Chapter 13
Metal–Organic Framework-Based Nanostructures for Biomedical Applications

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1 Introduction: Metal–Organic Framework-Based Nanostructures

The nanomaterials are the foundations of nanoscience and nanotechnology. Recently, nanomaterials have been assisting various fields of nano science as it acquires outstanding fundamental properties and structural features in between those of atoms and bulk materials. The self-assembly of nanomaterials which opened a new window of research through the controlled formation of nano-sized particles with distinctive chemical, biological, optical, magnetic, and electronic properties. Various metal nanomaterials of gold, silver, platinum, metallic oxides

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nanoparticle of titanium, silicon, zinc, iron, and semiconducting nanomaterials as zinc sulfate, and cadmium sulfate are used as carrier or marker depending on a purpose used for biomedical applications (Yaqoob et al. 2020; Maddela et al. 2021). Recently, in the development of nanotechnology, organometallic nanoparticles (OMNPs) with metal–organic frameworks have now emerged in order to enhance the structural potential when compared to nanoscale particles (Zhang et al. 2020). Metal–organic frameworks are usually amorphous nanomaterials also known as coordination polymers attached to metal nanoparticles that were first unearthed by Robson in 1989. Since this discovery, many researchers around the globe took interest in the engineering and evolution of MOFs for nano biomedical, drug delivery, catalysis, separation, magnetism, storage, luminance, biosensing, and many more applications. However, metal–organic framework-based nanostructures (MOFsN) are considered as the new cohort organometallic hybrids that might also be classified according to the dimensions and order of organic–inorganic material participating into the synthesis. As the development of nanotechnology progressed, many researchers studied the synthesis, characterization, functionalization, and biotoxicity of MOFsN. Due to this advancement, a structured understanding was developed about numerous MOFsN being promising platforms for biomedical applications. In 1989, the metal–organic-based structural frameworks, also known as porous materials, were first synthesized, and reported by B. F. Hoskins et al. (Hoskins and Robson 1989; Zhang et al. 2020). The MOFsN frameworks are organic–inorganic metal combined crystalline complex materials with a systematic arrangement of positively charged metal ions surrounded by linker such as organic molecules. The metal ions at the center that form a bond with functional groups of the organic linkers together produce a repeating, cage-like structure. As an emerging and favorable class of potential hybrid materials, it has drawn great consideration for various applications due to their unique features, high porosity, a wide range of void shapes, higher surface areas, and multifaceted structural frameworks. Numerous potential applications of MOFsN have been reported such as drug delivery systems, biosensing, biocatalysts, magnetic resonance imaging (MRI), optical molecular imaging, separation, magnetism, and energy (Yang and Yang 2020).The MOFsN possess not only porosity type materials but also shows a nanometer scale size with enhanced surface activities due to organic linkers, which leads to a great superiority in the field of biomedicine (Meng et al. 2020). The MOFsN frameworks were synthesized by using chromium metal at central with 1,3,5-benzene tricarboxylic acid or trimesic acid and 1,4-benzenedicarboxylic acid as organic linkers. The first time loading and releasing activities of MOFsN for the Ibuprofen drug encapsulation to enhance control drug release profiles were studied by Ferey et al. in 2006 (Horcajada et al. 2006). Several studies have been reported on surface modification of metal nanoparticles using multiple functional groups, for instance, biological molecules and fluorescent materials as organic linkers for the synthesis of MOFsN through the various synthetic methodologies. These innovative surface modifications show major advantages for the development of liquid separation, liquids purification, gas separation, electrochemical energy storage, chemical catalysis, sensors, and many biomedical applications. The research and development in the area of

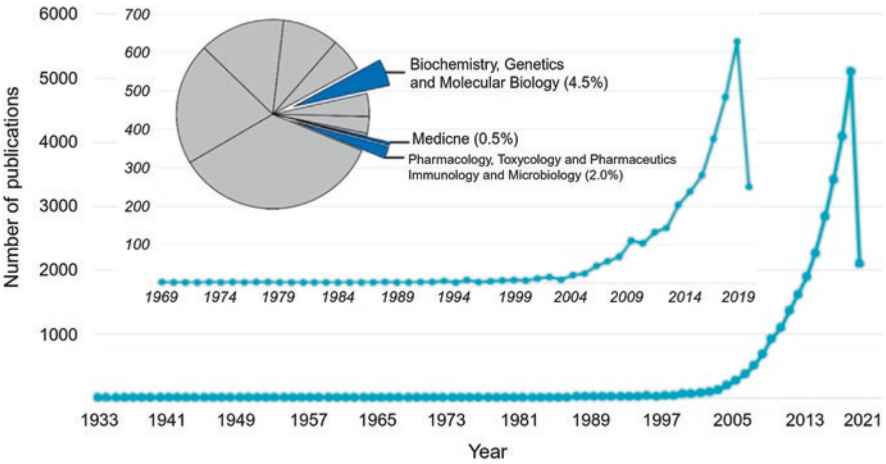

Fig. 13.1 Publication rate of work carried out on MOFs over time particularly in the biomedical applications (Barbosa et al. 2020) (Copyright 2020, Chapter 4, Metal-Organic Frameworks for Biomedical Applications, Page: 69–92, Elsevier publication)

MOFs as given in Fig. 13.1 with respect to publication in this area (Barbosa et al. 2020). Also, work done in the area of biomedical sciences is also highlighted.

1.1 Synthesis and Structural Properties of MOFsN

The synthesis of the MOFsN could be obtained through surface functionalization of metal with organic linkers such as simple organic molecules, biomolecules, dendrimers, polymers, amino acids, supramolecular, which eliminate several difficulties correspond to the stability, size, and structural properties. Jian Wang et al. reported and elaborated four categories of the surface modifications of metal NPs along with advantages and deficiencies molecular frameworks (Zhang et al. 2020). These categories are (a) covalent post-synthetically modification, (b) coordination modulation and coordinative post-synthetically modification, (c) noncovalent post-synthetically modification, and (d) modifications on the external surfaces of MOFs (Fig. 13.2).

1.1.1 Covalent Post-Synthetically Modification

The modification that deals with the metal are generally covalently conjugated with drugs or biomolecules organic linkers to the metal, which consist of the click chemistry and conjugation reacting mechanisms (Fig. 13.3).

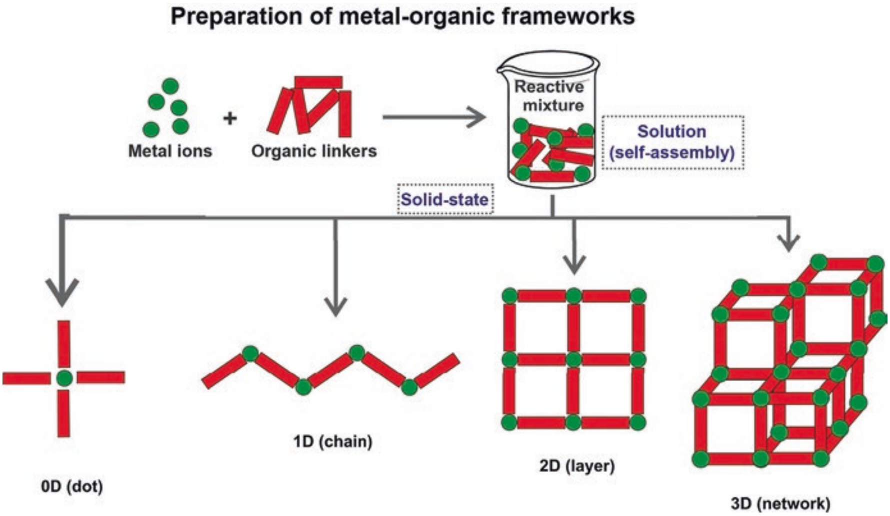

Fig. 13.2 Representation of the synthetic approach of MOFsN and their self-assembly in different dimensionalities. (Barbosa et al. 2020) (Copyright 2020, Chapter 4, Metal-Organic Frameworks for Biomedical Applications, Page: 69–92, Elsevier publication)

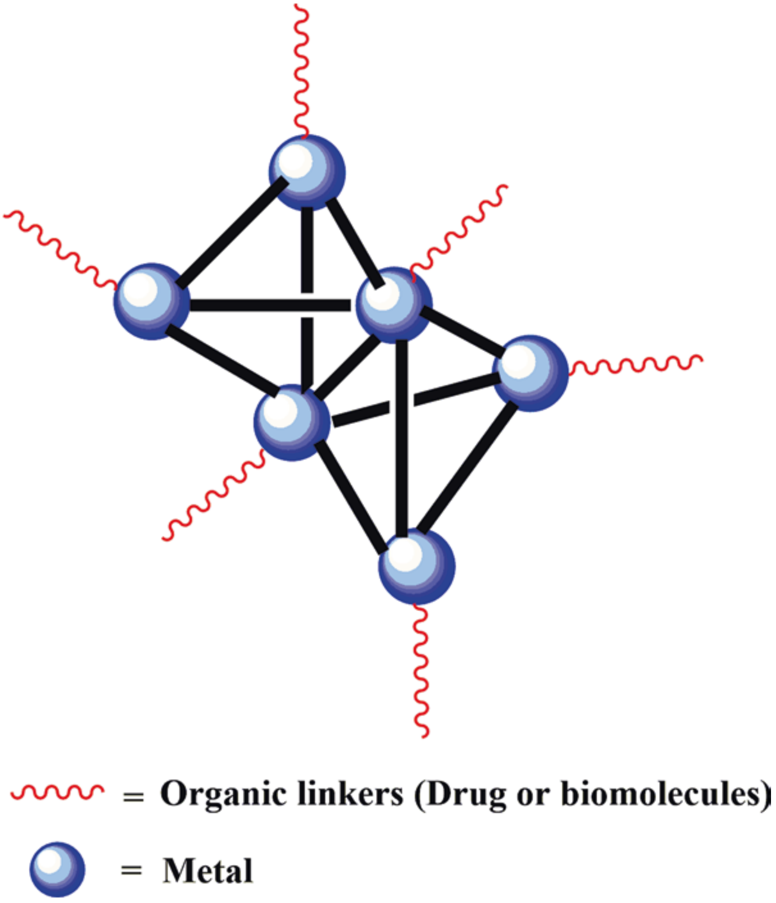

Fig. 13.3 The conjugation reacting model of the covalent post-synthetically modification

The drugs and biomolecules can covalently bind to the metal in MOFsN. In 1999, the first effective covalent post-synthetic modification of MNPs was carried out by Kiang et al. (Kiang et al. 1999). Furthermore, many researchers put their sincere efforts on covalent post-synthetic modification by using organic linkers like peptides, DNA, amine-modified cytosine, carboxylic acids, hydroxyls and thiols, green fluorescent protein, and biomacromolecules such as nucleic acid and protein and further studied for development of numerous applications in the field of biochemical and biomedical sciences (Begum et al. 2019; Kalaj and Cohen 2020; Ivancova et al. 2019; Guo et al. 2020). However, successful covalent conjugation of biomolecules is possible due to the presence of electrophiles in MOFsN with a strong binding ability (Nowroozi-Nejad et al. 2019).

The covalent conjugation plays a critical role for structural and functional control in MOFsN responsible for generating porosity and flexibility, which are afforded for designing materials specifically moderated toward future potential applications (Vardhan et al. 2019). Currently, covalent post-synthetically modified MOFsN show significant applications, and their physicochemical and biocompatible properties make them encouraging materials for drug storage, sustainable drug delivery systems, bio imaging, biosensing, magnetism, and gas adsorption (Chen and Wu 2018; Cui et al. 2018; Rojas et al. 2019).

1.1.2 Coordination Modulation and Coordinative Post-Synthetically Modification

The organic linkers such as drugs, biomolecules are coordinated to the metal for the synthesis of MOFsN through coordination chemistry, which includes ligand interchange. The coordination mechanisms are possible when the sidechain of the molecules has active functional moieties that bind to the metals for the genesis of networks with a higher degree of dimension (Cai et al. 2019a). The active terminals are the structural feature that facilitates amino acids (amino acids with carboxylic groups which provide a sequence of strong coordination approaches because of their huge negative charge density) and peptides to coordinate with central metal at definite angles and directions for the formation of MOFsN through coordinate post-synthetically modification (Rojas et al. 2017).

Generally, coordinative post-synthetically modification is significant to modify the surface functionality of MOFsN for developing biomedical applications, which can be possible during the synthetic methods (Segura et al. 2019). The major advantage of the coordination modulation synthetic method is the active surface modification of MOFsN, which is carried out during the synthetic process with biomolecules or simple organic molecules acting as interlocutors or modulators.

Many researchers have reported in situ coordination modulation process on surface modification by using DNA, biotin (Gkaniatsou et al. 2017), folic acid, porphyrin, phosphates, thiols, carboxylates, and imidazoles on the surfaces of MOFsN (Forgan 2019; Gkaniatsou et al. 2017; Abánades Lázaro et al. 2020; Kan et al. 2018; Park et al. 2016; Röder et al. 2017; Wang et al. 2018).

He Tin et al. have reported that the MOFsN microcapsules have a crystalline type material and rigid reticular structures that were prepared by using polymers or supramolecules through coordinative post-synthetically modification (He et al. 2018). They have expanded a competitive coordination modification in order to synthesize this MOFsN based microcapsules with new bowl-like structures. The formation of bowl-like structures of MOFsN is due to partial disintegration through the competitive reagents. In addition to this, flexibility is introduced into the rigid skeletons which is an innovative approach in designing MOF-based microcapsules with novel structures.

Hence, coordination mechanism is significant to produce extended active surfaces of MOFsN network structures, though green and scalable synthesis with very high chemical stability and better porosity. These types of MOFsN contain a high degree of dimensionality and fundamentally the most attractive structural features associated with their use as ligands also called surface ligand exchange (Cui et al. 2020).

1.1.3 Noncovalent Post-Synthetically Modification

The noncovalent post-synthetically modification consists of molecular interacting mechanisms such as electrostatic interaction, hydrogen bond interaction, Vander Walls forces, and dispersion forces. These molecular interactions between organic linkers and metals generate intermolecular forces (IMF) which are responsible for the binding of metal with molecules having active functional moieties.

However, MNPs are not stable and get agglomerated quickly they are stabilized using various stabilizing agents like PVA, PEG, citric acid, and so on (Zhao and Asuha 2010; Laurent et al. 2008). The MNPs of 1–100 nm size have been extensively studied, and their colloidal suspensions used as ferrofluids having many potential applications in electronics, material sciences, pharmaceutics, tissue engineering, biophysical, nanomagnetic thin films, nanomagnetic coating, magnetic biosensor, interacting activities inducing agent, biomedical, and biochemical sciences (Obaidat et al. 2019). Apart from having fundamental scientific interests of MOFsN, they can also assist in the development of novel applications in various electrical, industrial, and medical fields. Their exceptional and novel size dependent properties have developed remarkable research for designing new applications in nanotechnology and biomedical sciences (Jiang et al. 2019). Their synthesis and surface engineering are widely been studied due to their potential applications in magnetic fluids (Wu et al. 2016), catalysts (Cardoso et al. 2018), biotechnology, magnetic resonance imaging (Zhou et al. 2019), data storage (Noqta et al. 2019), DNA separation (Noqta et al. 2019), alternative current (AC) magnetic field-assisted cancer therapy (Shengzhe Zhao et al. 2020), and environmental remediation of heavy metals (Jawed et al. 2020; Thakare et al. 2021), drug delivery, and hyperthermia treatment (Gholami et al. 2020). Due to their versatile applications, the stability of dispersed MNPs plays a critical role with a milder tendency for self-aggregation via coulombic forces (Yew et al. 2020). However, the MNPs are not stable and get agglomerated quickly and can be stabilized by using surfactants such as SDS, CTAB, MTOAC, Tweens, cinnamic acid, oleic acid sorbitol, and zwitterions (Ansari et al. 2020). The MNPs are involved for suitable surface modifications by several coating agents for instance dimercaptosuccinic acid (Gutiérrez et al. 2019), dextran, starch, PEG, chitosan, proteins, amino acids, silica, and others (Nosrati et al. 2017). In 2011, Wiogo et al. have described a stabilization of MNPs in biological media by a fetal bovine serum to increase the surface area to modify the MNPs for in vivo biomedical uses (Wiogo et al. 2011).

The tribasic citric acid was used by (Cheraghipour et al. 2012) to stabilize the superparamagnetic nanoparticles which not only increases the dispersity of MNPs in water but the terminal carboxylic group can give more sites for surface modification (Cheraghipour et al. 2012). Thus, MNPs could play a critical role in molecular, bimolecular, and electronic interactions with various stabilizers for maintaining their stability to optimize their structural and geometric activities. The dispersion studies of surface engineered MNPs with polar protic solvents such as water, ethanol, and buffers (phosphate and tris) have been reported (Pandya and Singh 2015). The studies on nonaqueous dispersant medium with a series of organic acids and dendrimers with their increasing alkyl chain have been reported by S. R Pandya et al. (Pandya and Singh 2015). Furthermore, they studied their dispersion activities and optical behavior directly with aprotic polar, protic–aprotic, and dendritic–aprotic polar solvents as dispersant systems. The dispersion activities and optical behavior in a series of first-tier dendrimers for their perfect stabilized aggregation and this impact of aggregation have been monitored through their UV interactions. An impact of a series of FA, OA, and CA that produce H+ in 1:2:3 ratios could critically influence their size and aggregation patterns. However, the above-mentioned studies are simple in nature and even enhance the purity and stability effects of the nanoparticles. The molecules like nucleoli, peptides, cysteine, pyrene, PEG, glucose dehydrogenase, and methylene green have been used and linked to the surface of MOFsN through controlled supramolecular interactions and several strong interactions (Komiyama et al. 2017).

1.1.4 Modifications on the External Surfaces

These modifications are commonly known as the absorbent mechanism and consists of the conjugation of biomolecules to the silica coating on the MOFsN. The organic linkers can be reformed on the outer surface of MOFsN by using silica-coated surfaces as an active absorbent required to adhere to the additional drugs or biomolecules to the surface of MOFsN. Several researchers and their coworkers successfully attached the biomolecules such as oligopeptide, folic acid, on the surface of MOFsN with a silica coating for developing sustainable and targeted drug delivery systems (Siafaka et al. 2016; de Araújo 2017; Achilefu and Black 2018). The difficulties of silica coating methods are sometimes toxicity caused by excess use of silica and hence creates a challenge for the developing applications (Gubala et al. 2020). The MOFsN has exceptional structural properties and evolution in the field of nanotechnology, hence, there are lots of studies on synthetic processes and post synthesis surface modifications of MOFsN for biological applications.

2 Biomedical Applications of MOFsN

Currently, investigation of MOFsN has attracted much attention to develop biomedical applications (Sun et al. 2020) because MOFsN are shown to have a hollow structure with some extraordinarily larger surface areas inside the molecules (Zeng et al. 2015). The organic–inorganic metal-fused systems might be easily reformed due to the organic branched linkers with active functional groups and synthesized through the self-assembly mechanism of metal-attaching species, which leads to M_4 type (multipurpose, multitasking, multitracking, and multifaceted) properties. The MOFsN have well-defined porosity types of structures that makes them different from other nanoparticle structures with higher potential activities and M_4 properties required for various biochemical and biomedical applications. MOFNs have drawn attention due to their various potential uses in the field such as gas storage, bio separation, biocatalysis, photonics, biosensing, MRI, pharmaceutics, biocatalyst, and biomedicine (Horcajada et al. 2012). Figure 13.4 depicts various functional applications of MOFsN in the various field of sciences (Fig. 13.5).

2.1 *Drug Delivery Systems*

Developing a sustainable and targeted drug delivery system is essential and significant to reduce side effects with increasing therapeutic efficacy of drugs through metabolic actions. Well-defined structure, larger surface area, outreach porosity, multi fabricated pore size, and outstanding surface functionalization of MOFsN are considered as encouraging nanocarriers for efficient drug delivery systems (Sun et al. 2020). Hence, exceptional chemical and physical properties such as surface adsorption, covalent binding, encapsulation, and functional molecules as building blocks of MOFsN make them significant nanocarriers for targeted and intracellular drug delivery system.

Recently, MOFsN is evolving hybrid high porosity nanomaterials that are assembled from metal ions or clusters associated with organic linkers and they have ever-increasing attention due to the exceptional physical structures and wider potential applications (Cao et al. 2020). The MOFsN along with high absorptivity, porosity, controlled drug-release mechanism, large storage capability, and hydrophobic (non-polar)–hydrophilic (polar) nature have shown potential use for sustained and targeted drug delivery mechanism by accommodating drug molecules through conjugation or encapsulation (Rasheed et al. 2020; Cunha et al. 2013). The structural features of MOFsN enabled high drug loadings efficiency with controlled release moderated by simulated physiological and chemical conditions for hydrophilic and hydrophobic drugs (Horcajada et al. 2010; Wang et al. 2020). Table 13.1 summarizes some reported applications of MOFsN in the drug delivery system.

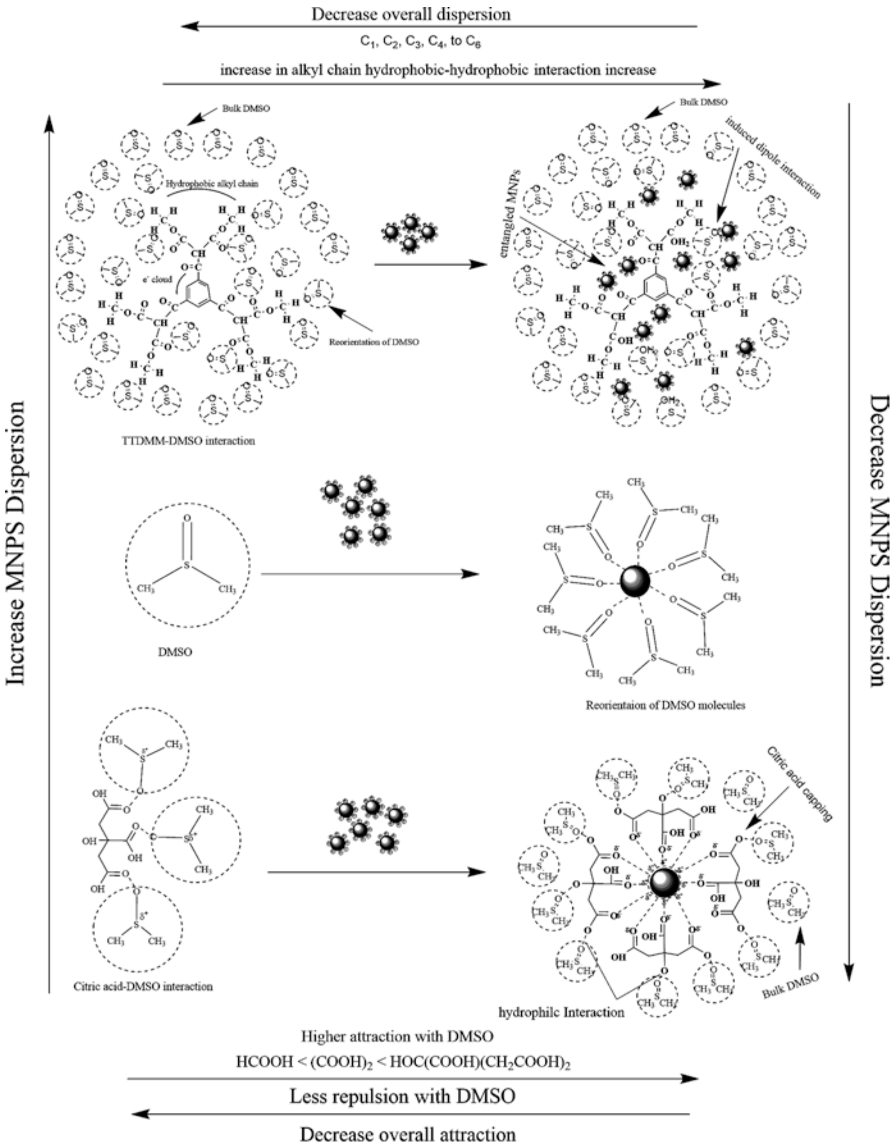

Fig. 13.4 The illustrations representing the surface coating of magnetic nanoparticle as the core for better stabilization (Pandya and Singh 2015)

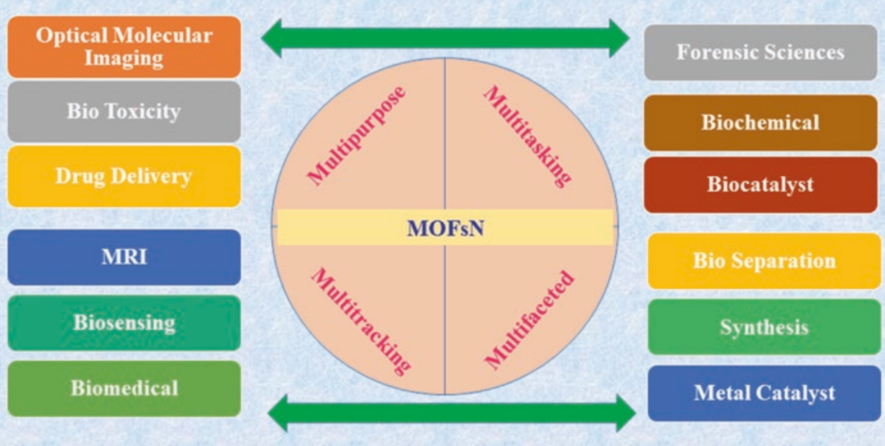

Fig. 13.5 The functional applications of MOFsN-based materials in various field of sciences

2.2 Magnetic Resonance Imaging (MRI)

MRI is an impressive diagnostic analytical tool for noninvasive (does not include a break in the skin) tomography of the inside arrangement and functions of living organisms as well as local properties of tissues that provides high longitudinal resolution images and deep tissue penetration without any involvement of radioactivity (Chen et al. 2020a; Brown et al. 2014). Basically, due to limited resolution, low imaging depth of penetration, poor spatial resolution, and low sensitivity in MRI, it becomes necessary to use contrast agents that play a vital role to improve MRI sensitivity through refining the contrast in areas with brighter or darker signals that are regularly administered in high doses (Boxerman et al. 2020). To overcome this problem, various studies have concentrated on developing multitasking imaging contrast agents or probes that incorporate several image improving activities into a particular system to achieve multitracking imaging functions in MRI (Shang et al. 2017). In this context, MOFsN has attracted great attention as promising MRI contrast agent attributable to its exceptional paramagnetic/superparamagnetic properties which can create large magnetic centers under the influence of an external applied magnetic field (Wong et al. 2020; Giliopoulos et al. 2020). Hence, such central shell hybrid MOFsN provides an ideal platform for targeted delivery of other imaging and beneficial agents to unhealthy tissues because they are effective at very lower concentrations and can also be engineered target specific through surface modification using essential molecules (Chowdhury 2017). Also, MOFsN with carboxylate as organic linkers shows a high capacity for drug loading or release and T_2-weighted (MRI sequence to quantify effectiveness) MRI properties with low toxicity (Li et al. 2015; Horcajada et al. 2010).

Meng et al. reported MOFsN having Fe^{3+} assembled octahedral structure by using a solvothermal reaction and graphene oxide (GO) as an organic linker,

Table 13.1 Some reported applications of MOFsN in drug delivery system

Metal/oxide	Organic Linker	Drug	References
Zn_4O	3,5-Dimethyl-4-carboxypyrazolato	5-Fluorouracil, caffeine, benzocaine, and para-amino benzoic acid	Noorian et al. (2020)
Zn (II)	Imidazole and polyacrylic acid	Doxorubicin	Cai et al. (2019b)
SiO_2	Poly(ethylene glycol) modified folic acid (PEGFA)	Doxorubicin	Xie et al. (2018)
Zr	Diaminostilbenedicarboxylate	Ibuprofen	Sarker et al. (2019)
Fe (III)	1,3,5-Benzene tricarboxylic acid	Caffeine	Cunha et al. (2013)
Fe/La	Benzene-1,3,5-tricarboxylic acid	Doxorubicin	Lin et al. (2019a)
Zr (IV)	1,4-Benzenedicarboxylate	Caffeine	Kandiah et al. (2010)
Fe (III)	Pyridine-3-carboxylic acid	Nicotinic acid	Miller et al. (2010)
Zr	Phosphonoacetate ligand	Cisplatin	Lin et al. (2019b)
Fe (III)/Fe_3O_4	Carboxymethyl dextran, trimesic acid	Doxorubicin/daunorubicin	Cherkasov et al. (2020)
Zn	$(CH_3COO)_2$ and imidazolate-2-carboxyaldehyde (2-ICA)	Methylprednisolone	Xu et al. (2020)
Cu	Gelatin microsphere biopolymer	Methotrexate	Md et al. (2018)
Zr (IV)	Amino-triphenyl dicarboxylic acid	Doxorubicin	Chen et al. (2018)
Zn	Terephthalic acid	Oridonin	Chen et al. (2019)
Cu/Zn	1,2-Bis(4-pyridyl)ethylene/hydrogel	Antibacterial effects	Gwon et al. (2020)
Fe	Sodium dodecyl sulfate (SDS)	Insulin	Zhou et al. (2020)
Fe	O-carboxymethyl chitosan	Doxorubicin	Lin et al. (2020)
Zr	Triethylamine	Camptothecin	Chen et al. (2020b)
Mg	Tetrakis (p-benzoic acid) pyrene	Fluorouracil	Hu et al. (2020)
Fe	Trimesoyl1,3,5-trimethyl malonate ester (TTDMM) dendrimer	Silibinin and methotrexate	Pandya and Singh (2016)

offering a strong T_2-weighted contrast with low cytotoxicity (Meng et al. 2017). D. Zhang et al. reported innovative cell membrane-coated porphyrin MOFsN based O_2-evolving photodynamic therapy (PDT) for homologous cancer cell targeting along with MRI and fluorescence imaging (dual mode imaging) biomedical applications (Zhang et al. 2019). The MOFsN has a superparamagnetic nature accountable for the enhancement of contrast to distinguish death and live tissues with limitless penetration and admirable imaging aptitude in MRI which could serve as robust and innovative materials to develop biomedical applications (Peller et al. 2016).

Hence, MOFsN are transpiring hybrid materials made up of metal ions/clusters as a core attached to organic linkers and their ability to transport huge numbers of paramagnetic and superparamagnetic metal ions (Pei et al. 2014). These MOFsN are considered as superlative and potentially offer advantages as MRI contrast agents and enhanced attention due to the probability of three-dimensional (3D) images with high longitudinal resolution (Qin et al. 2017).

2.3 Biosensor

Recently, several research scientists have been working on new and novel applications of MOFsN to exploit them as electrode triggered materials that are required for evolving electrochemical activity with high selectivity and sensitivity to diagnose trace amounts of biologically active molecules. Physicochemical properties such as pore sizes, high surface areas, multitasking surface activities with active sites of MOFsN are responsible for their use as an ideal biosensor agent for electrochemical reactions (Wu et al. 2015; Carrasco 2018). The reported typical data of the MOFsN used as a biosensor for various biomedical sensing is given in Table 13.2 (Zhou et al. 2018).

Generally, post-modified methods were used for the synthesis of MOFsN-based electrode biosensors with the linking of $-NH_2$ or $-SH$ functional groups and many others (Yang and Yang 2020). Some have rarely been reported MOFsN with significant electrochemical activity as electro biosensors without post-modification synthetic methods (Liu et al. 2017b). However, some of most electrochemical active MOFsN restrict over application in the field of electrochemistry detection due to poor water stability, which is related to electrochemical reactions generally carried out in a water environment (Fang, Zong, and Mao 2018; Taylor, Dawson, and Shimizu 2013). The MOFsN-based biosensors categorized in groups such as raw MOFsN, grafting approach, and bulk MOFsN according to their complexity and concerning the preparation methods for biosensor development (Carrasco 2018). The MOFsN having controlled size, shape, and morphology along with unique conductive properties and their preparation includes inorganic metal and organic linkers that have significantly enhanced the performance for biosensor development (Yang et al. 2018).

Table 13.2 The reported data of MOFsN based biosensors (Copyright 2018, Nanoscaled Metal-Organic Frameworks for Biosensing, Imaging, and Cancer Therapy, Advanced Healthcare Materials 7 (10): 1800022 (1–21))

MOFsN	Analyte	Recognition method	Recognition limits	References
H(2)dtoaCu	ds-DNA	FBS	1.3×10^{-9} m	Chen et al. (2013)
Zn(II)-MOFs	HIV ds-DNA	FBS	10×10^{-12} m	Zhao et al. (2016)
PCN-222@SA	DNA	ES	0.29 fM	Ling et al. (2015)
Dy-MOFs	Ebola virus RNA sequences	FBS	160×10^{-12} m	Qin et al. (2016)
MIL-101	Thrombin; oxytetracycline	FBS	15×10^{-12} m; 4.2×10^{-9}	He et al. (2017)
Cu-3(BTC)(2)@ SiO_2/BDC-PANI	Atrazine	CIS	0.01×10^{-9} m	Chen et al. (2017)
Hemin-MOFs/ PtNPs	FGFR3 mutation gene	ES	0.033 fM	Bhardwaj et al. (2015)
Fe-MIL-88B-NH_2	Alpha-fetoprotein	CMA	3 pg mL^{-1}	Zhou et al. (2016)
Au/hemin@ MOFs	Thrombin	EAS	0.068×10^{-12} m	He et al. (2017)
Fe3O4/g-C3N4/ HKUST-1	Ochratoxin A	FAS	2.57 ng mL^{-1}	Hu et al. (2017)
AuNPs/Ce-MOFs	Lipopolysaccharide	EAS	3.3 fg mL^{-1}	Shen et al. (2016)
Pt@ UiO-66-NH2	Telomerase activity	ES	$2.0 \times 10^{(-11)}$ IU	Ling et al. (2016)
516-MOF	Vomitoxin; salbutamol	EBS	0.70 pg mL^{-1}; 0.40 pg mL^{-1}	Liu et al. (2017a)
Mn-BDC@ MWCNT	Ascorbic/uric acid, dopamine	ES	0.01; 0.002; 0.005×10^{-6} m	M.-Q. Wang et al. (2016)
Ag@Au nanoprism MOFs	Glucose	PBS	0.038×10^{-3} m	Huang et al. (2017)
MIL-100(Cr)-B	H_2O_2	ES	0.1×10^{-6} m	Dai et al. (2017)
pFeMOF/OMC	H_2O_2	ES	0.45×10^{-6} m	Liu et al. (2017b)
R-UiO	Intracellular oxygen	RLS	–	Xu et al. (2016)

FBS Fluorescence biosensor, *FAS* Fluorescent aptasensor, *ES* Electrochemical sensor, *EAS* Electrochemical aptasensor, *EBS* Electrochemical biosensor, *CIS* Conductometric immunosensor, *CMA* Chemiluminescence metalloimmunoassay, *PBS* Paper-based biosensor, *RLS* Ratiometric luminescent sensor

3 Conclusion

The MOFsN are an interesting class of organic–inorganic metal combined porous crystalline nanomaterials with a systematic arrangement of positively charged metal ions surrounded by multifunctional organic molecules or ligands and have attracted increasing attention in current years in fundamental scientific interest and potential attractive several applications. The MOFsN consider as M_4 (multipurpose, multitasking, multitracking, and multifaceted) types materials with innovative and improved structural activities which play an extremely important role in increasing the biomedical and biochemical applications. Besides this, MOFsN as nanosized materials with variable physical, chemical, and biological properties that are more efficient as compared to bulk materials. The modern innovative and possible applications required a better potential metal–organic nanostructure-based formulations with extraordinary structural activities perceived as a tool and riders for biomedical applications such as drug delivery, MRI, biosensors, biocatalyst, bio separation, and many more associated with a decrease of environment and human health risks features. According to the intensified investigations on MOFsN exhibit important advantages and outstanding materials with minimized toxicity, which shows impacts at all stages of the development and evaluation of biomedical applications, which will increase their use in research areas. More active surface functionality of MOFsN could be designed and synthesized in order to meet the increasing biomedical requirements. MOFsN are excellent contrast agents that provide a new platform for the detection and diagnostics therapy in MRI. The synthesis and characterization of MOFsN for biocatalysts and bio-separation, biosensor, purification, drug delivery, medicine, energy-harnessing, and energy-storage fields show high growth and significant increase during the last decade. The scope and focus of this chapter are to study the strategies of MOFsN fabrication and its use for the expansion of biomedical applications.

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