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Review Article

Recent Progress In Metal Organic Framework As Drug Delivery Platform

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ABSTRACT

Recently, there has been a rise in interest in the emerging topic of porous coordination polymers and metal organic frameworks. The storage and separation of gases, sensors, catalysis, and functional materials are just a few of the applications that these microporous materials have discovered in the last ten years. Better coordination of organic frameworks with porous metals is needed. Polymers with particular functions. Gaining a thorough knowledge of the connection between is a crucial topic. Employing contemporary theoretical methods, one can determine molecule characteristics and structures, preferred adsorption sites, and attributes. It is essential and crucial to develop a regulated drug delivery system in order to minimize adverse effects and improve the therapeutic effectiveness of medications. The scientific community has paid close attention to metal-organic frameworks (MOFs) and nanoscale MOFs (NMOFs), porous hybrids built by polydentate bridging ligands and metal-connecting nodes. Superior porosity, compositions and architectures, and simpler surface modification. Encapsulate small compounds in monodisperse zeolitic imid-azolate framework-8 (ZIF-8) nanospheres. The single-crystalline, homogeneous 70 nm ZIF-8 nanospheres with small-molecule encapsulation are identified by electron microscopy, powder X-ray diffraction, and elemental analysis. Several little compounds, including the anticancer medication camptothecin and fluorescein, were encapsulated inside the Framework for ZIF-8. ZIF-8 nanospheres with fluorescein are being evaluated in MCF-7 breast cancer cells. Cell line showed low cytotoxicity and internalisation of cells. MOF-based drug delivery systems (DDSs) with high drug loading capacity, strong physiological stability, and great biocompatibility and targeted, controlled medication release.

INTRODUCTION

After the introduction of MOFs in 1995, the field started to pick up steam in the late 1990s. Williams

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et al. presented a study on MOFs called HKUST-1 in 1999 that were constructed from copper-based clusters and benzene tricarboxylic linkers. Metal-organic frameworks (MOFs), which self-assemble from organic linkers and metal ions or clusters, are a potent platform for creating functional materials and are an active research area of porous materials [1]. Porous coordination polymers (PCPs), also known as metal-organic frameworks (MOFs). They are crystalline materials with highly ordered structures made up of networks made of single metal ions or metal clusters joined by multidentate organic groups functioning as bridges Linkers. In 1960, the phrase coordination polymers first arose. however, significant advancement in this sector has largely come from When Yaghi and associates first used the term "metal-organic" in 1995 frameworks (MOFs) (MOFs). Polyhedral metal-organic compounds PMOFs are different from conventional MOFs, which feature significant voids. and pores with open channels [2]. Up till now, a number of synthetic methods have been investigated for the creation of PMOFs. Among the simplest methods to embellish them. The goal of changing the physico-chemical characteristics of the organic spacer bearing is either by post-synthesis modification or functional groups. The synthesis of MOF by using metal atoms as connectors and organic linkers was shown in Fig.1.

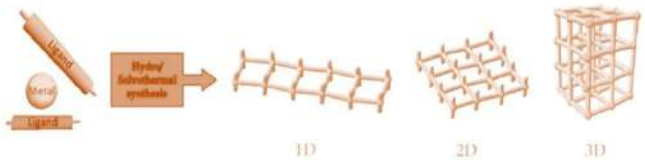

Fig.1 of Synthesis of MOF by using metal atoms as connectors and organic linkers.

Due to its intriguing multifunctionality, metal-organic frameworks (MOFs) have recently experienced significant development in the field of material science. New ordered porous MOFs display a number of benefits. like a lot of surface area, customizable composition and structure, sufficient biocompatibility, and biodegradability in nature. Thousands of MOFs have currently been reported, but the majority of They were utilised in a few strategic fields, including chemical sensors and gas separation. With the advent of MOF applications in biomedicine, an increasing number of Researchers have dedicated their time to studying these topics, such as gas delivery and storage. medication delivery, transmitter, and Among them, MOFs have been a potential tool to increase the potency of already-available medications and reduce side effects [3]. Much research had been done, particularly in the area of cancer therapy. For instance, Zheng and his coworker have utilised ZIF-8 in reports to Horcajada et al. have effectively loaded busulfan into an encapsulate of doxorubicin MIL-100. Various MOF structures such MOF-5 structure, HKUST structure26, UiO-66 structure as shown in in Fig.2.

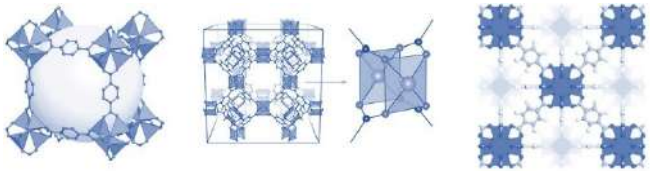

Fig.2 (a) MOF-5 structure, (b) HKUST structure26, (c) UiO-66 structure.

One of the deadliest illnesses in recorded human history is still cancer. It poses a serious threat to world health, endangering both wealthy and developing nations. A number of many cancer therapies, including surgical procedures, chemotherapy , radiation, and frequently combined therapies are necessary to treat or manage certain malignancies. Drug delivery techniques often rely on one of two organic or inorganic, carries. organic transporters like liposomes The medicines are enclosed in micelles and polymersomes. drug [4]. They are biodegradable, have biocompatibility, and can chemically altered to enhance their release characteristics and raise their buildup at the

location of the tumour. Zn-TDPAT type of MOF structures shown in Fig.3.

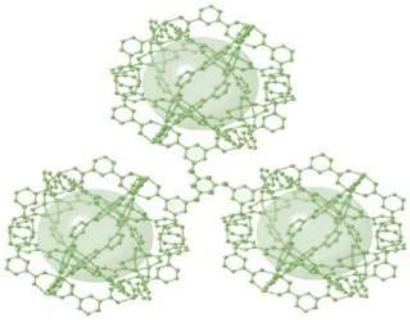

Fig.3 of Structure of Zn–TDPAT.

However, because their porosity is poorly defined and their contacts with the drug are weak, these carriers experience uncontrolled release. The second variety Iron oxide nanoparticles are an example of inorganic nanovehicles. Quantum dots, carbon nanotubes, and other nanoparticles are either conjugated to the therapeutic molecules or provide the agent with a lot of surface area to encapsulate (and thereby adsorb. The main negative They have poor biocompatibility (i.e., high immunogenicity). Therefore, the creation of a substitute is necessary immediately. safer and more effective drug delivery system. The another type of MOF UMCM-2: two Zn4O cluster coordinated to three T2DC structure shown in Fig. 4.

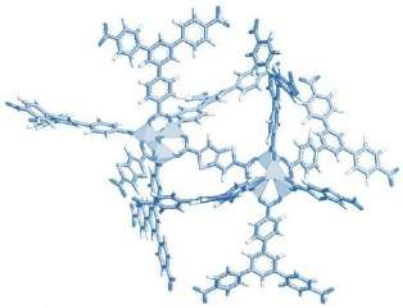

Fig.4 Structure of UMCM-2: two Zn4O clusters coordinated to three T2DC.

Every year, millions of people die from cancer, a threat to their health. The most popular kind of treatment is still chemotherapy. However, due to inherent constraints, such as unfavourable side effects, the traditional direct administration of medicinal medications to patients is no longer appropriate. poor biodistribution and pharmacokinetics[5].

1.1Merits and Demerits:

Merits:-

- Large intestinal interspaces.
- Porous structure.
- Abundant active sites.
- Facile preparation

Demerits:

- Poor conductivity.
- High cost of MOF;s matrix.

3. Formulation aspects of MOFs

3.Production techniques

4.Applications

5. CURRENT Status of MOF

6. FUTURE PROSPECT

1.2 Linkers:

1 Dicarboxylic acids:

Eg:- Oxalic acid, malonic acid, succinic acid,glutaric acid, terephthalic acid.

2.Tricarboxylic acids:

Eg:- Citric acid trimesic acid.

3 Azoles:

Eg:- 1,2,3-triazole, pyrrodiazole.

4 Amines:

5.Nitrates:

1.3 Formulation and Composition of MOF:

MOF composed of two major components are as follows:

1.Metal ion or clusters:-

Eg:- Zn(II), Cu(II), Fe(III), Zr(IV).

2.Organic molecules or linkers:-

Eg:-Benzenedicarboxylate(BCD), Biphenyldicarboxylate(BPDC), Terphenyldicarboxylate (TPDC).

1.4 Synthesis of MOF's

Synthesis with drug loading shown in Fig.5.

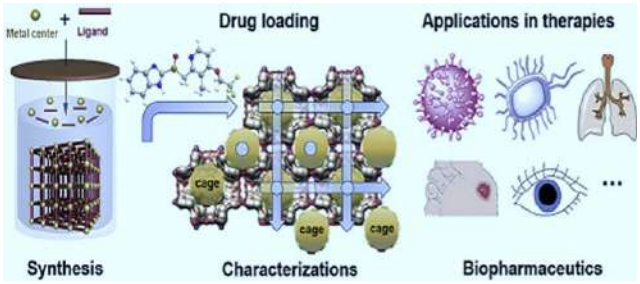

Fig.5 of Synthesis with drug loading of MOFs.

Metal-organic framework are synthesized by following methods:-

A. Hydrothermal and solvothermal methods:-

a). The synthesis process involves generating single crystals from an aqueous solution under high pressure and 400C temperature in an autoclave.

Eg:- Control grain size, crystalline phase, particle morphology, surface chemistry.

b).An autoclave that has been heated to a temperature over the boiling point of the preferred solvent is used to seal the precursor after combining it with the appropriate solvent.

Eg:- Copper terephthalate MOF's using solvothermal process employing dimethylformamide as solvent heating the reaction to 120C for 24hrs.

Merits:-

- Promote the solubility of involve segments.
- Nucleation growth.
- High crystallinity.

Demerits:-

- Long reaction time.
- Large amount solvents.
- Easy to produce byproducts.

B. Microwave and ultrasonic synthesis:-

Electromagnetic waves having frequency between 300 and 3000 MHZ are known as microwaves. Two components of radiation on the impact of electricity and magnetism on chemical formation. Insufficient maximum MV energy (0.037 kcal mol) to break chemical bonds in most organic molecules. For instance, MIL-101 contains microwave radiation to create the terephthalate limker. When considering MOF's industrial uses, ultrasonic synthesis is a quick and environmentally friendly process. Eg:- Nickel-based MOF's. The microwave synthesis shown in Fig.6.

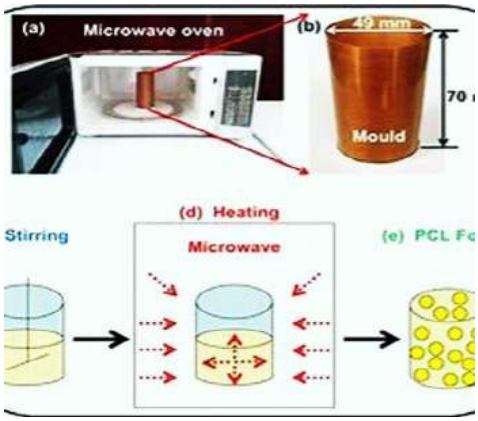

Fig.6 of Microwave synthesis.

Merits:-

- A Facile and rapid strategy.
- Small and uniform particles of MOF's.

Demerits:-

- Formation of secondary phase.

C. Mechanochemical synthesis:-

The chemical route involves the formation of four transient intermediary phases before the MOF-74 end product crystallises. It has been looked at how to make MOF-74 mechanically and chemically from ZnO and 2,5-dihydroxyterephthalic acid utilising DMF as a liquid addition.

Merits:-

- High efficiency.
- Less or no solvents.

Demerits:-

- Decreased pore volume.
- Lower crystalline.

D. Electrochemical synthesis:-

When MOFs are synthesised, metal ions are added electrochemically rather than through the solution of the appropriate salt or through their production after the reaction of the metal with the acid.

Merits:-

- Continuous operation.
- Lower demands of solvents.

- Mild reaction conditions.
- Short reaction time.

Demerits:-

- Under N2 atomosphere.
- Varied structure.
- Lower yield.
- Easy to produced byproduct

E. Microemulsion synthesis:-

Three homogeneous microcrystals were produced by this controlled morphology synthesis process using Co-MOF-74 crystals.

Merits:-

- Different particles with controlled composition and morphology.

Demerits:-

- Low yield of products.
- Toxicity of solvents and surfactants.

F. Diffusion synthesis:-

CD-MOFs and Contra-diffusion method synthesis solutions are separated by porous membranes to form the vapour dissusion technique, and MOF-70 is manufactured using diffusion methods.

G. Continuous flow synthesis:-

Zirconium-based MOFs UiO-66 were created in a reactor utilising supercritical carbon dioxide, and parts of the reactor, such as the thermocouple and back pressure regulator, were identified. Carbon dioxide pressurised for reactor use was provided by a gas cylinder.

Merits:-

- Rapid synthesis.
- Good porosity
- Controllable particle morphology

Demerits:-

- Easy to produced byproducts.
- Difficulty in MOF's isolation.
- Large amount solvents.

H. Spray-drying synthesis:-

This synthesis approach and strategy makes it possible to build multicomponent MOF superstructures and encapsulate superstructures.

I. Solvent evaporation synthesis:-

It entails dispersion in a volatile solvent like dichkoromethane and emulsification of the polymer in an aqueous phase. ETHYL ACID with CHLOROFORM.

Application of MOF's:-

A. Gas storage and separation:-

MOFs' internal nanopores can be used to store gas. A way for separation that is energy-efficient is provided by MOF-based membranes.

B. Catalysis:-

The original development investigations of these materials used MOF's as heterogenous catalysts, a sector that has shown tremendous expansion in recent decades.

C. Removal of harmful and toxic chemicals:-

Adsorption characteristics of different MOF-based materials were evaluated and compared to commonly used adsorbents.

D. Sensing:-

For bioimaging, MOF's sensors published results based on lanthamide ion luminescence quenching. Water vapour and oxygen are detected via MOF-based sensing.

E. Nonliniar optics:-

Many optical applications, including optical signal processing, optical computers, ultrafast switches, ultrashort pulsed lasers, sensors, and laser amplifiers, depend on it.

F. Magnets:-

For the immobilisation of enzymes, the use of nanozymes, and the development of novel functional nanomaterials, we need a magnetic metal organic framework.

G. Solar fuel energy:-

transforming solar energy, primarily through solar-driven conversion, into fuels. Utilizing sunlight, carbon dioxide and water vapour are directly converted to hydrocarbon fuel.

H. Metal corrosion inhibition:-

Inhibition Corrosion entails the development of a coating, sometimes a passivation layer, which blocks corrosive substances from reaching the metal.

I. **Biomedical application:-**
In biological applications such as drug delivery, biosensing, bioimaging, biocatalysis, drug transporters, and contrast agents, MOFs offer a lot of potential.

1.4 Evaluation of MOF's:-

A. **Size:-**
Zetasizers and mastersizers assess particle size and zeta potential to determine size.

B. **Morphology:-**
By using an atomic force microscope, a scanning electron microscope, and a transmission electron microscope, morphology can be determined.

C. **Encapsulation:-**
By using HPLC and ultracentrifugation, encapslation is determined.

D. **Stability:-**
The stability chamber determines stability.

E. **Crystalization:-**
PXRD, DSC, and Raman spectroscopy are used to determine crystallisation.

F. **Polymorphism:-**
DSC, XRD, and Raman spectroscopy are used to determine polymorphism.

G. **Drug release:-**
By using a franz diffusion cell and a dialysis bag, drug release is determined.

1.5 Structure of MOF:-

A coordination polymer typically consists of organic groups acting as linkers and metal atoms acting as connectors. The environment for geometry and coordination is solely dependent on the metal's properties. Unlike zeolites, which are constructed of MOFs are composed mostly of tetrahedral building blocks, but can also be created from a wide range of inorganic pieces. For a specific shape, a restricted number of high-symmetry topologies of fragment It is feasible to achieve stable networks [16].

There are just a few high-symmetry topologies that can produce a stable network for a particular fragment shape. Consequently, for a specific form, a variety of chemicals should be possible to prepare. having the same preferred topology and just nature-based differences an isoreticular series, and the length of the linkers.

1.6 MOF's as drug delivery:-

When the right MOFs are used to manage drug delivery, bioactive compounds enclosed within metal organic frameworks can slowly release and supply increasing amounts of energy. Pure absorption of the target site repeated dosage, high dose required, changes in plasma drug level, poor tissue biocompatibility, serious toxicities, side effects, and premature excretion from the body from conventional DDS incapable to sustained release. Inorganic components like as carbon nanotubes, grapheme magnetic nanoparticles, iron oxides, silicon-based compounds, and gold nanoparticles were employed in many DDS developed to decrease side effects and boost treatment efficacy.

1.9 MOF's as targeted drug delivery:-

For luminescence sensing, photofunctionality, and chemical species detection in cancer therapy, MOFs are frequently used. Organic ligands, metal ions, and dyes contained in MOFs all contribute to the optical and photonic properties that are induced in MOFs. To circumvent the lack of specificity of conventional chemotherapeutic drugs, molecular targeted treatment has emerged. Cancel cells that have developed resistance can evade the cytotoxicity of both more modern molecularly targeted therapies as well as more traditional chemotherapy. Nanocarriers can accumulate in tumours thanks to a tumour biology trait called passive targeting that improves permeability and retention. Active targeting is accomplished by combining compounds that

attach to overexpressed antigens or receptors on target cells with nanocarriers delivering chemotherapeutics. The ability of anticancer medications to effectively treat cancer after administration to pass through bodily barriers and reach desired tumour tissue with little loss of volume or activity in blood circulation. Drugs should be able to kill tumour cells with precision once they have reached the desired spot without harming healthy cells. Nanoparticles may be able to meet both requirements for a successful medication delivery method.

1.9 Biocompatibility of metal-organic frameworks:

Several novel framework materials have been developed, and parameters for drug loading into them have been established, all riding on the popularity wave of MOFs as drug delivery agents. framework cracks have been confirmed, and the medication Evaluation of release from MOFs has been done. Though, the problems with biocompatibility and material destruction are not completely evident in biological media and demand additional study, data gathering, and ensuing data evaluation [19].

New medications and dosage forms must meet a number of conditions in order to be used in biomedicine. In order to have the intended therapeutic effect, it is crucial to administer the correct dose, while decreasing the patient's suffering. In fact, because of the It is crucial to choose the metal location out of the MOFs in light of its toxicity. Iron and zinc in particular are significantly high quantities are found in the body and Having high LD50s (half-lethal dosages), which makes They are most favoured for the creation of novel MOFs. Any Check for biorelevance in any molecule or ingredient. utilising Bertrand's diagram, which illustrates the connection between toxicity and the provided dose, the ideal physiological response, and the body's insufficiency, dose.

1.10 Computer simulation for the rational design of MOF-based materials for targeted drug delivery:-

The approaches utilised for the design of novel materials have been significantly extended by the use of computer simulation. Computational techniques can help with from the start, optimise and direct the experiment. levels of completion. Computer simulation can be used to study the self-assembly, structural and dynamic properties of the obtained aggregates, drug loading capacity, distribution and localization of TA molecules in the cavity of the container, stability of TA container complexes, mechanisms and rate of TA release, and more as applied to the design of drug delivery systems. to create or enhance the potential targeted drug delivery systems' competitive sorption and release, and to delivery.

1.11 Screening of framework materials:-

Because drug delivery systems have intricate, hierarchical structures, computer simulations of these systems must also include these characteristics. the least three things make up the collection of modelling components: the TA, its container, and the medium it is presented in interacting container system (for the convenience, the The latter is referred to as a biomedium). Consequently, before It is a simulation of the overall system operation. need to address several major issues that bring us closer to comprehending how the system works function. Understanding the mechanism of TA action, resolving the container structure, determining interaction parameters between the container and the medium, and estimating the strength of the interaction between the TA and the medium are particularly important. container. Consequently, computer simulation of the operation of Using framework materials for medication distribution is a complex, labor-intensive problem.

1.12 Modelling of the sorption of drug molecules in the framework cavities:-

The adsorption of drug molecules in the framework cavity serves as the primary design principle for drug delivery systems made of framework materials. Consequently, comprehension of the adsorption and development of the A crucial component of future development and studying these resources A simulation on a computer An invaluable tool that describes the sorption process in both qualitative and quantitative terms (using current levels of computational chemistry). According to the severity of the issue, and a suitable simulation method should be selected from a wide range of techniques with varying degrees of accuracy and dimension.

a) Quantum chemical calculations:-

Methods of density functional theory have been increasingly popular because to the ideal trade-off between precision and the minimal amount of processing time needed with modern computers. finding widespread application in modelling MOFs.165 The essential The selection of the exchange-correlation functional is problematic. (just functional from hereon) to convey the dependency of a multielectron's potential energy based on a specific set of electron densities parameters and approximations.

b) Monte Carlo method:-

For describing adsorption processes in the cavities of framework materials or other meso- or macroporous materials, force field-based and Monte Carlo approaches are frequently preferred. microporous substances. The two most well-liked such calculations, such the Metropolis algorithm The configurational bias algorithm 194 and algorithm 193.

C) Molecular dynamics:-

Molecular dynamics is yet another crucial technique for simulating MOF-based drug delivery devices. This approach shows that the course of The system's specific atoms are determined by integration of the equations of Newtonian mechanics motion. A system in the traditional molecular dynamics is regarded as consisting of point atoms with forces acting between them, indicated by efficient potentials.210

d) Molecular docking:-

It was suggested to employ molecular docking, which is typically used to model how proteins bind to drug molecules or to other proteins212, 213, to explore how pharmaceuticals interact to MOF pores. 183 This approach is centred on the pursuit of new configurations of estimation of the change in molecule after being bound in response to a shift in the positions of elements of a model system.

1.13 Multifunctional MOFs for Cancer:-

There are still many issues that need to be resolved, such as the current treatment modality, which is still restricted to traditional chemotherapy and whose therapeutic efficacy is constrained by multidrug resistance, despite the widespread development of numerous MOF-based therapeutic platforms in recent years. An enormous amount of work has gone into creating diverse theranostic nanomedical platforms, including adaptable MOF-based medicinal and/or diagnostic devices, to circumvent disadvantages to establishing superior anti-tumor effectiveness Core-shell MOFs nanocomposites have a high effectiveness. showed incredible promise as platforms for nanomedicine.

A. Polymer-Coated MOFs for Cancer Theranostics:-

By altering the thickness of the silica shell, the nanocomposites may be able to effectively regulate the release of Pt species, according to the controlled release behaviour of silica-coated NCPs. c(RGDfK) generated from silyl was then grafted onto the pre-fabricated nanocomposites' surface to promote cellular absorption. In vitro tests demonstrated The Pt-based NCPs have strong anticancer efficacies and good biocompatibility.

B. Magnetic Core–Shell MOFs for Cancer Theranostics:-

Because of its outstanding magnetic properties, using iron oxide as a core to create MOF-based theranostic probes for cancer diagnosis and treatment has received significant attention. characteristics in MRI, magnetic hyperthermia, and magnetic division Fu and colleagues, for instance, reported a theranostic core-shell nanocomposite of Fe3O4@UiO-66 that simultaneously done MRI in vitro and drug delivery in person.[19] The DOX and UiO-66 were enclosed in the shell UiO-66. The capacity to quickly gather the powerful superparamagnetic core Fe3O4 under an external magnetic field and ensure its in MRI.

C. Other Versatile Core–Shell MOFs Nanocomposites for Cancer Theranostics:-

In addition to the magnetic core-shell MOFs discussed above, great effort has been made to construct multifunctional core-shell MOFs as effective theranostic nanoplatforms. theranostic systems, as well as numerous adaptable MOF core-shell nanocomposites have demonstrated Applications for nanomedicine have a lot of potential.[19] For instance, Wang and colleagues presented the adaptable Mn3[Co(CN)6]2@ Synergistic SiO2@Ag nanocube platform treatment for cancer.

D. Flexible MOF-Based Theranostic Nanoplatforms:-

Due to the easy integration of multifunctional components by inclusion and post-synthetic alterations of MOFs, along with the mature synthesis of MOFs, recent developments in MOF preparation techniques have paved the way toward multitargeted nanomedical applications in both diagnostic and therapy. Besides the methods outlined above, drug compounds Using simple building elements for MOFs is one way to allow for future theranostic or multimodal development NPs. Dastidar and colleagues, for instance, reported several By including nonsteroidal anti-inflammatory drugs, MnII MOFs the organic linkage 1,2-bis(4-pyridyl)ethylene and medications (NSAIDs) (L) as a component of the material for drug delivery and cell imaging. For cell imaging, both of the synthesised MOFs demonstrated promise. due to the imaging agent L and the medication delivery molecules comprised.

1.14 Encapsulation strategy:-

The coordinated connections of inorganic metal/metal cluster nodes with organic polydentate ligands in an endless array result in MOFs, which are unique reticular hybrid solids. a predictable and tuneable amount of "void" volume, such as channels, cavities and pores. DNA or RNA, enzymes, etc. successfully been enclosed.

A successful encapsulation depends on the chosen cargo's chosen pore structure and the MOF carrier's pore size matching. In this regard, it appears that there are insufficient microporous MOFs for use in practise. The design and construction of this have required extensive work. production of MOFs with a higher pore size to accommodate greater cargos, as well as to increase loading capacity, but the pore size could have a number of negative impacts, such a burst. cargo release and decreased delivery effectiveness

Several novel approaches have been used to overcome this constraint he fundamental metal-ligand connection of amorphous MOFs (aMOFs), which have very disordered structures but preserve via use of heating, pressure, and electrical discharge, crystalline counterparts and ball-milling procedures, which have already found some practical applications, are significant because of the intriguing guest entrapment in their permanently collapsing porous frameworks; 13 for For instance, these aMOF were recently utilised with efficacy in medication delivery with a customised timing for release. 14 Hydrophilic model drug calcein (cal) was successfully

encapsulated by Orellana-Tavra et al. a molecular size greater than the UiO-MOF pore) into nanosized Zr-UiO-66 MOFs with 4.9 weight percent loading [22].

1.15 MOF As Drug Nanocarriers:-

Large surface areas, highly organised porosities, and well defined structures that are inherent to MOFs give these materials the capacity to load and release various cargos, particularly medicinal medicines[25]. 2006 saw Férey initially suggested that MOFs offer potential in due to their large loading capacities and controlled release characteristics, medication delivery. MIL-100 and MIL-101, two Cr-based MOFs that they constructed from trimers of With 0.35 g g-1 of IBU/dehydrated MIL-100 and 1.4 g g-1 of IBU/dehydrated MIL-101, metal octahedra and di- or tricarboxylic acids, which demonstrated exceptional IBU adsorption. IBU's release kinetics were examined in simulated bodily fluid at 37 °C, and the results showed that after 3 and 6 days, respectively, MIL-100 and MIL-101 completely released IBU. Compared to MCM-41, a comparable substance, these two hybrid In simulated bodily fluid, solids demonstrated comparable IBU doses and kinetics, particularly MIL-101(Cr), which may be attributed to due to the increased interactions with IBU and higher cage sizes. Notably, a novel MOF-based technique was created in this paper. delivery of drugs. Some low toxicity MOFs have been used for the delivery of therapeutic molecules while taking into consideration the toxicity of chromium compounds. For instance, there are numerous Fe-based MOFs provide numerous options for achieving an appropriate controlled different pharmacological substances are released [25].

1.16 Stimuli-Responsive MOFs for Drug Delivery:

Smart materials have drawn a lot of interest, particularly in the area of bioapplications. Stimuli-responsive MOFs have been among them and have made interesting candidates for controlled drug release. Single-stimulus and multiple-stimulus responsive MOFs are the two main types for stimuli-responsive MOFs. In this section, we introduce several stimuli-responsive MOFs, including those that respond to a single stimulus and those that respond to several stimuli. accomplish controlled medication distribution after activation by a variety of stimuli, including temperature, ions, magnetic field, and pH, pressure as well as light. The Stimuli-Resoensive MOFs for drug delivery shown in Fig.7.

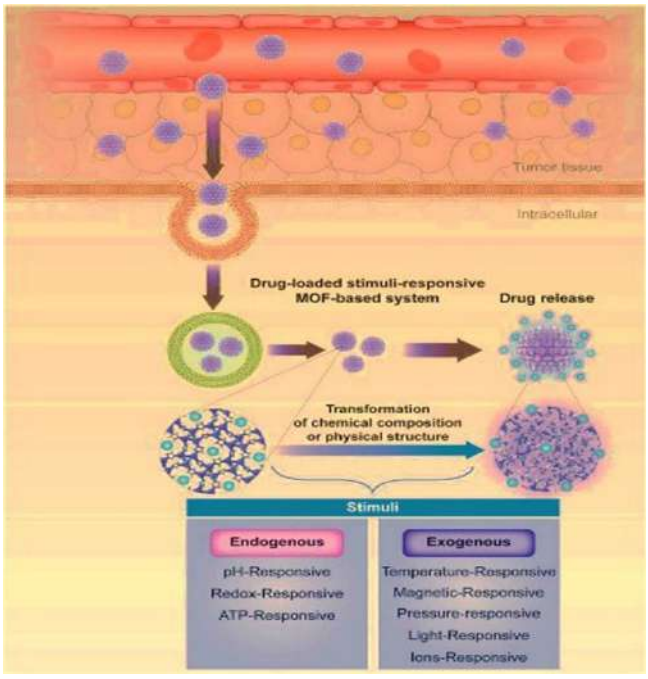

Fig.7 of Schematic illustration of metal–organic frameworks (MOFs)-based stimuli-responsive system for drug delivery.

A. Single-Stimulus-Responsive MOFs for Drug Delivery:-

a. pH-Responsive MOFs:-

Because of the acidic tumour microenvironment and the sensitivity of coordination bonds to external pH, pH-responsive MOFs—a class of porous MOF nanocarriers activated by external stimuli—are the ones that have received the most attention in research, particularly for cancer therapy. Numerous studies have examined MOFs' pHresponsive characteristics for medication delivery and cancer up until this point. treatment.

An Fe (bbi) MOF, for instance, was described by Huang et al. built from bbi and 1,1′-(1,4-butanediyl) bis (imidazole) iron ions using a deposition technique. encapsulation in place of Doing so only required adding DOX to the bbi solution. As anticipated, the loaded DOX could be released (Figure 3a). due to the sensitivity of the coordination when the pH is lowered relationship with the sour surroundings. In order to effectively control over the MOF's quick disintegration of the hosting material, a layer of silica was applied to its surface. the DOX release. The conjugation of folic acid was more significant. to the prepared nanocomposites' surface for focused delivery of drugs . As a result, the MOF-based medication vehicle demonstrated a pH-dependent progressive release pattern, and high antitumor effectiveness.

b. Magnetically-Responsive MOFs:-

Due to their potential advantages in magnetic separation, magnetic targeting, magnetic resonance imaging (MRI), and magnetic hyperthermia, magnetically responsive systems enable diversity in drug administration. One of these is the use of magnetically directed anticancer medication delivery. to target therapeutic probes with drugs at tumour locations in order to increase therapeutic effectiveness since its initial invention by developed the 1960s by Watson et al. Candidate nanocarriers based on MOFs for this type of distribution strategy are typically core-shell MOFs. NPs, such as Fe3O4, were frequently utilised as magnetic cores with MOF shell.

c. Ion-Responsive MOFs:-

A novel drug delivery method has been introduced via ion-responsive MOFs. Strong electrostatic interactions between the medicines and the frameworks in such drug carriers regulate the diffusion. and medication release. Consequently, powerful electrostatic interactions Because the release of ionic medications is a chemical stimulus-responsive mechanism occurring solely through ionic frameworks, the relationship between ionic drugs and ionic frameworks has drawn particular interest. exchange. The Rosi group, for instance, created an anionic Zn8(ad)4(BPDC)6O, 2Me2NH2, 8DMF, and 11H2O by incorporating zinc acetate dihydrate and biphenyldicarboxylic acid into adenine combinations.

d. Temperature-Responsive MOFs:-

Typically, materials that are sensitive to small temperature changes at the physiological temperature of 37 °C are referred to as temperature-responsive nanocarriers. PNIPAM, or poly(N-isopropyl acrylamide), is a potential component for thermosensitive materials. smaller critical solution temperature drug nanocarriers. When the temperature drops down below its cloud level [76] PNIPAM exhibits hydrophilicity and has a tendency to dissolve in water at the critical point (Tc, about 32 °C), although it can also agglomerate. As a result, Sada et al. showed a switchable UiO-66- Nanocarrier for PNIPAM (Figure 5a). By soaking the UiO-66-PNIPAM in guest solutions, resorufin, caffeine, and procainamide were loaded in the nanocarrier, and the release behaviours were then observed. were measured at either 25 or 40 °C.

e. Pressure-Responsive MOFs:-

The aforementioned responsive MOFs have been designed with a delayed release time and improved therapeutic efficacy to prevent the early release of medicines before they reach at diseased tissues. Pressure has also been used for controlled drugs in addition to the aforementioned generally discussed stimuli. release. Recently, a Zr-based MOF was reported by Qian and colleagues. constructed from zirconium clusters and (2E,2E′)-3,3′-(2-fluoro-1,4-phenylene) diacrylic acid (F-H2PDA) with high model drug 58.80 wt% diclofenac sodium (DS) loading capacity because of its expanded organic spacer and improved polarity.

1.17 Multiple-Stimuli-Responsive MOFs for Drug Delivery:-

The ability to accurately distribute medications in the body utilising single-stimulus-responsive MOF drug carriers is limited by the complexity of the human body environment. To increase loading capacities and chemotherapeutic efficacy, multiplestimuli-responsive MOFs are a preferable substitute. One example of a quickly evolving supramolecular compound is pillararenes. hosts, since their initial discovery, have received extensive research. in 2008 by Ogoshi et al. This is because of their advantageous characteristics, such as their unique structure, ease of functionalization, and favourable host-guest interactions. Undoubtedly, this new a class of macrocycles is advancing materials science and supramolecular chemistry.

Our research team worked hard to create such adaptable medication nanocarriers. Multiple-stimuli-responsive drug delivery has quickly developed, according to gated materials rapid development.

2. Introduction of Zeolitic Imidazolate Framework-8 (ZIF-8):-

The metal-organic frameworks known as zeolitic imidazolate frameworks are topologically isomorphic to zeolites. By using the melt-quench procedure and the first melt-quench, ZIF glasses can be created. NEennett et al. initially created and reported ZIF glass in 2015. ZIF are made up of immidazolate linkers that bind tetrahedrally coordinated transition metal ions, such as Fe, Co, Cu, and Zn.[28].

2.1 Structure of ZIF:-

After melting, the structure of melt-quenched ZIF glasses preserved short-range order, such as chemical configuration and coordinative bonding, but lost long-range order in the Rasmus et al. produced ZIF.

ZIF-8 structure. In (a) the single crystal structure; in (b) ORTEP diagram of the asymmetric unit of ZIF-8 shown in Fig.8.

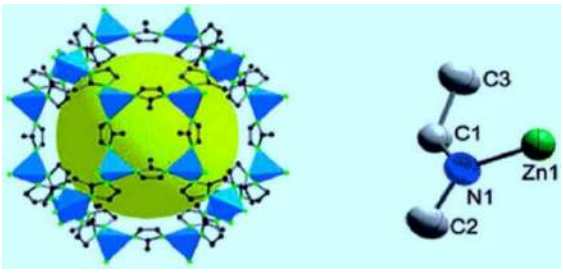

Fig.8 ZIF-8 structure. In (a) the single crystal structure; in (b) ORTEP diagram of the asymmetric unit of ZIF-8 (reproduced by permission, from ref. 180).

2.2 Synthesis of ZIF:-

Solvothermal and hydrothermal processes are used to create ZIF. From a heated solution containing hydrated metal salt, IMH solvent, and base IMH linkers, crystals gradually form. ZIF architecture. Synthesis of ZIF shown in Fig.9.

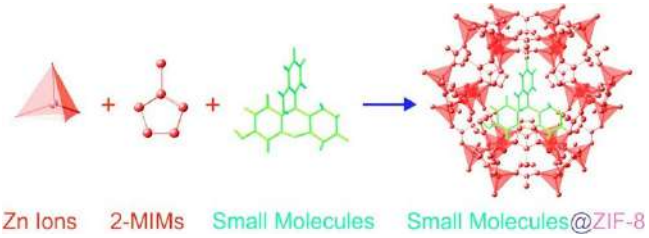

Fig.9 Synthesis of ZIF-8

2.3 Solvents:-

ZIF alternate solvents include methanol, ethanol, isopropanol, and water in addition to the amide solvent N,N-dimethylformamide (DMF).

Polymers:-

Polyethylene oxide, polypropylene oxide, polyvinylpyrrolidone, polydiallyldimethylammonium choride.

2.4. Target action of ZIF:-

ZIF target on directly target on cell or cancer cell and shows their effect. The Target action of ZIF is shown in Fig.10.

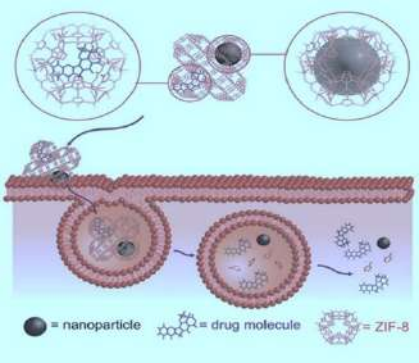

Fig.10 Target action of ZIF-8

2.5 Applications:

1. Application to carbon capture.
2. Gas seperation.
3. Other separation applications.
4. Catalysis.
5. Sensing and electronic devices.
6. Drug delivery.

DISCUSSION

This review of more than 200 scientific papers on MOFs shows that these substances will once again have a promising future since they consistently demonstrate the ability to address the most pressing problems of the third millennium. The numerous articles that have been published on the topic show that this field of chemistry is constantly expanding. Numerous ongoing studies on MOFs are focusing on potential new applications like drug release, sensing, water purification, air quality management, and magnetic materials, even though many of the studies on MOFs still focus on the potential for absorbing in empty space and releasing hydrogen and carbon dioxide molecules. Numerous obstacles, including poor selection, low capacity, and high expenses, should be removed as quickly as feasible in order to achieve meaningful outcomes in these areas.

We conclude by presenting a straightforward, environmentally safe approach for the one-step, room-temperature synthesis of two highly biocompatible MOFs and MOFs with embedded drugs. It was discovered that the drug-embedded MOFs released the drug when a biomimetic system like liposomes was present. This is the first time dox has been released from a dox-embedded MOF using liposomes. Additionally, we firstly demonstrated the successful three-day release of the medication from MOF-drug composites under low-acidity circumstances. The simplicity and industrial viability of the drug-embedded MOFs' synthesis as well as the delayed distribution of dox using external stimuli make the current work innovative. We anticipate that this research will soon present fresh chances in the field of biomaterials science. MOF as drug delivery very helpful because drug encapsulated in metal organic framework so it shows less toxicity than other drug delivery and quick response shows than another drug delivery system. MOF are also useful as targeted drug delivery an so drugs incorporated in MOF then the drug act on selected organ or tissues or cell and shows therapeutic effect with less toxicity so this MOF as drug delivery system very banificial for cancer treatment because MOF based Drug delivery forms target action on cancer cell or tumor and directly act on it and showas their therapeutic effect.

FUTURE PROSPECTIVES

In conclusion, we reviewed recent notable developments in the utilisation of NMOFs for cargo delivery and divided the cargo-delivery strategies into three categories: encapsulation, direct assembly, and post-synthesis. The porous architectures and customizable NMOF carrier compositions of the first two represent traditional methods. The final one, on the other hand, is a novel approach that is based on the easy chemical modification property of NMOFs. CUS, ligand defects from the metal nodes of MOF, and functionalities found in the linkers of the frameworks provide accessible anchorages for additional cargo loading. Additionally, each strategy's characteristics, noteworthy advancements, and practicable treatments for limiting cargo release and enhancing therapeutic

effectiveness have all been thoroughly discussed. Utilizing computational techniques like density functional theory calculations, large canonical Monte Carlo simulations, and molecular dynamics simulations, the loading and unloading of cargos at the atomic level within the pores of MOF have been thoroughly studied. 36 These studies were extremely helpful in understanding the interactions between cargo and MOF and in guiding the design and synthesis of MOF-based cargo-delivery systems, in addition to demonstrating the potential uses of MOF as cargo carriers. Many obstacles still need to be carefully considered, though. Last but not least, a thorough evaluation of the in vivo safety of MOF nanocarriers is required, as well as a comprehensive understanding of the "ADME" ("absorption- distribution- metabolism- excretion") mechanism. Although MOF nanoparticle bioapplication is still in its early stages, substantial advancements have already been made since the first publication on MOF for cargo loading, and it is anticipated that they will result in significant advancements in nanomedicine.

CONCLUSION

In conclusion, we have covered recent major developments in MOF drug delivery, particularly for cancer therapy and/or diagnosis. As shown below, a wide variety of outstanding MOF-based platforms, including individual MOF systems, functionalized MOF formulations, and current collaboration systems, have been created for innovative nanomedical applications. Before such nanocomposites may be used in clinical settings, there are still several issues that need to be solved for these systems. By choosing endogenous building components or functionalizing MOFs with bioactive molecules, future research may concentrate on the creation of non-toxic MOF carriers to minimize adverse effects. Systematic in vivo investigations are necessary to optimize the performance of MOFs prior to therapeutic applications, and in vitro systematic research of the stability and degradation process of MOF-based nanocarriers are also required.

In conclusion, we have created a perfect DD based on ZIF-8 nanospheres that is excellent for cellular absorption and has a size of 70 nm. We show that the ZIF-8 frameworks have a high degree of control over how many small molecules are loaded. We come to the conclusion that this particular inclusion method involves in situ trapping, which makes it applicable to tiny molecules with various physicochemical characteristics. The ZIF-8 sphere has a mild cytotoxicity that is equivalent to that of other organic and inorganic drug carriersIn conclusion, a nanoscale multifunctional MOF based DDS was created starting with a biocompatible MOF MIL-101 using a practical and "green" one-pot post-synthetic method. This biocompatible and biodegradable MOF-based DDS, in our opinion, can eventually function as a potential platform for cancer therapy.

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