Application of Zn-MOFs in Treating Cancer

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Abstract. Metal-organic frameworks (MOFs) are extremely porous crystals belonging to metallic complexes, made up of metal ions or clusters and organic ligands via coordinative bonding. The construction of tailored MOFs has attracted increasing interest over the past few decades. Particularly, a variety of applications for the delivery of drugs using MOFs are being investigated. MOFs were initially employed to deliver small-molecule medications. In this article, the construction of electrochemical (EC) biosensors based on MOFs that are directed toward certain analytes are mainly introduced. The classification of MOFs for drug-delivery systems (DDSs) based on the types of constitutes is presented in this article as an overview and point of view of MOF-based DDSs, among which, Zn-based MOFs are one of the best choices to be used in cancer treatment. This article demonstrates the advantages of Zn-based MOFs in cancer treatment compared to their counterparts.

Keywords: Metal-organic frameworks; nanoscale; Zn(II); cancer.

1. Introduction

The essence of MOFs is porous coordination polymer [1]. This kind of complex combines the characteristics of organic and inorganic. Organic allows biocompatibility, and inorganic enables the adsorption and desorption of drugs. In this case, one of the most important applications of MOFs is drug carriers in medical treatment, such as treating cancer. Among various MOFs, Zn-based MOFs are suitable to be used in drug delivery [2], as Zn(II) is not only non-toxic but also supports nanoscale structures which benefits the efficiency of drug delivery.

The key to lowering mortality rates and raising survival rates is early cancer diagnosis [3]. Therefore, it is crucial to create methods that are reliable, sensitive, quick, and efficient for finding cancer biomarkers or alive cancer cells. In this case, an efficient biosensor is essential in cancer treatment. Because MOFs provide ideal settings for anchoring biorecognition molecules, they are excellent options for building electrochemical(EC) sensors. Ultrahigh sensitivity or ultralow limit of detection are also reasons for choosing MOFs.

In this article, the reason why Zn-based MOFs deserve to be thought highly of when beating tumours has been explained. Advantages are discussed, and improving methods are given.

2. Advantages of Zn-MOFs in Drug Delivery

2.1. Nanoscale Drug Carriers

A new class of porous crystal material known as a MOF can be created by a method by which discrete elements spontaneously interact close to one another to form an organised structure, that is to say, organic ligands and inorganic metal ions combine via coordination bonds. Prepared MOFs display several promising properties, such as an adjustable structure, a large surface area, variable pore size, a variety of metal centres and ligands, and ease of functionalization, which has led to their widespread use in drug delivery, especially as a nanoscale drug carrier [2]. Zn(II) is a good choice to act as metal ions of MOF carriers because it is not poisonous [2]. An alternate technique is one-pot drug encapsulation. Both techniques involve putting the manufactured MOF nanocarriers into solutions that contain drugs.

Numerous nanocarriers have proven to be quite effective at stabilising compounds that are soluble and labile [3]. Solid lipid nanoparticles, MOFs, micelles, and mesoporous silica nanoparticles are some of these nanocarriers. The creation of nanoscale MOFs, which have a lot of potential for biological applications, has been made easier by the coupling of nanotechnology and MOFs [3,4]. Due to their distinctive qualities in comparison to other nanocarriers, nanoscale MOFs have generated a great deal of interest. With good loading efficiency, their high porosity enables the encapsulation of pharmaceuticals of various sizes [3].

Drugs encapsulated in nanoscale coordination polymers can also be released in four different ways: The four processes are desorption, degradation, diffusion, erosion, and so forth. In some cases, a single drug delivery system may experience multiple drug release mechanisms, but for a brief period [4].

Nanocarriers are much more efficient than their bulk coordination counterparts. Improving the medication release rate is essential in practice because a therapeutic amount rarely lingers in the human body for several days before it breaks down and then eliminates. The majority of the time, a period between a few hours and 24 hours is more suitable for controlling drug release in vivo [4].

A promising method for creating MOFs with a controlled size distribution is the template technique [5]. By changing the system's components, it was simple to regulate the size and shape of nanoscale templates.

2.2. Solubility and Stability in the Aqueous Phase

The environment in the human body is aqueous, thus drug carriers need to remain stable in blood and fluids, and be able to release the drug at certain organisms. Typically, bulk coordination complexes are harder to meet the condition. Chemotherapy is a crucial component of cancer treatment [4]. However, there are several issues with conventional chemotherapy, including limited bioavailability, unanticipated side effects from medication distribution, and the development of chemoresistance. To address these problems, multifunctional nanoplatforms for anticancer drug delivery have been developed. Targeted drug delivery systems can increase the effectiveness of a treatment by increasing pharmaceutical bioavailability while minimising side effects in normal cells [4].

The blood must be kept at a high initial particle size to provide extended circulation times [5]. To promote deep penetration, this particle must later be divided into smaller particles. To achieve this goal by surface alteration, there are two fundamental groups of techniques: responsive surface transformation size changes brought on by surface modification mediated by and the release of smaller particles [6]. MOFs have chemically reactive locations within their pores, which extends their potential performance in certain applications, unlike most porous materials. These MOF-based materials are useful for medication delivery since the size of these pores may be adjusted for each application[6].

3. Zn-MOFs in Targeted Cancer Treatment

3.1. MOFs as electrochemical biosensors

Nanoscale MOF-based EC biosensors are practical analytical instruments for the early detection of malignancies [3] due to their superior probe loading capacity and resistance to probe degradation. The detection selectivity of biosensors can be considerably increased by these characteristics. MOFs-based EC biosensors are capable of sensitively detecting several targets.

By connecting organic linkers to metal-based nodes, MOFs are created. Comparing typical inorganic porous materials to MOFs offers several benefits. More crucially, by altering environmental parameters like pH value, it is possible to prevent the breakdown of porous MOF exoskeletons and move them closer to biological preservation and medication delivery [4].

Nanoscale MOFs are a kind of essential materials owing to their adaptability, biocompatibility and porosity. According to previous research [4], increasing the concentration of the medication in the cellular compartment where it can exert its effects utilising MOFs will boost drug specificity and subcellular targeting. Research on nano-MOFs is now being done to use cellular assemblies for targeted delivery [4,5,6].

The coupled pore structures and the surface of MOFs can also be exploited to generate an efficient mass transfer, which is the second aspect. Because of their porosity, MOFs can be used with other functional materials together to improve sensing properties. Consequently, the distinctive MOF structures with superior EC biosensing capabilities for cancer diagnosis. However, immaculate MOFs encounter unheard-of difficulties such as poor electron conductivity, pricey ligands, huge particle size, and instability, which limits their capacity to be used in EC biosensors.

It is impossible to overestimate the value of MOF sensors. In addition to detecting cancer indicators, MOF-based EC biosensors, MOF-based composites, or heterostructures of several MOFs can recognise cells suffering pathological changes. The linked materials have good cell endocytosis, strong sensing potential, and outstanding cell imaging due to these inherent properties. To build advanced biosensors for the detection of tumour tissue, it is extremely desirable to manufacture additional MOF materials [3,7].

3.2. MOFs as Biomarkers

Whether containing volatile organic compounds or not is one of the most practical methods to distinguish tumours from healthy cells [6]. In vitro, volatile organic compound identification from cell lines is a useful technique to lessen the effects of external stimulation. Due to their complex matrix samples and trace concentration of volatile organic compound biomarkers, direct detection of these volatile organic chemical biomarkers is challenging without a highly effective sample pretreatment approach [5]. It is crucial to create an efficient extraction and enrichment method for the analytes before analysis.

Since MOFs have been used to detect many biomolecules in other contexts, MOF-based biosensors may also be useful for the early and extremely sensitive detection of cancer biomarkers. Functionalizing the framework enables the customisation of MOF characteristics as a result [7,8,9]. MOFs were combined with inorganic materials to enhance their unique properties. Nevertheless, it is important to look into the specifics of their relationship [10]. Inorganic nanoparticles, which are frequently used, control the tumour's location's photothermal effect [10]. The colour of bimetallic ZIF nanoparticles darkens as the Co concentration rises. The synthesis process resulted in Co-doped ZnO NPs with outstanding ferromagnetism, adjustable doping mode, customizable surface state, and catalytic activity [10].

Besides, MOFs are routinely combined with organic compounds to improve their functioning [10]. Organic chemicals can increase the mechanical properties of MOFs. By including organic components, the porosity structure of the MOFs can be altered to hasten to load. Organic substances can modify MOFs to improve their functionality [10]. Being biocompatible, nucleic acids are frequently used in biomedical therapy. However, they have little cellular uptake and degrade quickly. To successfully shield their nucleotides before releasing them into the cytoplasm, whole sequences of DNA and RNA have been set into holes in MOF. When the DNA skeleton is compromised, delivery rates are lowered [10].

As synthetic techniques have advanced and surface functionalization methods have arisen, the usage of MOFs in combination with biomolecules has benefited the advancement of biomedicine. Artificial MOFs with biocompatible features, therefore, have unignorable defences and distinctive biotic abilities. On the other hand, there is a need to improve the biological stability of MOFs. The asymmetric structure of molecules will impede producing MOFs. More research must be done on the factors that influence the induction and proliferation of biomolecules in the morphological structure [11]. The production of MOFs must be centred on clinical applications, and we must consider how to maximise the synergistic benefits of each component [10,11].

3.3. Zn(II) in Pores

Zinc-related MOFs are anticipated to be used in bio-application domains, particularly as drug carriers, due to the excellent low toxicity of zinc ions. Metals and several antibiotic medications have been shown to have an antibacterial effect together. It is frequently used in dermatology as an astringent, antimicrobial, anti-inflammatory, anti-dandruff, and cicatrizing agent. Zn(II) is frequently employed as a connecting point in nonlinear optically active MOFs to remove undesired signals from the visible spectrum. Besides, recent studies have documented the production processes of zinc-related MOFs as well as their toxicity, medical uses, and biocompatibility [5,12].

The enormous surface area and highly organised structure of MOFs make them special. Drugs can be loaded in a variety of ways, including by embedding them on the outside surface or encapsulating them inside the pores [5]. The easiest loading strategy to include pharmaceuticals in MOFs is the one-step method. Among this, the one-pot method is a cost-effective technique for drug loading during the synthesis of MOFs that not only speeds up the reaction process and minimises waste but also gets beyond the MOFs' restrictively tiny pore window.

An outer shell is needed. Both polymer and magnetic cores can act as shells owing to their versatile characteristics [2]. Additionally, low stability limits the creation, storage, and use of medicines [5]. Numerous medications are susceptible to oxidation, polymerization, deterioration, and crystallisation.

4. Configuration of Effective Zn-MOFs for Tumour Treatment

There are still several problems that need to be resolved for these systems before such nanocomposites may be used in therapeutic settings [8]. It is not enough to look at how nanocarriers affect healthy organs and how they might be used therapeutically. Furthermore, it is crucial to closely monitor the organism [9]. The absorption, distribution, metabolism and excretion processes must also be thoroughly understood because the clinical implementation of current imaging and therapeutic applications research is still years away [10,11,12].

4.1. Heterogeneous Surface of MOFs

As part of the coordination modulation approach of surface modifications, a monodentate ligand that is chemically and functionally equivalent to the existing multidentate organic ligand is simply introduced to the MOF synthesis reaction mixture. It is a modulator that regulates or stimulates crystal formation because the number of bridging sites is limited, in which case, monodentate and multidentate ligands will vie the opportunity to coordinate with metal ions [6,13]. The coordination modulation is influenced by a variety of factors, including reagent concentration, temperature and pH value. Additionally, depending on the conditions and makeup of the reaction, the overall structure of MOFs may change, which may have an effect either directly or indirectly on the properties of MOFs, including crystallinity. Despite some limitations, dentate ligands are an effective technique to change the surface of MOFs [6,7].

4.2. Stereo Structure of MOFs

In addition to possessing a large number of channels and porous architectures, MOFs also feature highly concentrated and evenly distributed active sites, which is favourable for product transport and diffusion [15]. Furthermore, MOFs' extremely uniform sizes and pore geometries are essential [8]. The catalytic centres of MOFs are typically constrained by the Lewis acid centres of coordinatively unsaturated metal sites and the active group on organic linkers. Due to these factors, MOFs only have a modest amount of catalytic activity, but there is good news a wide range of highly active species can reside as visitors in the pores of MOFs to produce nanocomposites based on MOFs for catalytic processes.

The study of MOFs-based nanozymes is a recent development with promising early results. The most current advancements in MOFs-based nanozyme design methodologies and multi-application has been described. Although research in this field is still in its infancy and is experiencing numerous challenges, MOFs-based nanozymes have already accomplished a significant lot [7,8,11].

Several problems persist despite the effectiveness of nano-MOFs-based enzymes in the treatment of cancer and other disorders. Before using nano-MOFs-based enzymes in clinical translation, their long-term effects must be verified in animal models [6,8,16]. Nanozymes based on MOFs has also significantly advanced the field of cancer malnutrition therapy [6,7,8]. However, complete tumour eradication is very difficult with fasting therapy alone since tumour cells may continue to obtain energy and nutrients through capillaries [8]. Therefore, a viable tactic for improving treatment effectiveness is to combine fasting therapy with several synergistic medications. Additionally, a thorough explanation of how various synergistic therapies work with each therapeutic modality is required to apply clinical translation [6,8].

5. Summary

Due to their advantageous properties, MOFs now play a greater variety of important roles in the treatment of cancer. Over the past few decades, interest in creating customised MOFs has grown. In particular, numerous MOF-based medication delivery applications are being researched. Initially, MOFs were used to deliver small-molecule pharmaceuticals. Additionally, it is described how to build EC biosensors based on MOFs that are targeted toward certain analytes to inspire further research on MOFs. Zn-based MOFs are among the best options for usage in the treatment of cancer. This article illustrates the superiority of Zn-based MOFs over alternatives in the treatment of cancer. However, the practical use of MOFs is constrained by a lack of biomedical expertise. To minimise unwanted impacts, more thought should be given to how they interact. The benefits and drawbacks of MOF composite materials must be assessed through actual clinical practice when theoretical research has evolved.

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