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Zeolite Nanoparticles For Dual-Use: Drug Transport And Environmental Detoxification

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Abstract:- This review investigates the potential of zeolite-based nanoparticles in contemporary pharmaceutical research, emphasizing their role in advanced drug delivery systems. When incorporated into polymeric materials, zeolites enable precise drug delivery due to their distinctive structural attributes, biocompatibility, and tunable properties. Furthermore, zeolites exhibit environmental remediation capabilities through ion exchange processes. Synthetic zeolites, equipped with controlled release mechanisms, display unique optical and electronic properties, broadening their applications across various domains. This study explores the significance of zeolites in both industrial and scientific settings, detailing their synthesis techniques and size regulation methods. The review highlights effective encapsulation and functionalization strategies for drug delivery, underscoring their contributions to drug stability and targeted administration. Advanced characterization techniques provide deeper insights into zeolite-based drug delivery platforms. Addressing concerns regarding potential carcinogenicity, the review evaluates environmental impact and risk assessment, emphasizing the necessity of safety measures in nanoparticle research. In biomedical applications, zeolites serve crucial functions as antidiarrheal, antitumor, antibacterial agents, and MRI contrast enhancers. Clinical studies featuring zeolite-based therapies demonstrate their potential in tackling a wide range of medical challenges. Ultimately, zeolite-based nanoparticles emerge as powerful tools for targeted drug delivery, exhibiting versatile applications and therapeutic benefits. Despite existing challenges, their unique properties establish zeolites as key players in the advancement of innovative drug delivery systems.

Keywords:- Zeolite based nanoparticles, Therapeutic potential, Targeted drug delivery, Drug stability

1. Introduction

The requirement for focused and regulated therapeutic delivery has led to the development of many new functional drug delivery systems. Liposomes, microspheres, dendrimers, solid lipid nanoparticles, and polymeric nanoparticles are among the numerous delivery platforms under investigation; however, none have successfully reached clinical application(1). Micro- and mesoporous inorganic materials, such as zeolites, have gained significant research interest for specific and regulated drug delivery due to their unique structural characteristics, biocompatibility, extensive surface areas, and adjustable physicochemical properties. Zeolites are incorporated into polymeric materials for therapeutic delivery through multiple approaches, including hosts, blends, composite structures, and gels(2). Their uniform pore geometry and ion exchange potential make zeolites central to drug delivery systems, enabling controlled drug release. The highly crystalline structure of zeolites renders them ideal candidates for hydrogel formulations used in therapeutic applications. They exhibit selectivity in absorbing both desirable and undesirable organic or inorganic compounds(3). Due to their morphology, zeolites effectively function as scavengers of toxic substances. In biomedical applications, zeolites are extensively utilized due to their capacity for cellular internalization via endocytosis and their remarkable biological durability, making them useful for DNA delivery to cells(4). Alongside these advantages, zeolites are widely available and cost-effective. Their chemical stability, biocompatibility, and adaptable structural properties further enhance their applicability. Additionally, variations in their structures and pore sizes contribute to their high drug-loading efficiency(5). Through ion exchange interactions, zeolites facilitate rapid drug release by means of high surface absorption. The superior capability of zeolite nanocomposites to efficiently encapsulate and release therapeutic agents makes them more effective for biomedical use than other porous materials(6). A primary challenge associated with zeolites is their potential carcinogenicity; however, this characteristic can be leveraged in cancer treatment by harnessing their antiproliferative effects.

1.1. Nanoparticulate drug delivery systems over conventional dosage forms

The development of nanoscale drug delivery methods has been prompted by the many biological obstacles that drug molecules must overcome. Their huge surface area and tiny size provide many benefits, including better distribution of poorly soluble compounds(7). Nanosystems may also effectively deliver medication molecules to the targeted tissue or organ because of their small size, which allows them to pass through inflexible cellular barriers. In addition to enabling the simultaneous release of medications at various speeds, these technologies are capable of efficiently encapsulating big molecules(8). Liposomes, niosomes, lipid nanoparticles, microemulsions, dendrimers, and polymeric nanoparticles are among the many nanoparticulate drug delivery systems that researchers are now investigating. Because organic materials are biocompatible and biodegradable, researchers have been concentrating on drug delivery systems (DDS) based on them for years(9). However, due to their versatility for conjugation with a variety of molecules, adjustable size and form, biocompatibility, and simplicity of functionalization, inorganic materials have garnered increasing attention in recent years for use in biomedical applications. Finding a new delivery method that tackles problems with medication loading and release is still highly important(10). By combining the benefits of both organic and inorganic DDS, the metal-organic framework (MOF) is one possible remedy. In some instances, the structures and characteristics of a certain subclass of metal-organic frameworks, called zeolite-like metal-organic frameworks (ZMOFs), are similar to those of conventional inorganic zeolites(11). The periodic pore patterns, characteristic cage-like cavities, and flexible intra- and extra-framework components of these ZMOFs give them remarkable properties(12). ZMOFs' variety of pore diameters is its main advantage as it increases their ability to load drugs and permits regulated drug release. Additionally, zeolites' pore sizes and surface properties may be altered to satisfy certain drug delivery requirements(13).

1.2. Importance of zeolite-based nanoparticles

An ordered porosity structure is a characteristic of zeolites, which are aluminosilicates. Natural, synthetic, and zeolitic imidazolate frameworks are the three main categories into which they are divided according to the silica-to-aluminum composition(14). Zeolites' ion exchange characteristics are provided by the densely packed networks of ALO_4 and SiO_4 units that create mesoporous cavities(15). Zeolite crystals' exterior surface area increases as they are lowered to the nanoscale, improving their ability to interact with macromolecules. By

combining the benefits of conventional zeolites with nanoparticles, this nanoscale alteration makes zeolites efficient in treating serious illnesses like cancer and facilitating the regulated release of medications(16). Optimizing the physicochemical characteristics of zeolite nanoparticles to increase drug loading and delivery efficiency is a major area of current study(17).

2. Search strategy and selection criteria

This paper's main emphasis is on zeolites and drug delivery methods based on zeolite nanoparticles. For this study, a thorough literature search on zeolites as a new area in nanoparticulate drug delivery was carried out using online public databases with search engines that can handle certain keyword combinations(18). PubMed, SCOPUS, SciDirect, Google Scholar, Hindawi, clinicaltrials.gov, Google Patents, and Wiley Online Library were among the databases that were chosen. ((Zeolite) AND ((zeolite-based drug delivery) OR (nanoparticles)) AND ((zeolite safety considerations) OR (nanoparticles)) AND ((zeolite-based clinical trials) OR (zeolite framework)) were among the Boolean keyword combinations that were used in the search(19). The selection of the papers in this evaluation was based on how well they addressed the subject. Furthermore, open-access publications with original research on in vivo and in silico investigations, randomized clinical trials, cohort studies, meta-analyses, and systematic reviews were given preference throughout the selection process(20). In order to find additional relevant studies that were missed by the first database search, reference lists from published review papers were also reviewed. To find articles that were not easily found via database searches, subject-matter experts were engaged(21). No limitations were placed on the publishing type in order to broaden the span of the literature evaluated, guaranteeing the inclusion of journal articles, reviews, guidelines, and correspondence. Publications from every nation were taken into account, but only English-language articles were included in order to avoid mistakes brought on by poor translations(22).

3. Zeolite nanoparticles: types, synthesis and characterization

3.1. Types of zeolite-based nanoparticles

Zeolites' three-dimensional arrangement and porous characteristics describe their complex crystalline structure. With T denoting either a silicon or an aluminum atom, these aluminosilicates have a well-organized structure made up of tetrahedral units, or TO_4, with an oxygen atom serving as a bridge between them(23). Water retention and cation exchange activities are greatly aided by the vast cavities found inside the zeolite structure. Zeolites are often described by the generic chemical formula Ma/n [AlaSibO_2]. The qH_2O In this formula, n stands for the cation charge, while M stands for elements like Sr, Ba, Ca, Mg, Li, K, or Na. While the q/a ratio goes from 1 to 4, the b/a ratio fluctuates between 1 and 6. Figure 1 below shows a two-dimensional schematic illustration of the zeolite framework. Both naturally occurring and chemically manufactured zeolites are possible. In Fig. 2, their categorization is shown. Volcanogenic sedimentary rocks are the primary source of natural zeolites, whose existence has been well-documented. Among the most frequently occurring zeolites are laumontite, phillipsite, mordenite, chabazite, stilbite, analcime, and clinoptilolite(24). A broad range of geological formations include these zeolites. Some varieties, such paulingite, offerite, and barrerite, are uncommon, however. Table 1 lists a variety of naturally occurring zeolites and their chemical formulae(25).

3.2. Fundamentals of zeolite-based nanoparticles

Zeolites are the subject of more and more drug development research because of their surface-adjustable and porous characteristics, which may be used for regulated drug delivery(26). Zeolites-based nanoparticles have drawn a lot of interest lately as possible catalysts and medicinal delivery systems. Understanding their functions in great detail is necessary to realize their full potential in a variety of sectors. The salient features of nanoparticles based on zeolites are described in this section. By virtue of their distinct structural characteristics, zeolites provide an ideal basis for the production of nanoparticles(27). Their stability is guaranteed by their crystalline composition, and their porous structure allows for effective drug encapsulation and distribution. The efficiency of nanoparticles is maintained under various circumstances and aggregation is avoided by encasing them in zeolite structures(28). Zeolites may also produce nanoparticles with exceptional catalytic capabilities. Zeolite-

based nanoparticles have become more well-known in the medical community for drug administration in recent years because of their carefully controlled pore diameters, which enable selective catalysis. These materials' regulated pore structures have led to their long-standing application in the chemical and petrochemical industries(29). Zeolites' porous structure enables efficient loading of pharmaceuticals, guaranteeing regulated drug release that targets certain regions most in need of therapy. While reducing side effects, this focused strategy increases the effectiveness of therapeutic therapies(30). Notwithstanding their many benefits, zeolite-based nanoparticles have drawbacks, including scalability and synthesis control. It is essential to overcome these obstacles if they are to be widely used and commercialized(31).

a) The capacity of zeolites to exchange ions is widely recognized. This characteristic may be successfully used to water purification and environmental remediation when paired with nanoparticles. Zeolite-based nanoparticles may help remove pollutants and impurities by selectively exchanging ions with water.

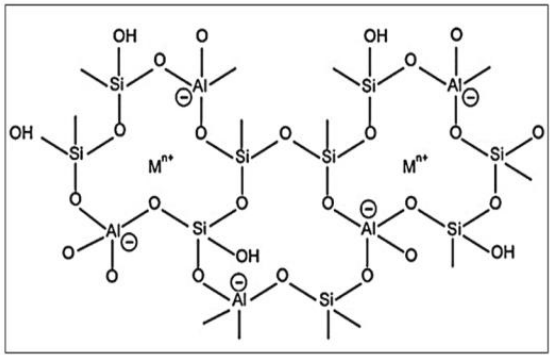
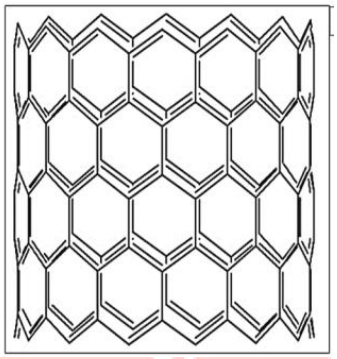


Figure 1 (a) Two-dimensional schematic representation of zeolite framework



(b) Zeolite Skeletal Arrangement.

b) In the domains of optics and electronics, zeolite-based nanoparticles exhibit unique properties. Adjustable electronic and optical characteristics result from the constricted gaps inside the zeolite matrix influencing the electronic structure of encapsulated components. These characteristics make them very promising for use in optoelectronic devices and sensors.

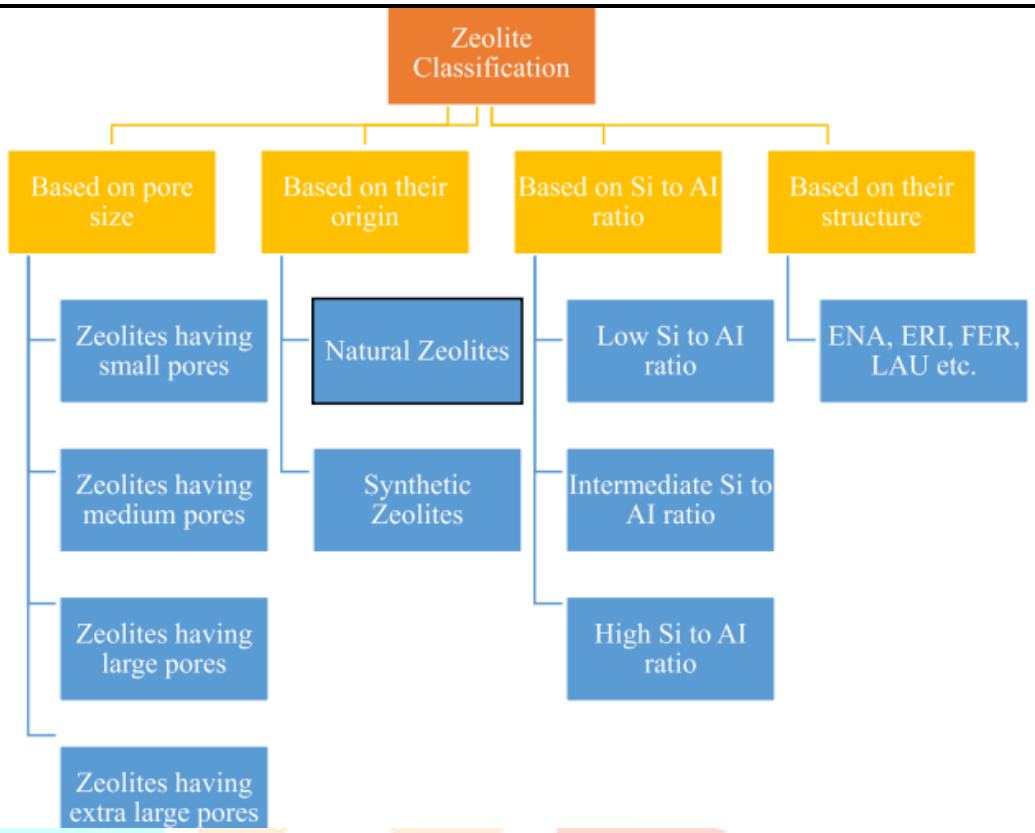


Figure 2 Classification of Zeolite based on different categories.

Table 1 List of some naturally found zeolites along with their chemical formula.

Some Naturally occurring zeolite	Chemical Formula
Clinoptilolite	(Na2,K2,Ca)3Al6Si30O72·21H2O
Chabazite	(Na2,K2,Ca,Mg)Al4Si8O24·12H2O
Analcime	Na16Al16Si32O96·16H2O
Ferrierite	[26 Mg]3Al6Si30O72·20H2O
Laumontite	Ca2Al8S16O48·16H2O
Scolecite	Ca4Al8Si12O40·12H2O
Heulandite	Al8Si28Ca4O68·24H2O
Phillipsite	(Ca,Na2,K2)3Al8Si10O32·12H2O
Mordenite	(Ca, Na2, K2)Al8Si40O96·28H2O
Stilbite	Na2Ca4Al10Si26O72·30H2O

3.3. Characteristics of zeolites

Zeolites are crystalline aluminosilicates with a variety of properties that make them indispensable for many commercial and scientific uses(32). On the basis of earlier studies, a thorough examination of these crucial characteristics has been assembled.

3.4. Methods for zeolite nanoparticle synthesis

3.4.1. Microwave and ultrasonic methods

Innovative zeolites may be synthesized using microwave and ultrasonic techniques, which allow regulated and effective procedures to speed up crystallization (Fig. 3). Ultrasonic-assisted synthesis helps dissolve precursors and encourages the nucleation of zeolite crystals, whereas microwave-assisted synthesis makes use of the unique heating characteristics of microwaves to ensure quick and even heating of the reaction mixture(33). For samples

with a high solid-to-liquid ratio, a number of research have shown how to synthesize zeolites from coal fly ash using microwave and ultrasonic-assisted microwave irradiation. In these investigations, the mass of coal fly ash is mixed with a volume of NaOH solution, with sonication added beforehand. Researchers have shown that zeolite formation is hampered by the combination of continuous microwave irradiation and the lack of traditional heating(34). Moreover, it has been shown that applying ultrasonic energy after hydrothermal treatment promotes the crystal development of zeolite nuclei.

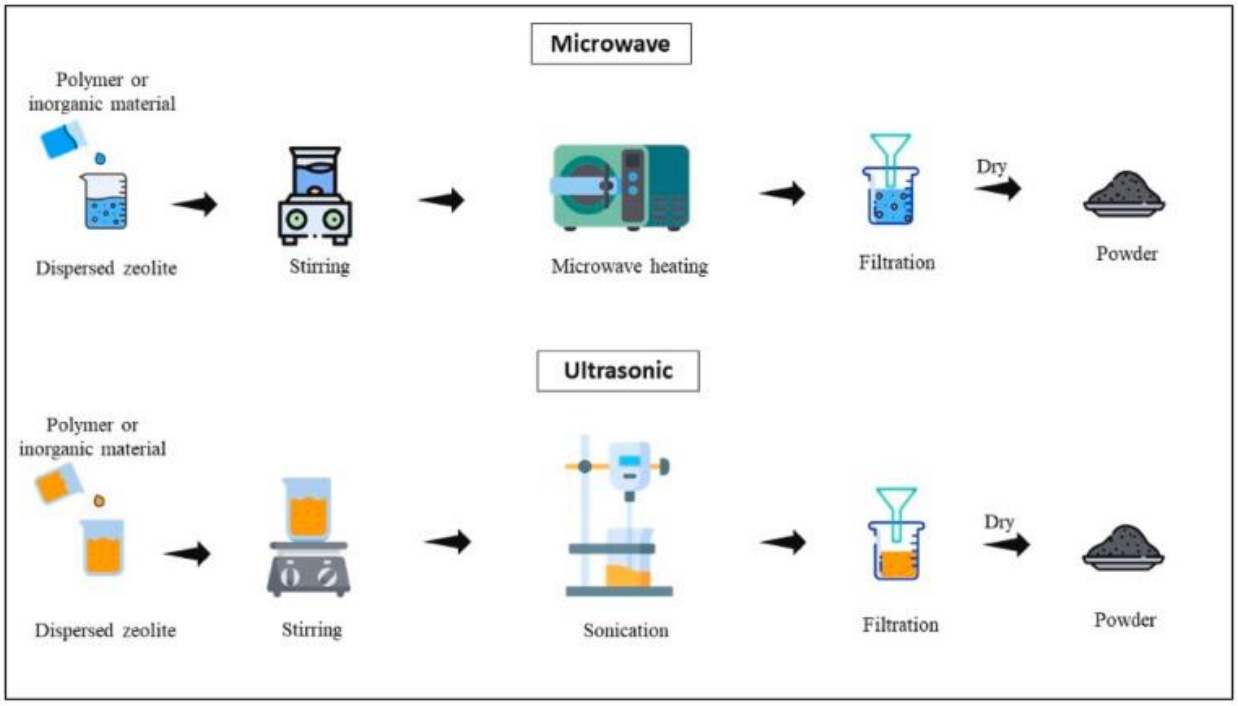


Figure 3 Preparation of Zeolite using Microwave and Ultrasonic Techniques.

3.4.2. Sol-gel and Co-precipitation methods

In the scientific community, sol-gel synthesis and co-precipitation are two well-known methods for creating zeolites, each with unique procedures and uses. Zeolite X particles were hydrothermally synthesized using alumina sol and the sol-gel technique (Fig. 4)(35). Alumina gel particles were found to aggregate close to micron-sized Zeolite X particles in a thorough microstructural analysis. Metal alkoxides, such as silica or alumina precursors, are hydrolyzed and condensed to start the sol-gel synthesis process(36). This process turns a solution into a gel, which solidifies to produce the required material. One benefit of this approach is that it makes it possible to produce many kinds of nanoparticles at once. Conversely, the co-precipitation method makes it easier for different substances to form from a solution at the same time(37). When silicon and aluminum source solutions are combined in zeolite synthesis, the pH level is a critical factor in starting the precipitation. To get the final zeolite structure, the resultant precipitate goes through a number of processes, including as aging, filtering, drying, and calcination(38). Microscopic study shows that while co-precipitation is a simple and economical method, it may provide somewhat less control over the end product's composition and crystallinity than sol-gel methods(39).

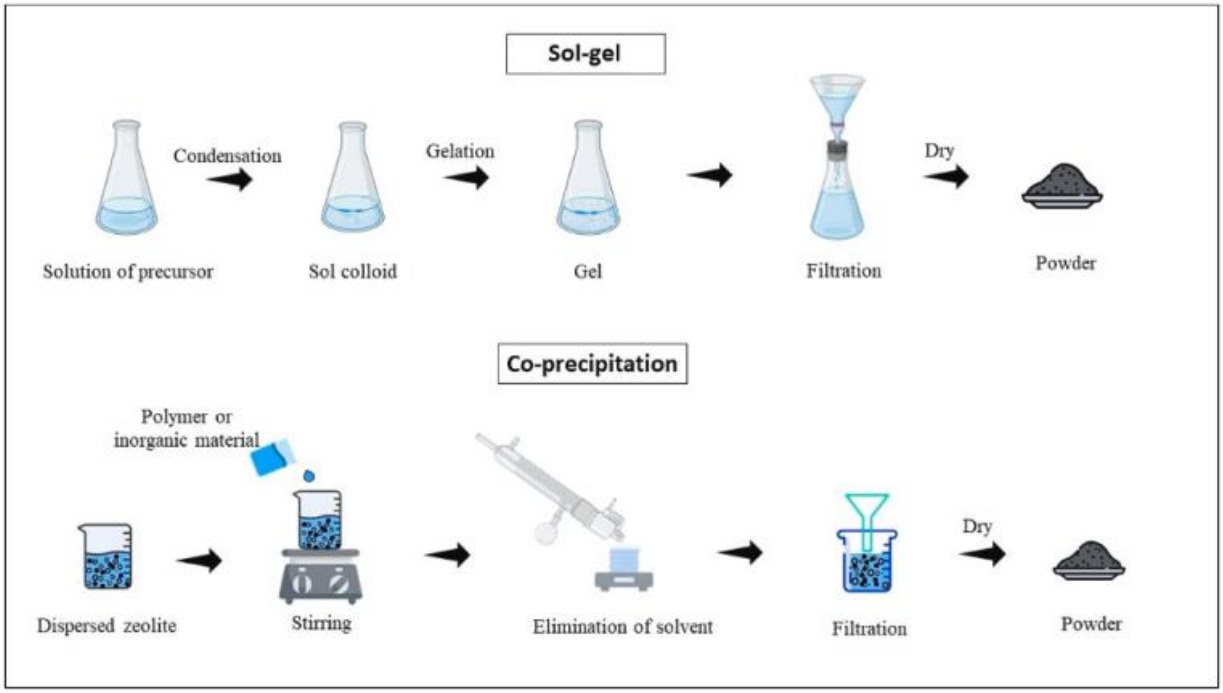


Figure 4 Preparation of Zeolite using Sol-Gel and Co-precipitation Techniques.

3.4.3. Hydrothermal and solvothermal methods

By mixing an aluminate mixture with a silica solution when organic bases and alkali hydroxides are present, the hydrothermal technique makes it easier for aluminosilicate gels to crystallize (Fig. 5). The type and pretreatment of precursors, temperature, pH, the mixture's reaction length, the amount of alumina and silica, and other parameters all have a substantial impact on the properties and synthesis of zeolites(40). Research on silica and alumina has shown that zinc-exchanged Zeolite A may be successfully synthesized by the hydrothermal technique, producing highly crystalline structures(41). Numerous studies have shown that the final crystal structure and the Si/Al ratio play a major role in the creation of various zeolite varieties. Solubilization methods have been used to passivate the surface of microporous zeolites in order to get over the usual diffusional restrictions(42). According to research, adding organic solvents helps regulate the formation of crystals. It has been shown that using single-component or mixed organic solvents, such as formamide, toluene, or a mixture of toluene and butanol, in place of a water-based crystallization medium inhibits aggregation and encourages the development of smaller (20–50 nm) and more evenly dispersed particles(43). This improves the structural consistency by increasing the dispersion of silanized zeolite seeds in the organic phase.

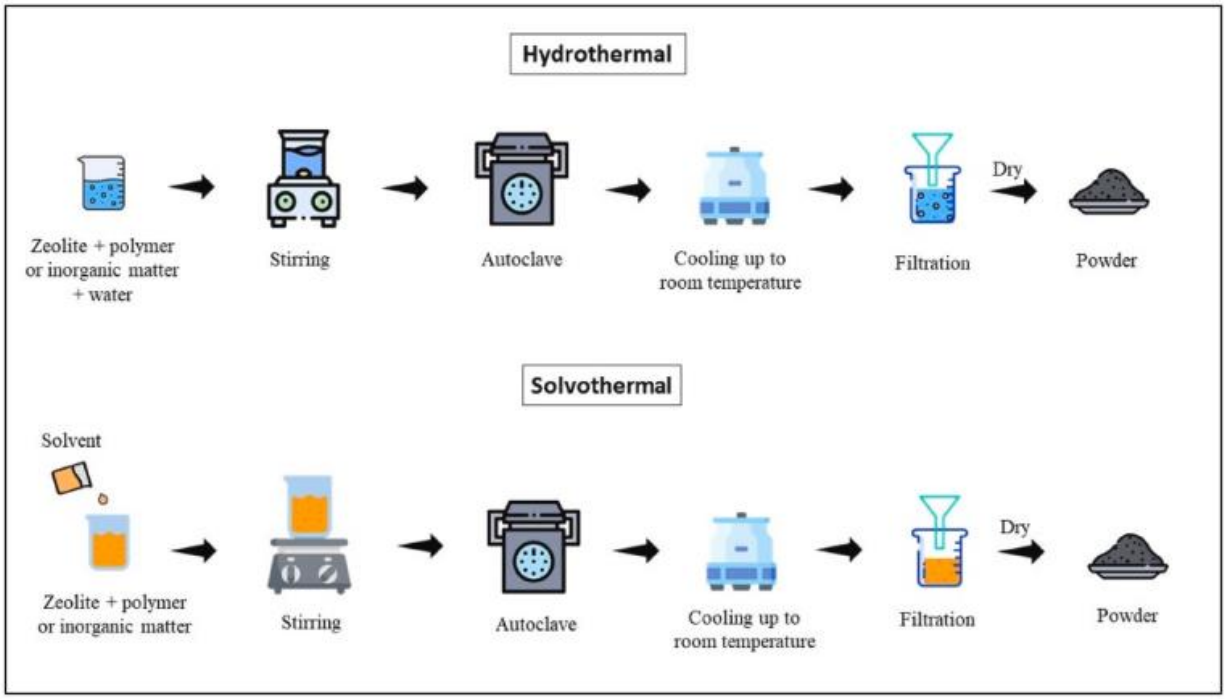


Figure 5 Preparation of Zeolite using Hydrothermal and Solvothermal Techniques.

3.5. Morphology and size control of zeolite nanoparticles

There is no denying the importance of zeolite morphology in influencing catalytic activity, selectivity, and stability; nonetheless, it is still difficult to provide accurate quantitative descriptors for these morphological effects. In order to shed light on the morphologies, structures, and chemical characteristics of zeolites, structural characterizations have been carried out. This has helped to clarify the complex link between zeolite structure and performance(44). By altering variables including temperature, alkalinity, pH, stirring rate, and reactant content, different organic template molecules have been used during synthesis to change the pore size and structure of zeolites(45). Reduced crystal size and a narrow particle size distribution have been associated with brief exposure of zeolite crystals to hydrothermal and microwave radiation. A single-step hydrothermal treatment was used in one research to create zeolite beta with a Si/Al ratio of around 18, which enabled the customized formation of either solitary nanocrystals or mesoporous aggregates(46). Zeolite beta nanocrystals with a diameter of 120–140 nm or 20–150 nm in mesoporous aggregates were the outcome of the size control that was accomplished. The produced samples' crystallinity was very similar to that of commercially available micron-sized zeolite beta, despite their diverse geometries(47). These samples had mesopore volumes of 0.4 to 0.5 cc/g and remarkable surface areas of over 600 m^2/g. A related research concentrated on controlling ZSM-5's morphology in connection to its diffusion characteristics. A total of thirty-five additives representing various functional groups and polarity were subjected to systematic testing(48). ZSM-5 with different morphologies, such as sheet-like, plate-like, and spherical structures of different sizes, were effectively created using this method. Notably, in C4 olefin cracking processes, the sheet-like shape showed excellent catalytic performance. All BEA-type silica crystals were prepared using a unique two-stage gel preparation method(49). While the second step regulated the amount of viable nuclei by pH adjustment and further aging in a basic solution, the first stage guaranteed the creation of stable nuclei at a neutral pH. This resulted in a narrow particle size distribution with crystal sizes ranging from 2 to 15 μm(50). Under simple circumstances, this novel synthesis method produced extremely hydrophobic BEA-type crystals with morphological variants ranging from well-developed truncated dipyramids to plate-like crystals. The complex interplay of shape, Si/Al ratio, and catalytic performance was investigated in the hydrothermal synthesis of ZSM-5 zeolite(51). A notable shift in the synthesis process was discovered by the kinetic investigation of crystallization at Si/Al ratios of 20 and 100. The gradual dissolution-recrystallization process gave way to a quick solid-state change when the Si/Al ratio rose, indicating how sensitive the zeolite morphology is to the circumstances of synthesis(52). The ensuing change in zeolite shape from clusters of small agglomerates to larger circular particles demonstrated the significant influence of the Si/Al ratio(53). A variety of H-ZSM-5 zeolites with different c-axis lengths and a constant sheet-like shape were synthesized in another work. Longer c-axis samples showed improved stability and catalytic activity, according to the results. To identify

the underlying processes, in-situ FTIR spectroscopy and time-resolved molecular dynamics simulations were used(54). As the intracrystalline dispersive behavior of olefins changed inside various channels of the zeolite structure, the findings demonstrated that anisotropy differences affected the catalytic performance(55).

3.6. Encapsulation and functionalization strategies

Zeolites are thought to be potential medication delivery vehicles because of their unique qualities. In one research, two different zeolite structures, Linde Type L and Faujasite, were combined with the anticancer medication 5-fluorouracil to create different drug delivery methods(56). Melanoma, breast cancer, and colorectal cancer cell lines were used in in vitro tests, while a chick embryo chorioallantoic membrane model was used in in vivo investigations. Notably, both experiments produced the best results for Hs578T breast cancer cells; however, 5-fluorouracil's efficiency was noticeably higher when it was encapsulated in Linde Type L zeolite(57). The results indicated that the uptake of zeolite nanoparticles was significantly influenced by the caveolin-mediated route. Faujasite and Linde Type L zeolites were used in another investigation on the potentiation of 5-fluorouracil. These zeolites effectively encapsulated the drug using sophisticated characterisation methods and hosted the drug with different particle sizes(58). The developed drug delivery devices significantly improved the impact of 5-fluorouracil on human colorectal cancer cell lines, HCT-15 and RKO, and in vitro drug release experiments showed fast release kinetics. With its effective zeolite-cell internalization and lack of toxicity to cancer cells, the zeolite-integrated drug delivery system provided a multidimensional boost to the effectiveness of traditional chemotherapy. The adsorption of isoniazid in Faujasite zeolite channels was investigated in a different research, with a focus on how pH affects the adsorption process(59). By illuminating the geometric configuration of drug molecules, saturation thresholds, and protonation states, molecular modeling studies provide a more profound comprehension of the drug-zeolite interaction. Drug release experiments highlighted the stability of the zeolite carrier and its possible use in antituberculosis therapy formulations, while the hybrid material, which was described at pH 3, proved to be an excellent isoniazid carrier(60). Another groundbreaking work addressed the problem of hypoxia resistance in solid tumors by examining the utilization of metal-containing nanosized zeolites as carriers for hypercapnic and hyperoxic gases in glioblastoma(61). The promise of the nanosized zeolite crystals in biomedical applications was further supported by their non-toxic profile in a variety of live species, such as mice, rats, and non-human primates.

3.7. Characterization techniques for zeolite-based nanoparticles

Zeolite nanoparticle characterisation is always changing, and new analytical methods have made major strides in recent years. These cutting-edge techniques have increased our knowledge of zeolite characteristics, opening up new possibilities for research and use(62). In order to maximize the performance of zeolite-based nanoparticles in drug delivery, adsorption, and catalysis, it is crucial to examine their structural characteristics, including surface area, pore size distribution, and crystal size(63). These nanoparticles have complex porous structures with clearly defined cavities and channels. Researchers can improve synthesis methods and increase the overall efficacy of these nanoparticles by conducting thorough structural analyses(64). The reactivity and functional characteristics of zeolite-based nanoparticles are largely determined by their surface chemistry. By identifying surface functional groups, spectroscopic methods like Fourier-transform infrared spectroscopy help designers create materials with specific catalytic or adsorption capabilities(65). Furthermore, the crystal structure is revealed by nuclear magnetic resonance and X-ray diffraction methods, which allow for the customisation of nanoparticle pore sizes and topologies for enhanced drug loading capabilities. Since the size and shape of nanoparticles have a major impact on cellular uptake and biodistribution, imaging technologies such as scanning electron microscopy and transmission electron microscopy offer important insights into particle size distribution, growth patterns, and morphology(66). These insights are crucial for customizing nanoparticles for drug delivery applications. When zeolite interacts with Fe3O4 nanoparticles, significant morphological changes have been seen, resulting in structural alterations. Additionally, studies on Fe-loaded ZSM-5 zeolite have shown the kinetics of nitrogen dioxide desorption and adsorption states using temperature-programmed desorption and infrared spectroscopy(67). These studies have revealed the formation of different adsorption species, such as nitrate, nitrosonium, nitrite, and dimerized nitrogen dioxide. Designing effective drug delivery systems requires a deep comprehension of the structural, morphological, and physicochemical properties of zeolite nanoparticles. This ensures better biocompatibility, controlled drug release, and increased encapsulation efficiency(68).

4. Applications of zeolite-based nanoparticles in drug delivery and biomedical applications

4.1. Controlled release mechanisms

Innovative drug delivery techniques, especially genetic drug delivery, have been developed at a fast pace by biotechnology and biomedical research. Numerous studies have shown that liposomes, carriers based on polymers, and particular micro- and mesoporous nanoparticles made of inorganic materials like zeolites have drawn a lot of interest because of their potential for controlled drug release(69). Numerous zeolites have been effectively used as drug transporters, including FAU, MFI, BEA, and CLI. Pore size, surface area, Si/Al ratio, and the hydrophobicity difference between the drug and the carrier are some of the variables that affect how well drugs are loaded and encapsulated inside various zeolite structures(70). The encapsulation process is endothermic, according to thermodynamic evaluations, guaranteeing that the medication release from zeolite nanoparticles stays within the dietary ranges that are advised for human consumption.

Because of their long-term stability and non-biodegradable character, natural zeolites provide sustained medication or nutrition delivery to specific areas. To better understand its drug release characteristics, methylpyridinium chloride, a cationic surfactant, has been added to chabazite, a naturally occurring zeolite and tectosilicate mineral that is closely linked to geminate. The diffusion coefficients of both the film and the particles were shown to be the main elements influencing drug release, while the distribution coefficient and film thickness were important factors in film diffusion. Particle diffusion was also strongly affected by ion exchange diffusivity. Clinoptilolite, another naturally occurring zeolite, was used as a porous matrix for the regulated release of vitamins A, D, and E in an oral drug delivery system(71). These zeolites have buffering qualities that help vitamins stay stable in acidic conditions and prolong their shelf life. Additionally, they increase the bioactivity of fat-soluble vitamins by shielding them from stomach acid. A modified clinoptilolite was encapsulated with diclofenac sodium and treated with cetylpyridinium chloride in order to examine the drug release behavior. Drug adhesion followed a pseudo-second-order process and was impacted by boundary layer diffusion. A prolonged release effect was achieved by modulating the drug release profile via the use of anionic exchange processes. Because of their altered release mechanisms and sensitivity to stimuli like pH shifts and electromagnetic fields, synthetic zeolites have shown to be superior to their natural counterparts. A research examined the impact of an electric field on the diffusion rate while creating a microporous zeolite Y alginate hydrogel for folic acid encapsulation. Results indicated that folic acid and zeolite's interaction was stronger as the aluminum level rose, limiting medication release—a phenomenon referred to as the "aluminum content effect." Furthermore, "anode folic acid electrorepulsion"—the electro-repulsive force between folic acid and a positively charged electrode in an electric field—was noted(72). Electrical conductivity improved when the Si/Al ratio in zeolite FAY rose, improving the mobility and diffusion of folic acid when electrical stimulation was applied. Drug release was also affected by crosslinker concentration; a larger crosslinker content resulted in a more sustained release via decreasing pore size. To aid in the release of enalapril maleate, zeolite L was created utilizing polyvinyl alcohol and pullulan cryogens. While the inclusion of zeolite-L nanoparticles reduced moisture absorption by the cryogen, resulting in structural alterations that improved drug release qualities, the porous nature of zeolite increased drug loading efficiency(73). This system operated according to the Korsmeyer-Peppas release model, in which the release of enalapril maleate was regulated by diffusion processes. Additional research investigated the use of Type A zeolites in conjunction with hydrogels based on natural polysaccharides for wound dressing applications, showing long-lasting therapeutic benefits. Since oxygen transmission is essential for wound healing, the addition of zeolites and other inorganic porous materials helped preserve it. Zeolite A-infused hydrogels were created using a membrane diffusion technique, and they demonstrated the capacity to release medications steadily, with an 86% release in only five hours(74). As porous drug delivery vehicles, zeolite A nanoparticles

increased hydrogel stability by promoting swelling characteristics while preserving oxygen transport rates. The bactericidal activity of zeolite type A was also examined. The antibacterial and wound-healing properties of a nitrous oxide-enriched version of zeolite A were assessed against both gram-positive and gram-negative bacteria. When nano-zeolite was added to a hydrophobic ointment basis, the water diffusion properties were diminished and the nitrous oxide release rate changed. This accelerated the healing process in the damaged region by slowing the adsorption and diffusion of exogenous chemicals via the porous network. Additionally, the inclusion of zeolite enhanced the therapeutic efficacy of stabilized ointment by controlling its release into the wound(75).

4.2. Theranostic applications of zeolite nanoparticles in cancer

Because zeolites are porous inorganic materials that may be loaded with a variety of medications, photosensitizers, fluorescent dyes, radioactive tracers, gas bubbles, and enzymes, they make intriguing theranostic platforms(76). In many applications, their capacity to encapsulate drugs and imaging agents has been widely recognized. Furthermore, studies carried out recently have validated their effective use for therapeutic objectives. A metal-organic framework (MOF), a hybrid structure that combines organic and inorganic materials, has gained popularity lately in biological applications(77). The zeolite imidazole framework is a well-known MOF that has been investigated for cancer theranostics. It is composed of imidazole or its derivatives and transition metal ions. In contrast to natural zeolites, ZIFs have a structural variant in which oxygen atoms are replaced by imidazolate anions, giving them the benefits of both MOFs and zeolites at the same time(78). These advantages include increased loading capacity, high porosity, and a large surface area because of the exposed edges of organic linkers. While retaining their chemical and thermal stability in alkaline or organic solvents, ZIFs can also be functionalized by adding active molecules or altering ligands. Other structural features of ZIFs increase their potential for use in medicine(79). Because of the moderate strength of their conjunctive bonds, they are stable in physiological conditions, but they break down slowly in environments that are slightly acidic. Because of the high affinity between ATP and Zn2+, certain ZIFs, including ZIF-90, degrade in response to subcellular adenosine triphosphate, allowing for the regulated release of drugs and therapeutic molecules at tumor locations. Additionally, the presence of imidazolate and Zn2+ groups, which are found naturally in biological systems, improves their biocompatibility. These characteristics have led to extensive research into ZIFs for drug administration, gas absorption, detection, and catalysis, especially in biological applications including biosensing, tumor imaging, and therapy(80). Iron oxide nanoparticles have been found to be an efficient contrast agent for MRI diagnostics when incorporated into porous zeolite nanocores. In addition to targeted medication delivery, zeolites have shown promise in the treatment of cancer by producing localized heat via magnetic hyperthermia, a phenomenon in which magnetic nanoparticles are subjected to an alternating magnetic field. T2-weighted MRI contrast is improved by zeolites' enhanced capacity to capture magnetic nanoparticles due to their porous nature. In one work, ferrous and ferric salts were mixed with NaY zeolite in a single pot to create a magnetic zeolite nanocomposite(81). Characterization demonstrated its effective deposition in breast cancer cells, and at high concentrations, it displayed non-toxic behavior. At a clinical field strength of 3T, the nanocomposite's efficacy as an MRI imaging probe was confirmed in vitro, resulting in a better dark contrast than control cells. Zeolite nanoparticles have also proven to be efficient carriers for delivering chemotherapeutic agents such as doxorubicin and paclitaxel to tumor sites. A research developed a ZSM-5 zeolite and chitosan core-shell nanodisk packed with doxorubicin for osteosarcoma therapy(82). The nanodisks were constructed with a 100 nm thickness and a 300 nm diameter, containing mesoporous architectures with 3.75 nm pore diameters. This pH-responsive nanoformulation revealed a high drug loading capacity of 97.7% and followed a regulated release profile that corresponded with the Korsmeyer-Peppas model. Pharmacokinetic assessments, serological tests, and histological examinations verified the effective release of doxorubicin from the ZSM-5/chitosan nanoformulation via cellular endocytosis, resulting to death in cancer cells. The pH-responsive technique provided excellent tumor suppression while reducing side effects, including cardiac toxicity(83). For cancer theranostics, multi-modal optical imaging in the second near-infrared window offers a sophisticated and accurate platform. Using zeolite-carbon-based nanozymes, which were first investigated as dual-modal near-infrared II photoacoustic and fluorescence imaging nanotheranostics, researchers have created a photothermal and catalytic synergistic therapy(84). Through carbon doping within its framework, the electrical structure of zeolite nano-Beta, which consists of a high surface area, three-dimensional, 12-ring pore system, may be changed from an indirect to a direct band gap. By taking use of ionic liquids' adsorption capacity, this change increases the emission of near-

infrared fluorescence(85). Analysis using transmission electron microscopy shows that cellular absorption is a major factor in this nanotheranostic tool's efficacy. During a six-hour incubation period with 4T1 cancer cells, studies demonstrated that these nanozymes were effectively absorbed by cells and that their structural integrity was maintained after cellular absorption.

4.3. Enhanced drug stability and bioavailability

Zeolites are aluminosilicate-based microporous crystals made up of a constantly growing three-dimensional network of AlO4 and SiO4 tetrahedra connected by common oxygen atoms to create an ordered system of channels(86). Drug molecules are stored in these pores and channels. Incorporating medications within a zeolite structure has been shown in several trials to improve their stability and bioavailability. Microporous faujasite zeolite has been shown by researchers to be very useful for encapsulating medications with low water solubility. To achieve this, the incipient wetness approach was used to introduce danazol into NaX-FAU. Drug loading was evaluated by thermogravimetric analysis and UV spectroscopy, which confirmed a 33.3% w/w drug loading efficiency(87). XRD and thermometry were used to assess the drug's crystallinity, which revealed that it was highly crystalline while preserving the original structure of the zeolite. Nitrogen sorption techniques used for texture examination verified that microporosity was maintained even after the wetness procedure. The stability of the formulation was maintained for six months by drug encapsulation inside zeolites, according to stability tests conducted under accelerated settings. When tested in simulated intestinal and stomach fluids, the dissolving profile of zeolite-encapsulated danazol revealed enhanced solubility in a variety of environments. An everted gut sac model used in ex vivo studies showed enhanced drug diffusion across intestinal membranes.

Zeolites were used to create a specific nano complex for vitamin encapsulation. Within the zeolite structure, the stability and regulated release of vitamins were investigated. A saturated solution including vitamins A, D3, and E was used to submerge natural powdered zeolite(88). For varying lengths of time—from two hours to four weeks—the samples were kept at room temperature. While the vitamin levels in the zeolite-containing samples were constant over time, the vitamin content in the control samples without zeolite declined(89). The size of zeolite particles, which ranged from 710 to 850 μm, improved vitamin retention in the surrounding environment. In simulated gastrointestinal circumstances, the zeolite-based samples showed greater release rates than the control. The usefulness of several zeolite types, including as BEA, ZSM, and NaX, for use in drug delivery systems based on nanomaterials was examined in further detail. The effectiveness of encapsulating indomethacin in zeolite nanoparticles was investigated(90). BEA and NaX showed excellent drug loading capacities and strong drug amorphization. The results of stress testing showed that the drug's loading capacity and characteristics remained the same. It was discovered that the aluminosilicate ratio and the crystallinity of drug particles affected the drug release profile in simulated gastric and intestinal fluids under both fed and fasted settings. Effective drug retention at the intended location without any harmful effects was established by cytotoxicity evaluations, such as MTT and flow cytometry tests(91). Research on curcumin's absorption characteristics in zeolite type 5A showed that a steady and consistent drug delivery mechanism was made possible by the pore structure of the material, which measures around 5 Å, in conjunction with Ca2+ cations present in the matrix. Increasing the curcumin content in the initial incubation solution improved drug-loading efficiency, according to UV-visible spectroscopy. Curcumin's incorporation into the zeolite pores was validated by DSC and XRD analyses, which also showed that the curcumin molecules and the zeolite had robust interactions(92). Hydrogen bonding was shown to be the main interaction mechanism promoting curcumin encapsulation by FTIR analysis. After loading, structural integrity was maintained, as shown by XRD and SEM tests. Another research investigated how laying hens' transporter gene expression, tissue accumulation, and zinc absorption were affected by the zinc-bearing zeolite clinoptilolite (ZnCP). Three dietary groups of laying hens were given various zinc sources over an eight-week trial: 0.46% ZnCP (80.50 mg Zn/kg diet), 0.23% ZnCP (40.25 mg Zn/kg diet), and Zn sulfate (80 mg Zn/kg diet, control). Zinc levels in the tissues of hens given 0.23% ZnCP were similar to those of the control group. Zinc buildup in the pancreatic and liver increased with a larger ZnCP inclusion of 0.46%. ZnCP incorporation was also associated with higher blood iron levels(93). Hens fed with ZnCP showed a substantial increase in jejunal metallothionein-4 (MT-4) mRNA expression. Additionally, higher ZnCP levels (0.46%) increased the expression of MT-4 in the pancreas and zinc transporter-1 (ZnT-1) in the jejunum. Additionally, the jejunum of chickens fed a meal containing 0.23% ZnCP had the greatest concentration of ZnT-2 mRNA. The results showed

that ZnCP was more bioavailable than Zn sulfate, as seen by higher expression of zinc transporter genes and improved tissue zinc accumulation(94).

4.4. Targeting ligands for specific cell interaction

To achieve successful therapy, various researchers have studied tailored nanoparticle-based drug delivery methods. Instability, insufficient drug release, and poor transport across biological barriers are the main problems with conventional therapy. Enhancing targeting effectiveness and dosage form stability has recently drawn a lot of attention from researchers(95). This has led to the introduction of a number of novel ligands and probes. Surface molecular imprinting technique, which entails attaching a substrate to a molecularly imprinted polymer, is a notable development in this area. The precise targeting of tumor cells is made easier by molecularly imprinted polymers that carry epitopes of proteins that are overexpressed in tumor settings. This strategy is appealing for targeted medication administration as it doesn't change the core nanoparticles' drug release profile.

The creation of fluorescent zeolitic imidazolate framework nanoparticles with doxorubicin at their center and a molecularly imprinted polymer coating to produce tumor-sensitive biodegradable nanoparticles is a new advancement in this sector. These nanoparticles showed significant growth inhibition in the tumor environment and efficient absorption by tumor cells. The creation of zeolite nanoparticles especially for laser-polarized NMR investigations is another advancement in this sector(96). PEG chains were added for in vivo studies, and peptides were attached onto these nanoparticles to guarantee effective biological targeting. By using sophisticated synthesis techniques, these nanoparticles were functionalized while maintaining the accessibility of noble gases within the micropores(97). Initial evidence for their potential in MRI applications came from scintigraphy research using radiolabeled nanoparticles to track their distribution in mice.

In radionuclide applications, one of the key hurdles is successfully binding bifunctional ligands. Nanotechnology solutions for the delivery of medicinal and diagnostic substances are currently being developed by researchers. It has been shown that negatively charged zeolite particles at the nanoscale may bond with positively charged gamma emitters(98). Improvements in receptor-specific chemicals, made possible by the shrinking of zeolite particles from the micro to the nanometer size, may have an impact on the future of targeted treatment based on nanoparticles. A peptide intended to target certain cell receptors in glioma cells was used to synthesis the sodium form of type A zeolite in a recent research. The nanozeolite's significant negative surface charge, which persists even after peptide conjugation, is a result of its high aluminum concentration(99). Because of their very negative zeta potential, the resultant nanoparticles were unable to aggregate. The produced system demonstrated potent cytotoxic effects and effectively bound to tumor cell receptors. The nanozeolite structure successfully held the radioactive material without leaking, according to radiometric measurements.

5. Toxicity and safety considerations

5.1. Biocompatibility and toxicity studies

Because of their high drug loading capacity and inherent biodegradability, ZIFs have drawn a lot of interest as pH-sensitive drug carriers. Modifying ZIFs with polydopamine (PDA) significantly improves their biocompatibility and helps control their rate of disintegration(100). Aside from the versatility of their micro-nano hierarchical structure, MOFs' natural degradation is a significant benefit in biological applications. MOFs are naturally biodegradable because to their coordinated metal ions and ligands. Nonetheless, there are benefits and drawbacks to this trait. The good news is that MOFs can be totally removed from the body via a regulated breakdown mechanism, which prevents them from building up in healthy organs(101). The drawback of MOFs is that they frequently break down too quickly for in vivo use, which may have serious negative consequences such cell death, anomalies in important organs, and even death in animal models.

One possible pH-sensitive drug delivery system for anticancer medications is the ZIF subclass of MOFs. Although it is stable under physiological settings, acidic environments cause it to degrade. In order to guarantee appropriate breakdown at the ideal pace and make it easier to remove nanocarriers when drug delivery is finished,

it is thus extremely desired to have precise control over MOF degradation and drug release. Changing these materials' surfaces is essential for reducing deterioration and enhancing biocompatibility(102). Heat-facilitated diffusion frequently facilitates drug release in the NIR-responsive drug-controlled release system. It has been shown that using PDA improves ZIFs' biodegradability and biosafety, enabling in vivo research.

Antimicrobial peptides (AMPs), also known as host defense peptides, are vital elements of many immune systems. Broad-spectrum toxicity against viruses, bacteria, fungi, and cancer cells has been shown for a number of AMPs. In contrast to traditional chemotherapy medications, AMPs derived from insects show targeted cytotoxicity against tumor cells while causing no harm to healthy human cells. These qualities help to increase the therapeutic results of cancer therapy. It has been discovered that Cecropins (CECs), a particular class of broad-spectrum antimicrobial peptides, inhibit the growth of cancer cells both in vitro and in vivo. One study used ZIF-8 nanoparticles to encapsulate CECs, which are generally not very bioavailable(103). The intracellular accumulation and cytotoxic activity of these peptides in cervical cancer cells were both markedly increased by this encapsulation.

Some zeolites have cytotoxic and carcinogenic properties despite their potential for use in medicine. Erionite is a fibrous zeolite that resembles asbestos in that it has a brittle, wool-like texture. Malignant mesothelioma and lung cancer have been related to exposure to this material. Surface area, pore size, surface charge, functional groups, and crystallinity are some of the structural features that affect these porous materials' biosafety(104). Because of its capacity to cause oxidative stress, upset the cytoplasmic calcium balance, cause callose synthesis, and impede root development, aluminum is a serious worry when it comes to the toxicity of zeolites in plants. High silicon-to-aluminum ratio zeolites are typically less hazardous. Dealumination is thought to be a useful technique for lowering the toxicity of synthetic zeolites by reducing their aluminum content.

The production of reactive oxygen species, which can increase toxicity, is largely influenced by surface reactivity. Research on zeolites' surface reactivity has shown how it affects the generation of hydroxyl radicals(105). Coating zeolite surfaces may improve their biocompatibility and lessen this problem. The morphology of zeolite particles also affects their interactions with biological systems. Selecting specific shapes, such as spherical or rod-like structures, has been shown to reduce toxicity. Additionally, surface modifications using various polymers can stabilize surface reactivity without significantly altering porosity, further improving their safety profile.

5.2. Toxicity and risk assessment of different zeolites used in drug delivery

Nanoparticles' reduced size may make them more dangerous or change the ways in which they cause toxicity. Toxicological data on one kind of nanoparticle cannot always be immediately applicable to another since naturally occurring nanoparticles and artificial nanoparticles vary in size, composition, and surface characteristics(106). Because of their size- and shape-dependent properties, which affect how they interact with biological systems, nanomaterial toxicity is a complicated subject to examine. The degree and methods of toxicity that silica-based nanoparticles cause in cells may be altered by functionalizing them. Important information has been gleaned from studies on the toxicity of crystalline silica, especially quartz and industrially significant zeolites.

Studies on the naturally occurring zeolite clinoptilolite indicate that it is typically harmless for both people and animals. Other research, however, suggests that breathing in crystalline silica particles of a respirable size may be dangerous and result in diseases like silicosis. It has been shown that both erionite and mordenite may induce mesothelioma and fibrosis in mice lungs, however erionite's effects are more noticeable(107). Erionite's thin, fibrous structure is thought to be the cause of its different toxicity from mordenite, which has a mixture of fibrous and granular particles.

The impact of crystal form is a feature that is often investigated in zeolite toxicity investigations. The shape of various forms of zeolite crystals is determined by their structure. The form of zeolite crystals may sometimes be controlled by altering the synthesis conditions(108). Results indicate that varying degrees of cytotoxicity are shown by fibrous and nonfibrous dust particles with comparable chemical contents. Fibrous erionite showed a much greater rate of superoxide species production than nonfibrous mordenite. These investigations highlight the

need of comprehensive material characterisation since toxicity is controlled by a number of parameters, including particle size, porosity, shape, surface area, functionalization, and surface treatment.

6. Potential areas of growth and research

Because of their unique structural features and better physicochemical qualities than other mesoporous nanomaterials, zeolite nanoparticles (NPs) have improved biocompatibility and optimal biomolecular transport capacities. They have better intracellular targeting effectiveness, more drug-loading capacity, and less cytotoxicity(109). These nanoparticles are essential for a number of biological uses, such as MRI contrast imaging and the usage of antibiotic, anticancer, and antidiarrheal medicines. They have also been investigated in research on hemodialysis treatments, drug delivery systems, dental applications, bone regeneration, and the evolution of Alzheimer's disease.

Since nanosized porous materials have shown to be good contrast agents, zeolites offer a great deal of promise to improve the quality of MRI imaging. They may bond with water molecules due to their high-spin metal content, which speeds up proton spin relaxation periods(110). Zeolites also modulate the immune system and have potential as adjuvants in cancer treatment. Additionally, giving activated TMA-zeolite to cancer patients and diabetics has been associated with a decrease in oxidative stress, which enhances general health.

Given the evolutionary nature of bacterial resistance to traditional organic antibiotics, medical researchers are always looking for new ways to counteract the emergence of multidrug-resistant microorganisms(111). Because of their high surface area-to-volume ratio and low toxicity, nanoscale solid materials have emerged as powerful antibacterial agents among these solutions. Using a transgenic mouse model of Alzheimer's disease (AD), research has shown that micronized zeolite (MZ) has antioxidant qualities that help slow down age-related neurodegeneration. Long-term MZ therapy was well tolerated; there were no side effects or indications of toxicity. Interestingly, MZ dramatically decreased Aβ42 levels in treated animals, which seemed to decrease amyloidogenic processing of Aβ.

Zeolite nanoparticles have been used in the creation of biosensors and diagnostic instruments for AD in addition to their therapeutic uses. Nanoscale zeolites have a much greater external surface area than their micron-sized counterparts, which makes them ideal for a variety of drug delivery applications(112). Additionally, adding targeting ligands to theranostic zeolite nanocarriers offers a particularly promising strategy for precision-based cancer treatments.

7. Conclusion

In modern therapies, the development of regulated and targeted drug delivery using novel functional systems is essential. Zeolites and other microporous and mesoporous inorganic materials have attracted a lot of attention from researchers because of their unique structural features, biocompatibility, vast surface areas, and modifiable physicochemical qualities. Metal-organic frameworks (MOFs) combine the benefits of inorganic and organic drug delivery by integrating both large and tiny pores, allowing for effective drug loading and prolonged release over time. Because they are porous, zeolites are great transporters for medications, allowing for more precise and efficient drug delivery. Zeolite nanoparticles (NPs) have been produced using a variety of synthetic methods, demonstrating their promise for theranostic and biological applications. Characterizing these nanoparticles' structural characteristics, such as surface area, pore size distribution, and crystal size, is crucial because of their complex porous architectures with accurately defined cavities and channels. To maximize their effectiveness in medication administration, adsorption, and catalytic applications, this characterisation is essential. Their possible toxicity is still a major worry despite their extensive usage in areas including MRI contrast imaging, antimicrobial

applications, anticancer and antidiarrheal therapies, and more. Surface changes that improve biocompatibility, however, may help overcome this difficulty. Zeolites' functions in medication delivery systems, dental applications, Alzheimer's disease research, and bone regeneration are also the subject of much investigation. An overview of clinical studies using zeolite-based nanoparticles is given in this paper. Even though these materials have many benefits, their wider commercialization will require overcoming obstacles including large-scale manufacturing and accurate synthesis control.

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