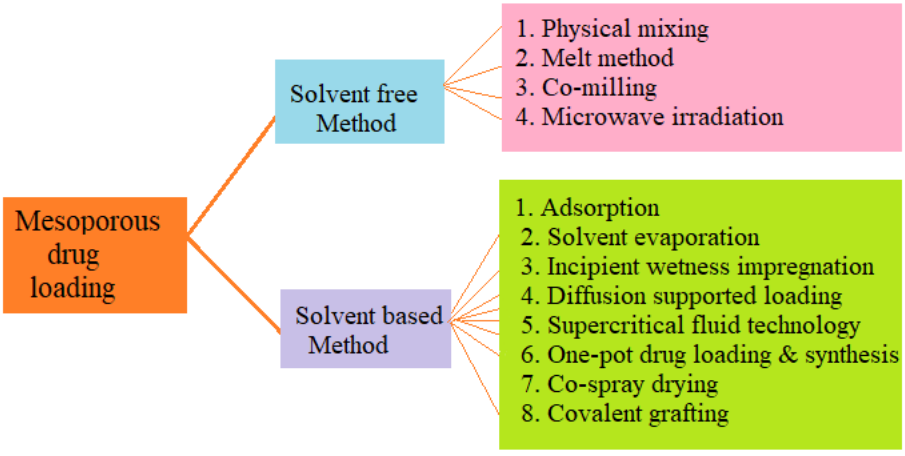

Figure 3: Different methods used to load drugs into Mesoporous SBA

a.Solvent-Based methods

Based on the available literature, a variety of drugs are frequently encapsulated using solvent-based methods such as solvent evaporation, adsorption, and incipient wetness impregnation (as summarized in Table 2). In this approach, the drug loading process typically involves the adsorption of drug molecules onto mesoporous silica particles through various interactions such as van der Waals forces, electrostatic binding, hydrogen bonding, or even covalent bonding [55].

The drug loading capacity of the mesoporous silica particles in wet methods is influenced by several factors, including the internal pore volume of the silica, the concentration of the drug in the solution, and the polarity of the solvent [56]. Therefore, optimizing these parameters can play a critical role in achieving efficient drug loading and effective drug release from the carrier material.

b.Adsorption method

One of the commonly used and straightforward methods for loading drugs into the pores of mesoporous SBA is the adsorption method. In this approach, an organic solution of the mesoporous silica particles is immersed in a concentrated drug solution. During this process, the drug molecules get adsorbed onto the pore walls of the mesoporous silica. The drug-loaded particles are then separated from the solution by either filtration or centrifugation, followed by drying to remove the adherent solvent [57].

The adsorption method is suitable for loading hydrophilic, hydrophobic, and thermally sensitive drugs [58]. However, this method also has several disadvantages, including the rapid adsorption of drug molecules onto the surface, which can potentially block the mesopores, making it unsuitable for poorly soluble drugs. Additionally, a high concentration of drug solution is required, leading to a large quantity of drug being wasted during the filtration or centrifugation process, making this method time-consuming [59]. The choice of solvent used for the drug loading process is also a crucial parameter that can affect the overall efficiency and effectiveness of the drug delivery system [60].

c. Incipient wetness impregnation method

The impregnation method is commonly used for the preparation of catalysts, but it is also suitable for loading drugs into mesoporous materials. In this method, a known volume of concentrated drug solution is added dropwise onto the silica, and the wet powder is allowed to dry, allowing the drug to diffuse into the pores through capillarity. The product is then washed immediately to remove any excess drug coating the external surface of the silica using a small amount of used solvent. The product is dried for approximately 24 hours using air and then placed under a vacuum for 48 hours at 40°C [61].

Charnay et al. reported that the washing step for eliminating APIs outside the pores significantly influences the drug loading efficiency. They observed a reduction in the amount of ibuprofen encapsulated onto the mesoporous material after washing the silica with ethanol, from 1350 to 500 mg/g. The impregnation method's main advantage is its ability to accumulate a larger quantity of drug into the carrier due to the large pore volume of the mesoporous silica. This method also allows for easy determination of the concentration of the drug loaded into the carrier [62].

However, this method has some disadvantages, such as the difficulty in achieving uniformity of drug distribution, and there is a high risk of drug crystallization on the outer silica surface, which can lead to plugging of the mesopores [63].

d. Solvent evaporation method

Another commonly used approach for drug loading is the solvent evaporation method, which involves a combination of adsorption and subsequent rapid solvent evaporation [64]. In this method, the mesoporous silica is dispersed in a volatile organic solution containing the drug, such as ethanol or dichloromethane. The solution is then dried by fast solvent evaporation using a rotary evaporator or heating to obtain the drug-loaded mesoporous silica material.

It should be noted that the solvent evaporation method may affect the physical state of the drug and the rate of drug release from the carrier [65]. He et al. suggested that the solvent evaporation method provides the drug molecules with enough time to rearrange and aggregate inside the mesopores, which can affect the drug's release behavior[66].

e. Diffusion supported loading (DiSupLo)

The DiSupLo method is a novel, efficient, and environmentally friendly approach for loading APIs into mesoporous silica. It was developed by Potrzebowski and his team and involves transferring a pre-homogenized physical mixture of API and mesoporous silica with the desired proportions of both components into an opened vessel and placing it in a closed vessel containing ethanol for 3 hours at room temperature (Fig. 4). The drug loading time is established experimentally using NMR measurements at 30-minute intervals. The layer thickness of the physical mixture should be small and optimized experimentally. Finally, the ethanol is removed by evaporation from the drug-loaded samples [67].

The DiSupLo method relies on the diffusion of ethanol vapor to the solid mixtures, followed by the penetration of vapors into the solid mixture, condensation, and dissolution of the drug. The dissolved API is then transferred into the pores of the mesoporous silica. This method is fast, requires minimal solvent, and does not need any special equipment. It is also capable of loading two or more components with the desired API composition, making it suitable for multi-component systems [68].

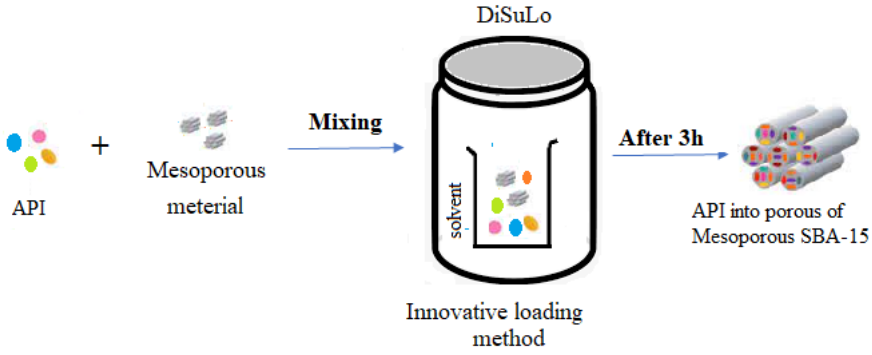

Figure 4:Schematic illustration of DiSupLo method for drug loading

f. Supercritical fluid technology (SCF)

Supercritical fluid impregnation is a method commonly used in the food and chromatography industries, as well as in drug loading into mesoporous silicas. In this technique, supercritical fluids such as carbon dioxide are used as solvents to load drugs into mesoporous silica [69]. The use of supercritical fluids in this technique has many advantages compared to organic solvents. Their specific properties, such as liquid-like density, gas-like viscosity, and high diffusivity allow for even impregnation and a shorter processing time than in the liquid phase. Additionally, supercritical fluids have very low interfacial tension, which allows for better control over the impregnation process. This method is also environmentally friendly as the supercritical fluid can be easily recovered and reused [70].

g. One-pot drug loading and synthesis procedure

This is a new and promising method for drug encapsulation, where the API is loaded into the mesoporous carrier during its synthesis. The traditional method of mesoporous silica production involves a gel-sol synthesis using inert surfactant micelles as a template, which is removed through extraction or calcination [71]. However, this method is time-consuming, multi-step, and has low drug uptake and burst release, which is not suitable for most applications. In contrast, the new approach combines mesoporous silica synthesis and drug loading processes, which overcomes these limitations and appears very promising for designing novel drug delivery systems [72].

Wan et al. presented research using the one-pot synthesis method by evaporation-induced self-assembly, where they introduced two drugs, the hydrophilic heparin, and the hydrophobic ibuprofen, into mesoporous silica. This new method is expected to increase drug loading efficiency, improve drug release behavior, and simplify the production process. Further research is required to optimize the drug loading process and explore its potential for different types of APIs and mesoporous materials [73].

h. Melt method

The melt method involves heating a physical mixture of the drug and mesoporous silica above the melting point of the API [75]. This approach is highly efficient and significantly reduces the time required for drug incorporation into the mesoporous silica. Potrzebowski et al demonstrated that the melt method is a much more efficient technique for confining ibuprofen in the pores of MCM-41 than the incipient wetness method. They established the percentage of mesopores filled by analysing the proton NMR spectra recorded at very fast rotation of the sample. However, this method is suitable only for drugs that have a low viscosity after melting and are thermally stable. It was observed by Mellaerts et al. that itraconazole was not successfully loaded into the pores of SBA-15 due to its high viscosity in a molten state, which prevented homogeneous drug distribution in the mesopores [61].

i. Solvent-Free method

Solvent-free methods have significant advantages compared to solvent-based methods, such as achieving a high degree of drug loading, being less time-consuming, and providing an easy way to predict drug concentration. Therefore, these methods are considered more environmentally friendly. Various solvent-free methods are used for the encapsulation of drug particles, including the melt method, microwave irradiation, and co-milling [74].

j. Melt method

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k. Microwave irradiation

This drug loading method is known as the microwave irradiation method, where a feedback system is used to control the temperature during the loading process of the API into the silica nanoparticles to protect the drug from degradation [75]. This technique has several advantages over traditional heating methods, including faster drug incorporation, increased drug loading capacity, and improved drug release profiles. Waters et al. demonstrated the effectiveness of this method by loading fenofibrate into various silicas, including SBA-15. The fenofibrate-loaded samples prepared by microwave irradiation showed higher and faster drug release compared to pure drug and samples prepared by other methods. This is attributed to the conversion of crystalline fenofibrate into an amorphous state, resulting in enhanced drug release [76].

l. Co-milling

The co-milling method is a popular technique for producing submicrometric particles and solid-state amorphization [77]. It is a simple and efficient technique that can be used on an industrial scale without time-consuming steps. However, during ball milling, it is essential to consider the resistance of the nanocarriers to mechanical stress. Shen et al. demonstrated that co-milling SBA-15 with ibuprofen resulted in a drug loading of almost 40%, indicating that the milling method is an efficient way of drug loading into mesoporous silica carriers [78].

Table 2. Review of drug loading methods usedfor mesoporous SBA in published papers

Drug	Mesoporous SBA type	Loading method	Reference
Atenolol III	SBA-16	Adsorption	Mehmood., et al.,[24]
Atorvastatin II	SBA-15	Solvent evaporation	Mellaerts., et al[25]
Carbamazepine	SBA-16 SBA-15	Adsorption Solvent evaporation	Mehmood., et al [24] Zhao., et al [28]
Celecoxib	SBA-15	Adsorption	Narayan., et al [31]
Cinnarizine, Danazol II and Diazepam II	SBA-15	Incipient wetness	Fulvio., et al [27]
Dasatinib II	SBA-15	Solvent evaporation	Jammaer., et al [34]
Fenofibrate	SBA-15	Incipient wetness Supercritical fluid technology Physical mixing	Goesmann., et al [38] Tanev., et al[39]
Furosemide	SBA-15	Solvent evaporation	Abdelbasir., et al [44]
Glibenclamide II	SBA-15	Incipient wetness	Agren., et al [45]
Ibuprofen	SBA-15	Adsorption, Incipient wetness Solvent evaporation, Melting Co-spray drying, Co-milling	Seljak., et al [51] Maleki., et al [52] McCarthy., et al [53]
Indomethacin	SBA-16	Solvent evaporation	Li., et al [54]
Itraconazole	SBA-15	Solvent evaporation Incipient wetness and Melting	Maleki., et al [52] Xie., et al [56]
Ketoconazole	SBA-15	Incipient wetness	Fulvio., et al [27]
Naproxen	SBA-15	Adsorption	Speybroeck., et al [60]
Nifedipine Phenylbutazone	SBA-15	Incipient wetness	Fulvio., et al [27]
Piroxicam II	SBA-15	Adsorption	Maleki., et al[52]
Prednisolone	SBA-15, SBA-3	Adsorption	Abd-elbary., et al [64]
Rufinamide	SBA-16	Adsorption	Ulrich., et al [26]

APPLICATIONS OF MESOPOROUS MATERIALS AS A DRUG DELIVERY SYSTEM

Mesoporous materials have a wide range of potential applications in the pharmaceutical industry due to their highly ordered mesoporous structures, large surface areas, and ease of surface modification. These properties make them ideal for various drug delivery applications such as targeted drug delivery, protein delivery, DNA/gene delivery, bio-imaging dyes, polymers, photosensitizers, biosimilars, active pharmaceutical ingredients, antibodies, catalysis, adsorbents, anticancer agents, antiviral agents, peptides, RNA, vaccines, dental grafting, and bone grafting. The use of mesoporous materials in these applications offers a promising approach for developing novel drug delivery systems with improved efficacy, safety, and biocompatibility [79].

a. Mesoporous material for immediate drug delivery systems

It is important to note that the use of mesoporous silica as a drug carrier has shown great potential in overcoming the limitations of hydrophobic drugs. Mesoporous silica-based drug delivery systems can provide immediate release, sustained release or controlled release of drugs by modifying the pore size, surface properties and chemical composition of the carrier [80]. The large surface area and high pore volume of mesoporous silica enable a high drug payload and help to maintain drugs in the amorphous or non-crystalline state, preventing transformations and improving drug dissolution and permeation. Additionally, mesoporous silica carriers offer excellent chemical stability and inert behavior, making them ideal for precise control of drug loading and release kinetics. This makes mesoporous silica a promising candidate for drug delivery systems, especially for hydrophobic drugs with poor solubility and limited applications [81].

b. Mesoporous material for sustained drug delivery systems

Sustained release dosage forms have a significant advantage as they maintain steady blood concentration for a prolonged period of time. Modified silica materials can achieve sustained drug release by the interaction between drug molecules and functional groups. Traditional mesoporous materials achieve sustained action by controlling their physical-textural properties, pore morphology, drug polarity, and amount of drug entrapped within the pores. Another approach is functionalization or grafting of mesoporous material with appropriate functional groups, which retards drug release from the mesopores mainly through diffusion mechanism. Different organic groups enhance attraction between drug and host molecule, leading to a decrease in drug release. The degree of drug release depends on the electrostatic force dominant between the host and guest molecule, hence selection of appropriate functionalization group depending on the chemical nature of the drug to be entrapped in mesopores is crucial [82,83].

Functionalization or grafting of mesoporous materials is a common approach to achieve sustained release of drugs. The appropriate functional groups can be grafted onto the mesoporous materials to retard drug release from the mesopores. This retardation is mainly achieved through the diffusion mechanism, where different organic groups can enhance the attraction between drug and host molecule, leading to a decrease in drug release. The degree of drug release depends on the electrostatic force that dominates between the host and guest molecule. Therefore, the selection of appropriate functionalization groups, depending on the chemical nature of the drug to be entrapped in the mesopores, is crucial to achieve sustained release of the drug [84].

c. Mesoporous material for targeted drug delivery system

Mesoporous materials possess numerous advantages, including good biocompatibility, excellent physicochemical and biochemical stabilities, and complete degradability [85]. These properties make them ideal carriers for targeted drug delivery systems. In addition to their various characteristic features, functionalization enhances the development of targeted or specific drug delivery systems by allowing for various parameters to be considered, such as the size of the drug molecule, drug loading efficacy, chemical nature of the drug, and hydrophilic or lipophilic properties. Targeted cancer therapies utilizing mesoporous materials may be more effective and safer for normal cells. They are used to obstruct the growth and spread of cancerous cells by directly interfering with specific molecules involved in tumor growth and indirectly stimulating the immune system [86].

d. Mesoporous materials for stimuli-responsive controlled drug delivery system

Stimuli-responsive drug carriers have shown great potential in reducing systemic toxicity and enhancing the therapeutic efficacy of APIs [87]. To achieve this, stimuli-responsive mesoporous silica materials have been developed by incorporating 'gatekeepers' over the pore entrance. The drug is trapped within the mesoporous silica carrier and cannot be released until exposed to specific external stimuli such as pH, temperature, photo irradiation or enzymes. These stimuli remove the gatekeepers, allowing for controlled drug release. Among various stimuli-responsive drug delivery systems, pH-responsive systems have been extensively studied due to the presence of pH gradients in different tissues and subcellular compartments [88].

II. CONCLUSION

Santa Barbara Amorphous (SBA) is a type of mesoporous silica with unique properties that make it an attractive candidate for drug delivery applications. The highly ordered, homogeneous structure of mesopores in SBA provides a large surface area and pore volume, which can be used to effectively entrap both drug molecules and pharmaceutical excipients.

The synthesis of mesoporous SBA typically involves the use of surfactants as templates, which are removed after synthesis to leave behind the ordered mesoporous structure. Characterization techniques such as X-ray diffraction, transmission electron microscopy, and nitrogen adsorption-desorption are commonly used to assess the morphology and properties of SBA.

Various types of SBA have been reported in the literature, including SBA-15, SBA-16, and SBA-3. These materials differ in pore size, pore volume, and wall thickness, and can be tailored for specific drug delivery applications.

Several drug loading methodologies have been developed for SBA, including physical adsorption, covalent attachment, and template-assisted loading. The mechanism of drug release from SBA typically involves diffusion of the drug through the mesopores or dissolution of the silica matrix.

SBA has been used in the formulation of various novel drug delivery systems, including nanoparticles, hydrogels, and coatings. Applications of SBA for drug delivery include improving the solubility and bioavailability of poorly water-soluble drugs, and providing sustained release of drugs over an extended period of time.

Overall, the unique properties of mesoporous SBA make it a promising material for the development of advanced drug delivery systems. Further research is needed to optimize the synthesis and drug loading methodologies, as well as to evaluate the safety and efficacy of SBA-based drug delivery systems in vivo.

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