Application of metal-organic frameworks-based drug delivery for different diseases treatment

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Abstract. The limitations of traditional drug delivery vehicles include low specificity, uncontrolled biodegradation, and are oftentimes associated with toxicity and serious off-target events. In addressing the biological relevance of an effective drug delivery system in improving the therapeutic efficacy of active ingredients, a variety of new approaches for drug administration have recently been developed. Remarkable breakthroughs following the emergence of nanotechnologies promoted metal-organic frameworks (MOFs) as viable drug delivery possibilities. They are characterised by large surface area and porosities, and hence, exceptional drug adsorption ability. Inorganic MOFs in particular offer high drug loadings and functionalisation capacity, enabling a high-efficacy drug administration route and controlled pattern of drugs' *in vivo* behaviours. This research encompasses the preparation of MOFs and their relevant drug delivery for different diseases treatment in biomedical field, which are classified according to four types of diseases including cancer, Alzheimer's disease, pulmonary diseases, and ocular diseases. A diverse of different MOFs have been designed to treat given their corresponding properties for these diseases. Experimental outcomes from each research are also analysed to evaluate the therapeutic effectiveness and biological applicability of proposed MOFs, which is expected to provide a new idea for efficient drug delivery in disease treatment.

Keywords: Drug delivery; MOFs; functional materials; disease treatment; application.

1. Introduction

While countless novel drugs have been formulated to treat complicated conditions, a wide range of constituent active ingredients have limited therapeutic efficiency due to related drawbacks that cannot be resolved without drug delivery systems (DDSs). The incompatibility of drugs with endogenous enzymes and biological fluids oftentimes leads to a short half-life in vivo, eventuating in issues such as low solubility, instability and rapid biodegradation. Meanwhile, without specified DDSs, low level of therapeutic specificity, inadequate drug transport to the tumour site and off-target side effects and toxicities are direct consequences of free movement of drugs in body. As a result, to improve the efficacy and bioavailability of medications, it is imperative to regulate the drug release patterns using DDSs. Through stabilizing drugs and targeting them to infected tissues, they can deliver drugs locally by the anticipated quantity and time with a controlled release profile. Consequently, effective DDSs can ascertain an optimal drug ratio at the tumour tissue, and meanwhile minimize systematic side effects. Hence, drug delivery is of great biological relevance in regulating the in vivo pharmacokinetic behaviours of drugs to maximize treatment efficacy.

To transport certain medications to a specific area of the human body and produce a desired therapeutic effect, different DDSs are utilized, and these used systems are usually required to be safe and efficient. Many strategies for drug delivery have been developed recently, where theranostics and co-delivery and stimuli-responsive tactics are a few of the new medication delivery techniques. A diverse of different medication delivery methods have been also developed. For example, by using a

layer-by-layer approach, 3D printing-based drug delivery technology can create 3D drug delivery formulations from digital designs, which makes it special for creating individualized biomedical devices. The most popular 3D printing method for creating specialized pharmaceutical formulations is fused deposition modeling. The microneedle-based transdermal drug delivery can speed up the creation of transdermal drug delivery systems. Because of the needle's diminutive size, it makes this technology more convenience and has more benefits. Since nanoparticles are made entirely of the active pharmaceutical ingredients without the use of any carriers or vehicles, nanocrystals significantly reduce the frequency of excipients used in the formulation, making it simple to achieve ultra-high loading capacities. Prodrug nanomedicines are also known as nanodrugs, prodrugs, or self-assembled DDSs.

The development of functional materials-based drug delivery methods has received increasing attention. As a new type of functional materials, metal-organic frameworks (MOFs) are a series of composites with a two- or three-dimensional periodic structure consisting of metal ions or ionic groups linked to organic ligands. MOFs show huge advantages as compared to conventional materials, which are surface functionalization and pore structure tunable [1]. The drug carrier is the medium for drug delivery, an important component of drug delivery and a major factor in achieving the advantages of sustained drug release. Compared to the present DDSs that is frequently only organic or inorganic substances, drug delivery methods developed around MOFs-based functional materials have even more unique advantages. For example, the prepared MOFs have higher drug loading, better biocompatibility and excellent therapeutic effect. In addition, MOFs have a number of characteristics that make them great choices as contrast or drug delivery agents, such as huge pore surfaces and volumes linked to strong drug adsorption capabilities. Functionalized interior (pore structure) and external surfaces can be used for reversible drug adsorption/desorption or surface modification to enhance in vivo stability or biodistribution [2]. These surfaces also allow for specialized host-guest interactions. And also, the drug release is controlled to prevent the well-known "burst effect".

Herein, this research mainly introduces the synthesis of different MOFs-based functional materials and their construction of drug delivery methods for disease treatment, including chronic obstructive pulmonary disease, cancer, Alzheimer's disease and ocular diseases. In this research, we aim to look at the use of MOFs made by different teams in four different diseases and analyze how they can be used to treat and overcome these diseases. For cancer, DDSs are a marvelous and effective way to deliver therapeutic agents to cancer cells. The main purpose of this research is to explain and help others to understand current met and unmet needs, and how can we overcome age-old barriers, such as Alzheimer's treatment, with innovative drug delivery technologies. This research highlights the biological relevance of metal organic frameworks in treating diseases through enhanced drug administration. In the context of pulmonary therapies, MOFs are expected to make constructive contributions to improving the effectiveness of aerosol delivery. In addition, this research describes the importance of MOFs in the treatment of disease through drug delivery. In terms of ocular therapeutics, MOFs open the door to eye treatments due to its particularity.

2. Different Diseases Treatment with MOFs-Based Functional Materials

2.1. Chronic obstructive pulmonary disease

The main characteristic of chronic obstructive pulmonary disease (COPD) is an excessively inflammatory response of the lungs to respiratory contaminants, mostly cigarette smoke, which results in restricted airflow. According to WHO's reports, lower respiratory tract infections and COPD are accountable for over 6 million deaths per year [3]. In addition to the pulmonary pathology, COPD is also correlated to multiple extra pulmonary side effects, including systematic inflammation, nutritional abnormalities and muscle dysfunction. Currently, inhaled therapy dominates in the treatment of COPD, however, the efficacy of many inhalation aerosol drugs is limited by indirect administration and inconsistent dosing. As a result, various novel ways are required to broaden the application of aerosol delivery.

For theophylline, Strzempek et al. synthesised the (Fe) MIL-100, which allows the drugs to be aerosol delivered without undergoing liver first-pass metabolism [4]. The MOFs was prepared by dissolving trimesic acid in a 1 M NaOH solution, and added dropwise into the iron (II) chloride tetrahydrate solution. Magnetic stirring operation for 24 hours was carried out and then it was further activated for 6 hours under 110 °C vacuum. It was then mixed with theophylline (presently dissolved in HCl solution, 0.03 mol/L). The composite was then centrifuged for 5 minutes at 6000 rpm, denoted as TP@Fe-MIL-100. By X-ray power diffraction (XRD) characterization, the resulting MOF's structure and crystallinity were assessed, as shown in Fig. 1. The intensity of reflexes was shown to decrease after theophylline encapsulation, where the relative position only shifted 2θ values right, confirming the MOF matrix's stability under the drug encapsulating process [4]. Frantz cells were used for the release investigations. Within the first 8 hours, 46% of the composite-loaded theophylline in the Franz cells was dissolved. In comparison, pure theophylline administration in body without MOF as DDSs contributed to a 95% drug dissolution in 3 hours. Hence, the reduced effects of burst release from the composite proved the potential of Fe-MIL-100 in drug transport with increased biocompatibility. Furthermore, the cytotoxic effects of Fe-MIL-100 (at various concentrations: 10~500 g/mL) on murine macrophages and epithelial human cells are also examined. Experiments indicated that although the vitality of these cells were decreased as the concentration of Fe-MIL-100 increases. Their overall morphology was unaltered and proliferation sustained (but at a lower rate). This demonstrated the pharmaceutical practicability of the proposed Fe-MIL-100.

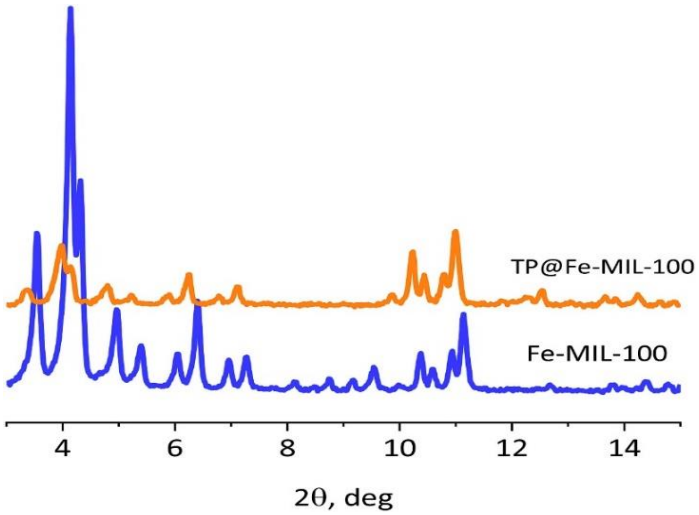

Fig 1. XRD characterization for the prepared MOFs-based functional materials [4].

Jarai et al. designed a new DDSs with the prepared UiO-66 nanoparticles [5]. The used MOFs-based functional materials were synthesized through adding $ZrCl^{4+}$ terephthalic acid mixture into anhydrous dimethylformamide and deionised water. Dissolving by sonication, the sample was heated and centrifuged along with the decanting of the supernatants. Then Rhodamine B (RhB) or dexamethasone (Dex) were post-synthetically loaded onto finished UiO-66 nanoparticles. The size and charge (range from -15 to -25 mV) of the MOFs was formulated within a favourable range for phagocytic uptake. Results indicated that even with defectiveness in UiO-66 nanoparticles, no significant impacts on the loading of RhB and Dex were found. The quantity of cargo adsorbed also corresponded with previous studies, with reported adsorption level of 0.15 milligram of RhB and 0.1 milligram of Dex per milligram of UiO-66. After loading, a portion of the loaded nanoparticles was redistributed into the ALF (pH 4.4) and PBS (pH 7.4), which represent extracellular and intracellular pH environments, respectively. Given that the UiO-66 must be internalised by cells to enable cargo release, the much quicker degradation profile of UiO-66 in ALF than in PBS (Fig. 2), indicating the advantages of the MOF as pH sensitive DDSs with properties of selective release in certain biological settings, such as the low pH tumour microenvironment. Moreover, the cytotoxicity of UiO-66 was evaluated through observing the viability of MH-S alveolar macrophages and A549 alveolar basal epithelial cells after treatment using the MOFs-based functional materials. No major reduction in cell

viability and functionality was observed, indicating good biocompatibility of the prepared UiO-66 nanoparticles.

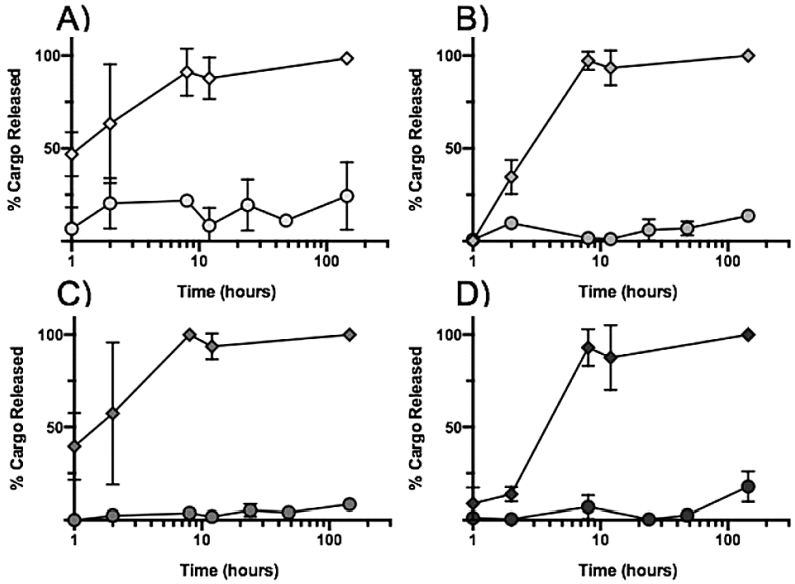

Fig. 2 Cargo released performance under different experimental conditions [5].

To improve the efficacy of vasodilator drugs that are used to mitigate the intensity of pulmonary arterial hypertension (PAH) as a complication of pulmonary diseases, Mohamed et al. put forward the pulmonary DDSs nanoMIL-89 [6]. The used MOFs was prepared by combining Trans, trans-muconic acid and iron (III) chloride hexahydrate in pure ethanol. Glacial acetic acid was also applied in an optimal quantity to regulate the size and distribution of nanoparticles. After heating and centrifugation, 20 mg of the nanoMIL-89 was added to a 5 mg sildenafil solution in PBS to finalise the sil@nanoMIL-89 precipitate. The suitable size and integrity of structure for MOFs after loading was verified using infrared/attenuated total reflection and XRD. Besides, the highest quantity of sildenafil that sil@nanoMIL-89 could release into the blood equalled to more than 51% of the drug's initial loading, indicating the high drug adsorption efficiency of the MOFs-based functional materials. The release experiment was also conducted in human plasma. The results show a continuous release of the drug in the first hour, which was sustained into the 6 h timepoint, but at a slower pace (Fig. 3). Notably, from the 72 to 96 h interval, pure sildenafil had deteriorated, while sil@nanoMIL-89 sample showed relatively high and constant amount of sildenafil. This illustrated the constant and controlled release kinetics of drugs offered by sil@nanoMIL-89. Additionally, different cells and the aortas of mice were prepared to evaluate the cytotoxicity of the synthesized materials. No significant decrease in the cell viability was recorded, while the sustained vasodilation effects effectuated by sildenafil remained unaltered, which indicates the biocompatibility and stability of sil@nanoMIL-89 for use in biorelevant settings.

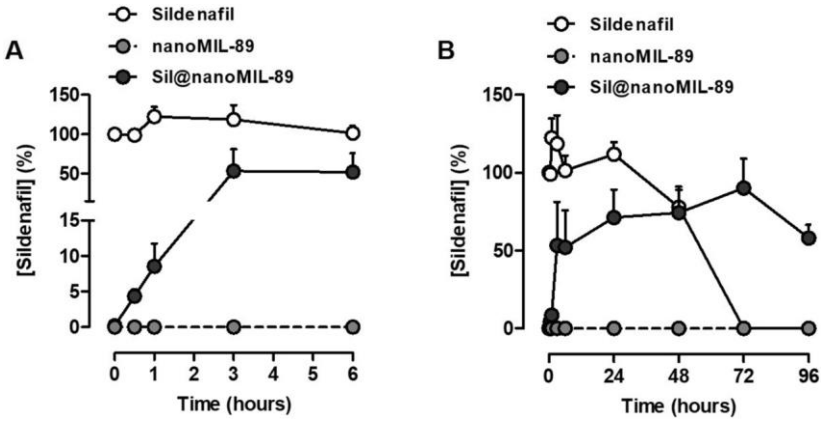

Fig 3. Sildenafil release by using the prepared functional materials [6].

2.2. Cancer

Cancer is a major risk to people's health throughout the universe that causes millions of deaths annually. For example, non-small cell lung cancer (NSCLC), which occur about 85% of cancer incidence, is the most common cancer to cause serious harm globally. For patients who have advanced NSCLC, platinum-based combination chemotherapy is recommended as the first line of treatment. By using automobiles that can safeguard drugs from degradation and deliver them successfully and safely to the target tissue, minimizing off-target events, the developing field of nanomedicine aims to address these problems. Nanomedicines could be one of an effective cancer treatment option. The DDSs is a remarkable and effective approach for transporting therapeutic agents to cancer cells. However, due to inherent restrictions, such as unfavourable side effects and poor biodistribution, the traditional practice of directly administering therapeutic drugs to patients is no longer appropriate.

Zheng et al. demonstrated that DOX encased by ZIF-8 can be used as a useful DDSs for treating disease [7]. pH-responsive MOFs was created by trying to induce DSF and DOX into ZIF-8, which was then encased with Cu^{2+}-tannic acid (TA) by Cu complex for enhanced chemotherapy. The Cu-TA complex, as well as bonds of compound (especially Cu-O and Zn-N) in ZIF-8, are not stable in slightly acidic conditions. As a result, the degradation of the synthetic material structure results in the release of DOX, copper ions, also DSF in the designed to simulate tumour microenvironment (TME). This degradation was explored, also it was discovered that NPs remained unchanged in neutral conditions but degraded in acidified PBS. The above synthetic biodegrades at a pH-dependent rate, demonstrating the rapid release of coated Cu and loaded medication in TME [8]. The anticancer effect of the used functional materials was enhanced by the chemotherapeutic action of doxorubicin, which strengthened the suppression of the anti-apoptotic NF-κB pathway.

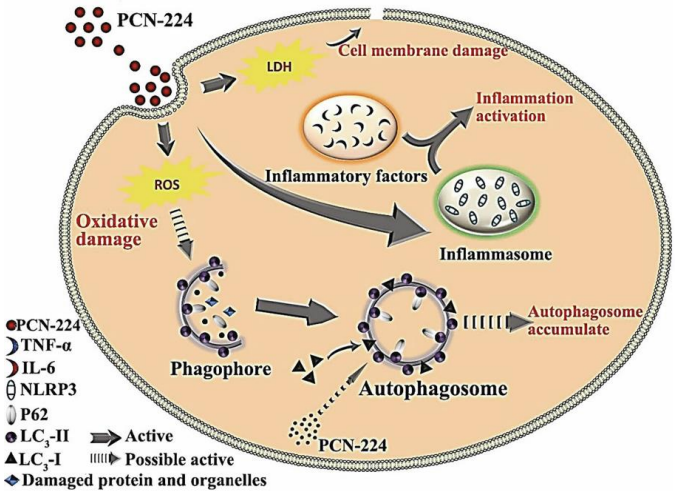

Fig 4. Potential mechanism of PCN-224-induced cytotoxicity [8].

Mallakpour and co-workers investigated the cellular effects of PCN-224 on human hepatocytes and mouse macrophages [8], as shown in Fig. 4. The Lactate Dehydrogenase (LDH) assay was used to investigate cell membrane destruction as the criteria for cytotoxic effects. The LDH performance improves dramatically as PCN-224 concentration rises, which demonstrates that the cell membrane is seriously damaged in all cells. The inflammatory index produced by PCN-224 was studied using the enzyme-linked immunosorbent assay (ELISA) on people's liver cells to measure IL-6 and TNF-α. The results show that PCN-224 promotes inflammatory reactions in these cells by stimulating them to release TNF-α in the daily dosage manner. To examine the biological effects in various cells, cytotoxicity, as seen in mouse macrophages, can be used to monitor infection and cell membrane damage. And also, the results show that the PCN-224 can cause cytotoxicity in a variety of cells, demonstrating harmful impacts are dose dependent. The increased LDH release in mouse macrophages cells demonstrates the annihilation of the cell membrane.

Carboxymethylcellulose (CMC) was loaded into the synthesised mesoporous structured UiO-66 MOFs for sensitive pH response as well as to serve as a connector to encompass the DOX

chemotherapy drug [9]. The loading capacity for the prepared MOFs-based functional materials was used to evaluate the experimental effect. Infrared and UV-Vis spectroscopic characterization methods are used for analyzing the loading of CMC and DOX, and the morphological features and crystal structure for the prepared MOFs were characterized by transmission electron microscopy and XRD. At 37 °C, the release of DOX was tested. At pH 5, the aggregate release of DOX might reach 78%. Because the CMC shrank and DOX is more soluble in an acidic medium. When pH was low, the release of DOX was better. According to the cytotoxicity study, the A549 cell viability was only 28% at DOX concentration of 4 μg/mL, which was lower than that of free DOX solution (47%). It has been shown that the prepared MOFs-based functional materials are an effective drug delivery for the release of chemotherapy drugs.

2.3. Alzheimer's disease

Alzheimer's disease (AD) belongs to the neurological condition that has the potential to develop. Memory issues, aphasia, visuo-spatial skills issues, and personality and behaviour abnormalities are only a few examples of clinical symptoms. According to AAIC, every three seconds, a new AD patient will be produce worldwide. The number of AD patients worldwide is expected to increase to more than 150 million by 2050. The mechanism of the AD needs to be deeply understood to find more useful treatments. Different biomarkers for AD have been discovered. For example, intraneuronal neurofibrillary tangles that are composed of amyloid-(A) are the two primary histopathological markers of the AD.

For the therapy of AD, Zhao et al. used the MOFs to a new drug delivery method [10]. This drug delivery system was created by post-synthesizing NOTA and DMK6240 over the outer surface of the Fe-MIL88B-NH_2. Researchers used the MTT method to test the toxicity of the used MOFs, where SH-SY5Y cells were exposed. The findings indicate that the MOFs is safe for normal tissues because no significant morphological changes were seen in the hippocampus, liver, kidney tissues or many other body organs. In another test, researchers found that in untreated okadaic acid group, the cell viability ratio was only 39%. However, with the MB treatment, the cell viability in the okadaic acid group increased to 62%. It demonstrates the potency of the prepared materials as a neuronal death inhibitor. When compared to the OA group, the outcomes reveal that rats given the prepared materials had a reduced escape delay, but the average swimming speed across all groups was virtually the same, indicating that the animals' regular physiological function is unaffected by the nanocarriers. These findings clearly imply that the anti-tau hyperphosphorylation impact of the prepared materials ameliorates memory loss in the engineered rats in experiment. The findings point to the prepared materials as a potential tau-targeting nanocarrier for the treatment of AD.

Wang et al. suggested another type of MOFs, PCN-224 nanoparticles for AD treatment [11]. The prepared PCN-224 nanoparticles underwent extensive experimental investigation by the researchers, and the results indicate that they are stable and safe to use. When NIR light was exposed, PCN-224 NPs were shown to limit Aβ accumulation and lessen A-induced toxicity. The capacity of photo-activated PCN-224 nanoparticles to inhibit Aβ-induced cytotoxicity in PC12 cells was examined. The outcome demonstrates that the cell viability increased to 90%, which is much greater than when PCN-224 nanoparticles were in a dimly lit setting. At the end, researchers developed a facile strategy, which they used PCN-224 nanoparticles to inhibit amyloid-β peptide into a β-sheet-rich structure with an NIR-light-induced in order to treat Alzheimer's disease and reduce an aggregation.

The primary cause of cognitive impairment in AD is the massive loss of neurons, but thankfully, exogenous neural stem cells (NSC) transplantation aids in self-repair following neurons loss. However, the brain cells of AD patients are constantly subject to high levels of oxidative stress. The loss of exogenous NSC and certain other symptoms may be caused by ongoing oxidative stress. Ceria-doped MIL-100 with excellent antioxidant activity was developed by Yu et al. to transport retinoic acid and siSOX9 to NSC [12]. Researchers created CeNPs/RA@MIL-100/siSOX9 (CeRMS), CeNPs@MIL-100 (CeM), and CeNPs/RA@MIL-100 syntheses (CeRM). On 11-month-old experimental transgenic mice, CeRMS and RNS were evaluated. The mice was tested with the Morris

water maze test after 5 weeks of NSC transplantation, and the evidence suggests that the nanoparticles could help triple transgenic AD mice's cognitive ability. Researchers also synthesized polyvinyl pyrrolidone-coated ceria, then coated with CeM. And high-resolution electron microscopy demonstrates that the encapsulation of ceria nanoparticles in MOF was effective. The PXRD patterns of the CeM after coating with MIL-100 further showed the CeM's effective fabrication, and X-ray photoelectron spectroscopy further established their potential SOD activity. Researchers used dynamic light scattering experiments to assess CeRMS's stability in various pH and conditions, and the results showed that the platform was rather stable overall. The results suggest that the used MOF could be useful for the treatment of AD.

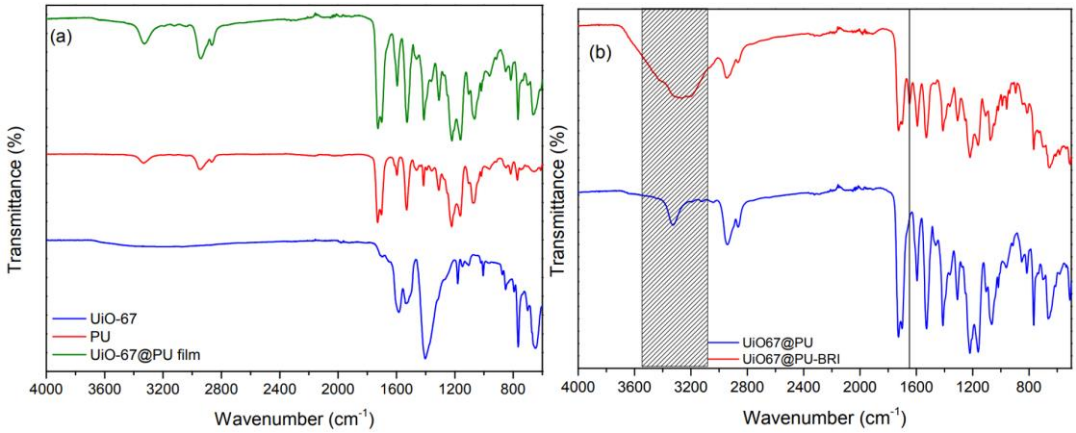

Fig 5. Infrared spectral characterization of the prepared materials [13].

2.4. Ocular therapeutics

A growing number of people are losing their vision due to eye diseases with the development of society. Anti-VEGF drugs have emerged as the mainstay of vision treatment. Despite the fact that anti-VEGF medicine helps a lot of people, there are still therapeutic limitations on how it should be administered and how long it should last. Anti-VEGF medication must be delivered intravitreally to properly treat these retinal disorders. The opportunity exists to reduce the requirement for repeated intravitreal dosing through the use of sustained pharmaceutical delivery systems. The physical and physiological restrictions of the ocular environment put constraints on the administration of ocular medication, necessitating optically neutral and restricted formulations or devices outside the visual axis. In order to safely and effectively deliver protein therapies for a prolonged period of time in the eye, new and improved methods are required. In addition, building some analytical models are crucial for translating laboratory findings into clinical trials because they assist anticipate therapeutic dosages and advance our understanding of drug destiny.

At present, a diverse of different drug delivery based on virous functional materials have been widely designed for ocular therapeutics, such as MOFs-based functional materials. For example, Silvestre-Albero et al. prepared a new MOFs-based composite film and used as the potential functional materials for drug delivery [13]. The surface morphology and internal structure of the prepared functional materials were characterized. As shown in Fig. 5, combined with spectroscopic instrumental analysis, it was confirmed that the prepared nanocomposite films could well load drugs and have good stability. These experimental results open the door for novel MOFs-based functional materials for drug delivery applications in ocular therapy.

3. Conclusion

This research mainly introduces MOFs-based functional materials for the development of different drug delivery systems and for the treatment of different diseases. To sum up, MOFs are promising and superb functional materials for applications in the biomedical industry. Due to their structure, composition, large surface area, and pore volumes, MOFs solve many medical challenges and provide

great assistance in drug delivery. This makes MOFs a promising new material for drug delivery. We can also conclude from the experimental results and data of the above studies that MOFs perform well while treating illnesses like cancer, Alzheimer's disease therapy, lung disorders, and ocular therapeutics. This solves many challenges in drug delivery and has made significant contributions to the advancement of medicine.

References

[1] Lázaro, I. A., & Forgan, R. S. (2019). Application of zirconium MOFs in drug delivery and biomedicine. Coordination Chemistry Reviews, 380: 230-259.

[2] Rojas, S., Arenas-Vivo, A., Horcajada, P. (2019). Metal-organic frameworks: A novel platform for combined advanced therapies. Coordination Chemistry Reviews, 388: 202-226.

[3] Bjork, E.M., Baumann, B., Hausladen, F., Wittig, R., Linden, M. (2019). Cell adherence and drug delivery from particle based mesoporous silica films. RSC Adv., 9: 17745-17753.

[4] Strzempek, W., Menaszek, E., Gil, B. (2019). Fe-MIL-100 as drug delivery system for asthma and chronic obstructive pulmonary disease treatment and diagnosis. Microporous and Mesoporous Materials, 280: 264-270.

[5] Jarai, B.M., Stillman, Z., Attia, L., Decker, G.E., Bloch, E.D., Fromen, C.A. (2020). Evaluating UiO-66 Metal–Organic Framework Nanoparticles as Acid-Sensitive Carriers for Pulmonary Drug Delivery Applications. ACS Appl. Mater. Interfaces, 12: 38989-39004.

[6] Mohamed, N.A., Abou-Saleh, H., Kameno, Y. et al. (2021). Studies on metal–organic framework (MOF) nanomedicine preparations of sildenafil for the future treatment of pulmonary arterial hypertension. Sci. Rep., 11: 4336.

[7] Zheng, H., Zhang, Y., Liu, L., Wei, W., Peng, G., & Nystroem, A. M. et al. (2016). One-pot synthesis of metal-organic frameworks with encapsulated target molecules and their applications for controlled drug delivery. Journal of the American Chemical Society, 138(3), 962-968.

[8] Mallakpour, S., Nikkhoo, E., & Hussain, C. M. (2022). Application of mof materials as drug delivery systems for cancer therapy and dermal treatment. Coordination Chemistry Reviews, 451, 214262.

[9] Xie, C., Guo, B., You, H., Wang, Z., Leng, Q., Ding, L. ET. Al. (2021). Synthesis and surface modification of mesoporous metal-organic framework (uio-66) for efficient ph-responsive drug delivery and lung cancer treatment. Nanotechnology, 32(29), 295704.

[10] Zhao, J., Yin, F., Ji, L., Wang, C., Shi, C., Liu, X., Yang, H., Wang, X., & Kong, L. (2020). Development of a Tau-Targeted Drug Delivery System Using a Multifunctional Nanoscale Metal–Organic Framework for Alzheimer's disease Therapy. ACS applied materials & interfaces, 12(40), 44447-44458.

[11] Wang, J., Fan, Y., Tan, Y., Zhao, X., Zhang, Y., Cheng, C., & Yang, M. (2018). Porphyrinic metal–organic framework PCN-224 nanoparticles for near-infrared-induced attenuation of aggregation and neurotoxicity of Alzheimer's amyloid-β peptide. ACS applied materials & interfaces, 10(43), 36615-36621.

[12] Yu, D., Ma, M., Liu, Z., Pi, Z., & Qu, X. (2020). MOF-encapsulated nanozyme enhanced sirna combo: control neural stem cell differentiation and ameliorate cognitive impairments in alzheimer's disease model. Biomaterials, 255, 120160.

[13] Gandara-Loe J., Souza B.E., Missyul A., Giraldo G., Tan J.C., Silvestre-Albero J. (2020). MOF-Based Polymeric Nanocomposite Films as Potential Materials for Drug Delivery Devices in Ocular Therapeutics. ACS Appl. Mater. Interfaces, 12(27), 30189-30197.