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UiO-67
A promising Drug Delivery Platform for Podophyllotoxin

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Abstract

In pursuit of development of a drug carrying platform for delivery of Podophillotoxin, an anti-cancer drug, a porous metal–organic frameworks (MOFs), UIO-67, was synthesized and used. The unique structure of UIO-67which are built of inorganic nodes and organic ligands lead to successful encapsulation of different ions and molecules.Following our recentstudy, UIO-67was prepared and characterizedusing variety of analytical methods containing FTIR, FESEM, and EDS.The loading and releasing profile of Podophyllotoxin in the synthesized platform UIO-67were evaluated. The in vitro cytotoxicity results revealed UIO-67- Podophyllotoxin was able to increase cytotoxicity compared to that of Podophyllotoxin on HT-29 cancerous cells indicating the remarkable role of this drug delivery system.

Keywords:UIO-67, MOF, drug delivery, Podophyllotoxin, Cytotoxicity

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Fig1. Placement of drug in the structure of MOF.

1. Introduction

Cancer as the most prevalent diseases worldwide is one of the main public health concerns. In spite of intensive efforts for treatment of cancer, the necessity of developing effective agents isn't ignorable [1]. Designing an ideal drug delivery system for targeting cancer cell is considered as a hot topic in life science research. MOFs with crucial features including high drug loading capacity, high surface area, as well as tunable pore size is used for drug delivery intensively[2]. MOFs plays an important role as an carriers in drug delivery because they are non-toxic as well as the uptake of drugs and getting across the cell membrane has been facilitated via controlling the size of MOFs[3].

Podophyllotoxin is anticancer drugs which is able to induces cytotoxic and increase DNA damage[4]. Although, Podophyllotoxinfrequently applied, developed drug resistance and severe side effects affected its clinical application [5]. Encapsulate of Podophyllotoxinusing various DDS could be an effective idea[6]. In present work, the drug loading capacity of i for Podophyllotoxinas an anticancer drug was evaluated. Upon exposure by Podophyllotoxinthe in vitro cytotoxicity against cancer cells were assessed.
Finally but contrary to the original goal of this project, which was to use a muff, because of the simpler and faster synthesis, we carried out this project with a MOF.

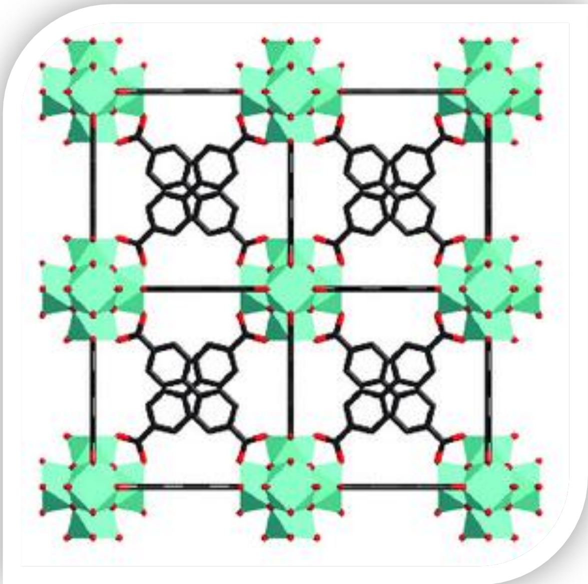

Fig2. Placement of Structures of UiO-67[26]

UiO-67 is a Zirconium-based metal-organic framework that features larger pore sizes compared to UiO-66. This is due to the longer structure of BPDC (UiO-67) as compared to BDC (UiO-66).
The structure and properties of two new UiO-67-type metal–organic frameworks, along with their linker synthesis and powder and single crystal synthesis, are presented. The new MOFs, UiO-67-Me and UiO-67-BN, are based on 3,3′-dimethylbiphenyl and 1,1′-binaphthyl linker scaffolds, and show a much higher stability to water than the thoroughly investigated UiO-67, which is based on the biphenyl scaffold. On the basis of structure models obtained from single crystal X-ray diffraction, it is seen that these linkers are partly shielding the Zr cluster. The new materials have higher density than UiO-67, but show a higher volumetric adsorption capacity for methane. UiO-67-BN exhibits excellent reversible watersorption properties, and enhanced stability to aqueous solutions over a wide pH range; it is to the best of our knowledge the most stable Zr-MOF that is isostructural to UiO-67 in aqueous solutions.

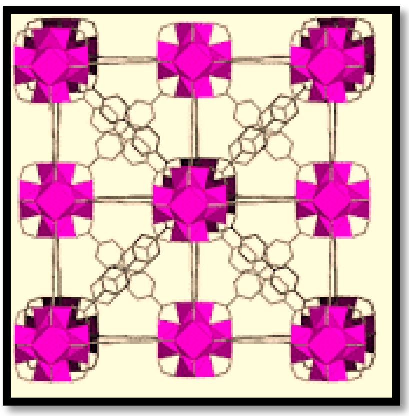

Fig3. Placement of Structures of UiO-67

Application

❖ Gas adsorption and storage:
- Carbon dioxide (CO_2)
- Hydrogen (H_2)
- Methane (CH_4)

❖ Neutralisation/detoxication of chemical warfare agents (nerve gas)
❖ Catalyst
❖ Biomolecular motor
❖ Biomedical imaging

Properties

Formula: $Zr_6O_4(OH)_4(BPDC)_6$
Surface area: up to 1970+ m^2/gr (BET)

NanoComposite

Nanocomposite is a multiphase solid material where one of the phases has one, two or three dimensions of less than 100 nanometers (nm) or structures having nano-scale repeat distances between the different phases that make up the material. [7]
The idea behind Nanocomposite is to use building blocks with dimensions in nanometre range to design and create new materials with unprecedented flexibility and improvement in their physical properties. In the broadest sense this definition can include porous media, colloids, gels and copolymers, but is more usually taken to mean the solid combination of a bulk matrix and nano-dimensional phase(s) differing in properties due to dissimilarities in structure and chemistry. [8]
The mechanical, electrical, thermal, optical, electrochemical, catalytic properties of the nanocomposite will differ markedly from that of the component materials. Size limits for these effects have been proposed.

1. <5 nm for catalytic activity
2. <20 nm for making a hard magnetic material soft
3. <50 nm for refractive index changes
4. <100 nm for achieving superparamagnetism, mechanical strengthening or restricting matrix dislocation movement [9].

Nanocomposites are found in nature, for example in the structure of the abalone shell and bone. [10] The use of nanoparticle-rich materials long predates the understanding of the physical and chemical nature of these materials. Some researchersinvestigated the origin of the depth of color and the resistance to acids and bio-corrosion of Maya blue paint, attributing it to a nanoparticle mechanism. From the mid-1950s nanoscale organo-clays have been used to control flow of polymer solutions (e.g. as paint viscosifiers) or the constitution of gels (e.g. as a thickening substance in cosmetics, keeping the preparations in homogeneous form). By the 1970s polymer/clay composites were the topic of textbooks, although the term "nanocomposites" was not in common use. [11]
In mechanical terms, nanocomposites differ from conventional composite materials due to the exceptionally high surface to volume ratio of the reinforcing phase and/or its exceptionally high aspect ratio. The reinforcing material can be made up of particles (e.g. minerals), sheets (e.g. exfoliated clay stacks) or fibers (e.g. carbon nanotubes or electrospun fibers). [12] The area of the interface between the matrix and reinforcement phase(s) is typically an order of magnitude greater than for conventional composite materials. [13] The matrix material properties are significantly affected in the vicinity of the reinforcement. Some scientists be aware that with polymer nanocomposites, properties related to local chemistry, degree of thermoset cure, polymer chain mobility, polymer chain conformation, degree of polymer chain ordering or crystallinity can all vary significantly and continuously from the interface with the reinforcement into the bulk of the matrix. This massive quantity of reinforcement surface area means that a relatively small amount of nanoscale reinforcement can have an observable effect on the macroscale properties of the composite. [14]

MOF

Metal–organic frameworks (MOFs) are a class of compounds consisting of metal ions or clusters coordinated to organic ligands to form one-, two-, or three-dimensional structures. They are a subclass of coordination polymers, with the special feature that they are often porous. The organic ligands included are sometimes referred to as "struts" or "linkers", one example being 1,4-benzenedicarboxylic acid (BDC).

More formally, a metal–organic framework is a coordination network with organic ligands containing potential voids. A coordination network is a coordination compound extending, through repeating coordination entities, in one dimension, but with cross-links between two or more individual chains, loops, or spiro-links, or a coordination compound extending through repeating coordination entities in two or three dimensions; and finally a coordination polymer is a coordination compound with repeating coordination entities extending in one, two, or three dimensions.[1]
In some cases, the pores are stable during elimination of the guest molecules (often solvents) and could be refilled with other compounds. Because of this property, MOFs are of interest for the storage of gases such as hydrogen and carbon dioxide. Other possible applications of MOFs are in gas purification, in gas separation, in water remediation,[2] in catalysis, as conducting solids and as supercapacitors.[3]
The synthesis and properties of MOFs constitute the primary focus of the discipline called reticular chemistry (from Latin reticulum, "small net").[4] In contrast to MOFs, covalent organic framework (COFs) are made entirely from light elements (H, B, C, N, and O) with extended structures.

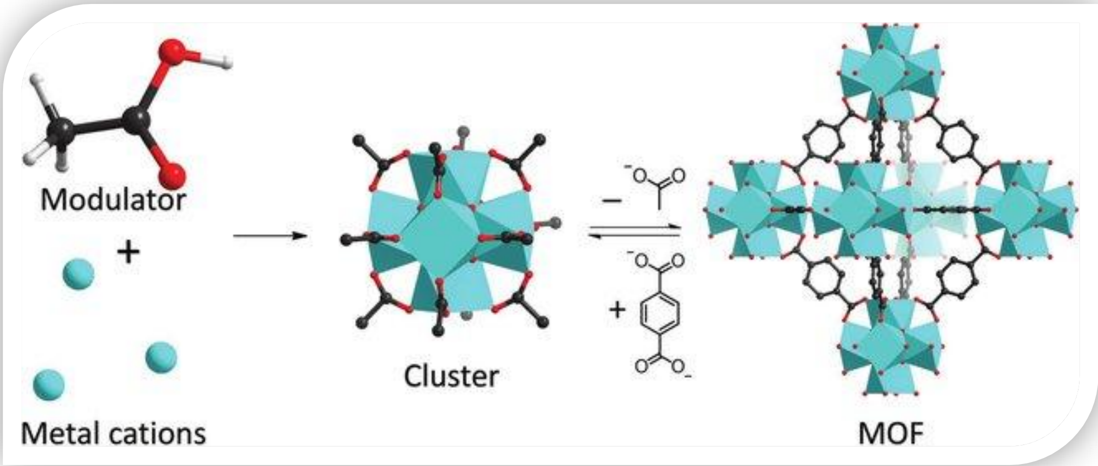

Fig4. Representative modulated synthesis [26]

Structure

MOFs are composed of two major components: a metal ion or cluster of metal ions and an organic molecule called a linker. For this reason, the materials are often referred to as hybrid organic–inorganic materials; however, this terminology has recently been explicitly discouraged.[1] The organic units are typically mono-, di-, tri-, or tetravalent ligands.[6] The choice of metal and linker dictates the structure and hence properties of the MOF. For example, the metal's coordination preference influences the size and shape of pores by dictating how many ligands can bind to the metal and in which orientation.

Classification of hybrid materials based on dimensionality

		Dimensionality of Inorganic			
		0	**1**	**2**	**3**
Dimensionality of Organic	**0**	Molecular Complexes	Hybrid Inorganic Chains	Hybrid Inorganic Layers	3-D Inorganic Hybrids
	1	Chain Coordination Polymers	Mixed Inorganic-Organic Layers	Mixed Inorganic-Organic 3-D Framework	
	2	Layered Coordination Polymer	Mixed Inorganic-Organic 3-D Framework		
	3	3-D Coordination Polymers			

To describe and organize the structures of MOFs, a system of nomenclature has been developed. Subunits of a MOF, called secondary building units (SBU), can be described by topologies common to several structures.

Each topology, also called a net, is assigned a symbol, consisting of three lower-case letters in bold. MOF-5, for example, has a pcu net.
Attached to the SBUs are bridging ligands. For MOF's, typical bridging ligands are di- and tricarboxylic acids. These ligands typically have rigid backbones. Examples are benzene-1,4-dicarboxylic acid (BDC or terephthalic acid, biphenyl-4,4'-dicarboxylic acid (BPDC), and the tricarboxylic acid trimesic acid.

Synthesis

General synthesis

The study of MOFs developed from coordination chemistry and solid state inorganic chemistry, especially the zeolites. Except for the use of preformed ligands, MOFs and zeolites are produced almost exclusively by hydrothermal or solvothermal techniques, where crystals are slowly grown from a hot solution. In contrast with zeolites, MOFs are constructed from bridging organic ligands that remain intact throughout the synthesis.[8] Zeolite synthesis often makes use of a "template". Templates are ions that influence the structure of the growing inorganic framework. Typical templating ions are quaternary ammonium cations, which are removed later. In MOFs, the framework is templated by the SBU (secondary building unit) and the organic ligands. A templating approach that is useful for MOFs intended for gas storage is the use of metal-binding solvents such as N,N-diethylformamide and water. In these cases, metal sites are exposed when the solvent is evacuated, allowing hydrogen to bind at these sites. Four developments were particularly important in advancing the chemistry of MOFs.
(1) The geometric principle of construction where metal-containing units were kept in rigid shapes. Early MOFs contained single atoms linked to ditopic coordinating linkers. The approach not only led to the identification of a small number of preferred topologies that could be targeted in designed synthesis, but was the central point to achieve a permanent porosity.
(2) The use of the isoreticular principle where the size and the nature of a structure changes without changing its topology led to MOFs with ultrahigh porosity and unusually large pore openings.
(3) Post- synthetic modification of MOFs increased their functionality by reacting organic units and metal-organic complexes with linkers.
(4) Multifunctional MOFs incorporated multiple functionalities in a single framework.

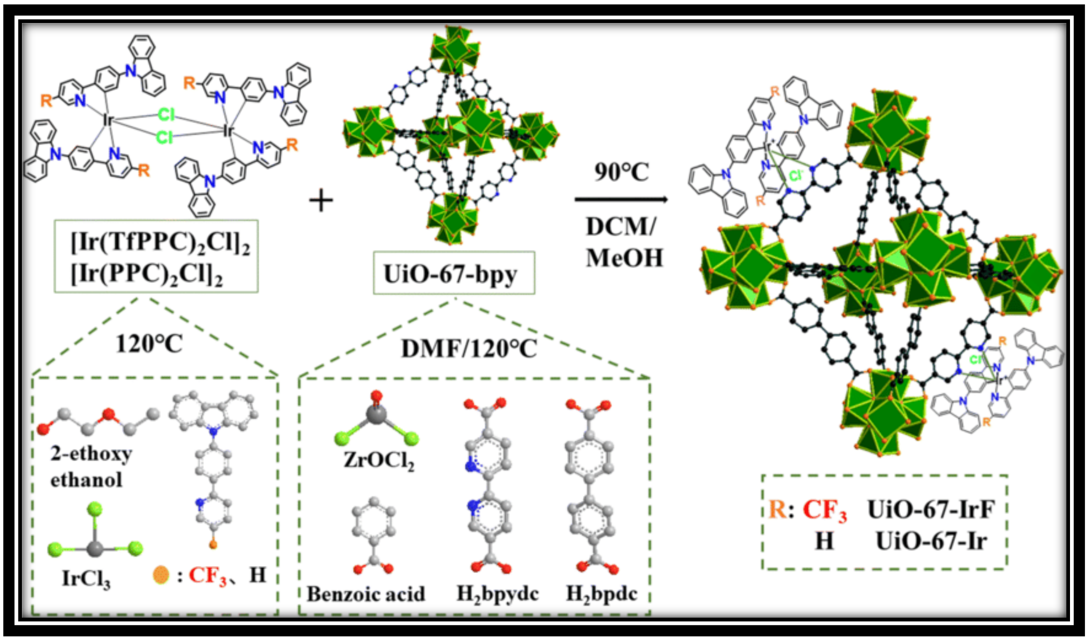

Fig5. Synthesis routine for UiO-67-IrF [28]

Since ligands in MOFs typically bind reversibly, the slow growth of crystals often allows defects to be redissolved, resulting in a material with millimeter-scale crystals and a near-equilibrium defect density. Solvothermal synthesis is useful for growing crystals suitable to structure determination, because crystals grow over the course of hours to days. However, the use of MOFs as storage materials for consumer products demands an immense scale-up of their synthesis. Scale-up of MOFs has not been widely studied, though several groups have demonstrated that microwaves can be used to nucleate MOF crystals rapidly from solution. This technique, termed "microwave-assisted solvothermal synthesis", is widely used in the zeolite literature, and produces micron-scale crystals in a matter of seconds to minutes, in yields similar to the slow growth methods. Some MOFs, such as the mesoporous MIL-100(Fe), can be obtained under mild conditions at room temperature and in green solvents (water, ethanol) through scalable synthesis methods.

A solvent-free synthesis of a range of crystalline MOFs has been described. Usually the metal acetate and the organic proligand are mixed and ground up with a ball mill. $Cu_3(BTC)_2$ can be quickly synthesised in this way in quantitative yield. In the case of $Cu_3(BTC)_2$ the morphology of the solvent free synthesised product was the same as the industrially made Basolite C300. It is thought that localised melting of the components due to the high collision energy in the ball mill may assist the reaction. The formation of acetic acid as a by-product in the reactions in the ball mill may also help in the reaction having a solvent effect in the ball mill. It has been shown that the addition of small quantities of ethanol for the mechanochemical synthesis of $Cu_3(BTC)_2$ significantly reduces the amounts of structural defects in the obtained material.

A recent advancement in the solvent-free preparation of MOF films and composites is their synthesis by chemical vapor deposition. This process, MOF-CVD,[19] was first demonstrated for ZIF-8 and consist of two steps. In a first step, metal oxide precursor layers are deposited. In the second step, these precursor layers are exposed to sublimed ligand molecules that induce a phase transformation to the MOF crystal lattice. Formation of water during this reaction plays a crucial role in directing the transformation. This process was successfully scaled up to an integrated cleanroom process, conforming to industrial microfabrication standards.[20]

Numerous methods have been reported for the growth of MOFs as oriented thin films. However, these methods are suitable only for the synthesis of a small number of MOF topologies. One such example being the vapor-assisted conversion (VAC) which can be used for the thin film synthesis of several UiO-type MOFs.[21]

High-throughput synthesis

High-Throughput (HT) methods are a part of combinatorial chemistry and a tool for increasing efficiency. Basically, there are two synthetic strategies within the HT-methods: On the one hand the combinatorial approach, here all reactions take place in one vessel, which leads to product mixtures and on the other hand the parallel synthesis, here the reactions take place in different vessels. Furthermore, a distinction is made between thin films and solvent-based methods. [22]

Solvothermal synthesis can be carried out conventionally in a teflon reactor in a convection oven or in glass reactors in a microwave oven (high-throughput microwave synthesis). The use of a microwave oven changes, in part dramatically, the reaction parameters. In addition to solvothermal synthesis, there have been advances in using supercritical fluid as a solvent in a continuous flow reactor. Supercritical water was first used in 2012 to synthesize copper and nickel-based MOFs in just seconds.[23] In 2020, supercritical carbon dioxide was used in a continuous flow reactor along the same time scale as the supercritical water-based method, but the lower critical point of carbon dioxide allowed for the synthesis of the zirconium-based MOF UiO-66.[24]

High-throughput solvothermal synthesis

In high-throughput solvothermal synthesis, a solvothermal reactor with (eg) 24 cavities for Teflon reactors is used. Such a reactor is sometimes referred to as a multiclav. The reactor block or reactor insert is made of stainless steel and contains 24 reaction chambers, which are arranged in four rows. With the miniaturized Teflon reactors, volumes of up to 2 mL can be used. The reactor block is sealed in a stainless steel autoclave; for this purpose, the filled reactors are inserted into the bottom of the reactor, the Teflon reactors are sealed with two Teflon films and the reactor top side is put on. The autoclave is then closed in a hydraulic press. The sealed solvothermal reactor can then be subjected to a temperature-time program. The reusable Teflon film serves to withstand the mechanical stress, while the disposable Teflon film seals the reaction vessels. After the reaction, the products can be isolated and washed in parallel in a vacuum filter device. On the filter paper, the products are then present separately in a so-called sample library and can subsequently be characterized by automated X-ray powder diffraction. The informations obtained are then used to plan further syntheses.

Reversible hydration and dehydration

During drying it comes to the removal of free and bound water from the crystal grid, which is then counterbalanced back in contact with materials such as stored grain and feed, pet litter, in flue gas to prevent condensation and the like. [19] Clinoptilolite stabilize moisture at a low dose of volume and avoid the adverse effects of water. [20]

Metal-organic frameworks (MOFs) are organic-inorganic hybrid crystalline porous materials that consist of a regular array of positively charged metal ions surrounded by organic 'linker' molecules. The metal ions form nodes that bind the arms of the linkers together to form a repeating, cage-like structure. Due to this hollow structure, MOFs have an extraordinarily large internal surface area.
Researchers have synthesized MOFs that feature a surface area of more than 7800 square meters per gram. To put this into context, if you could lay out the available surface area in a teaspoon of this material (around a gram of solid), it would cover an entire soccer field. MOFs offer unique structural diversity in contrast to other porous materials uniform pore structures; atomic-level structural uniformity; tunable porosity; extensive varieties; and flexibility in network topology, geometry, dimension, and chemical functionality. This allows researchers the successful control of framework topology, porosity, and functionality.
MOFs unique structure design and tunability –crystalline porous materials that are composed of both organic and inorganic components in a rigid periodic networked structure– is not readily accessible in conventional porous materials, e.g., purely inorganic zeolites. By making the MOF from different metal atoms and organic linkers, researchers can create materials that selectively absorb specific gases into tailor-made pockets within the structure. MOFs therefore offer great potential for their effective integration and exploration in various sensing applications. MOFs can be put together arbitrarily like Lego bricks and outperform every previously known class of material in terms of flexibility.

Short history and Background of MOFs

The physicochemical properties of materials are governed by the synergistic effects of structures and compositions, and MOFs are fascinating examples of how the unique structure of hollow-structured materials can provide a whole raft of advantageous features. Among them are enhanced surface-to-volume ratio; low density; microreactor environment; higher loading capacities; and reduced transmission lengths of mass and charge.
Consequently, the preparation of hollow structures for technological applications has long been a popular research field for chemists and materials scientists. However, the synthesis of porous or hollow-structured materials with controllable – and especially complex – structures and certain composition in a controlled manner has always been a challenge for scientists.
Enter MOFs – crystalline hybrid materials created from both organic and inorganic molecules via molecular self-assembly. Pioneered in the late 1990s ("Design and synthesis of an exceptionally stable and highly porous metal-organic framework") by Prof. Omar Yaghi at UC Berkeley, MOFs have become a rapidly growing research field. So far, more than 90 000 different MOF structures have been reported and the number grows daily. Though exciting, the sheer number of MOFs is actually creating a problem: It researchers propose to synthesize a new MOF, how can they know if it is truly a new structure and not some minor variation of a structure that has already been synthesized? To address the issue, researchers are using machine learning to develop a 'language' for comparing two materials and quantifying the differences between them.

MOF Applications

Numerous applications in many fields are being developed that exploit MOFs' cage-like structure, such as gas storage and separation, liquid separation and purification, electrochemical energy storage, catalysis, and sensing. In addition to direct applications, MOFs have been used as unique precursors for the construction of inorganic functional materials with unparalleled design possibilities, such as carbons, metal-based compounds, and their composites.
Currently, carbonaceous materials are attracting much interest for their extensive applications including adsorption, catalysis, batteries, fuel cells, supercapacitors, and drug delivery and imaging. In addition, some sensors are also one of the important applications of carbonaceous materials, because they are closely related to human health.
There are varieties of approaches for the preparation of these carbon materials, but among them, directly carbonizing from organic precursors is the most frequently used method to prepare nanoporous carbons due to its flexibility and simplicity. These materials present certain drawbacks, though, such as low surface areas, disordered structures, and non-uniform sizes, which will greatly limit their applications. However, researchers found that carbon materials derived from metal-organic frameworks (MOFs) could overcome these limitations.

Podophyllotoxin

Podophyllotoxin (PPT) is the active ingredient in Podofilox, which is a medical cream that is used to treat genital warts and molluscum contagiosum. It is not recommended in HPV infections without external warts. It can be applied either by a healthcare provider or the person themselves. It is a non-alkaloid toxin lignin extracted from the roots and rhizomes of Podophyllum species. A less refined form known as podophyllum resin is also available, but has greater side effects.

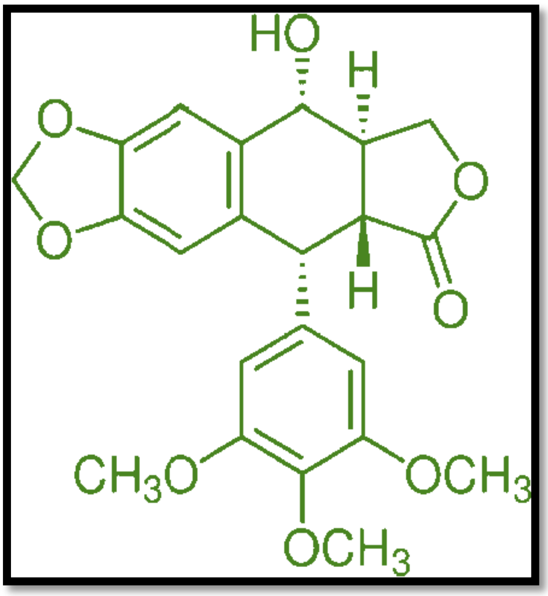

Fig5. Podophyllotoxin structure

Medical uses

Podophyllotoxin possesses a large number of medical applications, as it is able to stop replication of both cellular and viral DNA by binding necessary enzymes. It can additionally destabilize microtubules and prevent cell division. Because of these interactions it is considered an antimitotic drug. Podophyllotoxin and its derivatives are used as cathartic, purgative, antiviral agent, vesicant, antihelminthic, and antitumor agents. Podophyllotoxin derived antitumor agents include etoposide and teniposide. These drugs have been successfully used in therapy against numerous cancers including testicular, breast, pancreatic, lung, stomach, and ovarian cancers.

Podophyllotoxin cream is commonly prescribed as a potent topical antiviral. It is used for the treatment of HPV infections with external warts as well as molluscum contagisum infections. 0.5% PPT cream is prescribed for twice daily applications for 3 days followed by 4 days with no application, this weekly cycle is repeated for 4 weeks. It can also be prescribed as a gel, as opposed to cream. PPT is also sold under the names condyline and warticon.

Adverse effects

The most common side effects of podophyllotoxin cream are typically limited to irritation of tissue surrounding the application site, including burning, redness, pain, itching, and swelling. Application can be immediately followed by burning or itching. Small sores, itching and peeling skin can also follow, for these reasons it is recommended that application be done in a way that limits contact with surrounding, uninfected tissue

Neither podophyllin resin nor podophyllotoxin lotions nor gels are used during pregnancy because these medications have been shown to be embroytoxic in both mice and rats. Additionally, antimitotic agents are not typically recommended during pregnancy. Additionally, it has not been determined if podophyllotoxin can pass into breast milk from topical applications and therefore it is not recommended for breastfeeding women.

Podophyllotoxin cream is safe for topical use; however, it can cause CNS depression as well as enteritis if ingested. The podophyllum resin from which podophyllotoxin is derived has the same effect.

Mechanism of action

Podophyllotoxin destabilizes microtubules by binding tubulin and thus preventing cell division. In contrast, some of its derivatives display binding activity to the enzyme topoisomerase II (Topo II) during the late S and early G2 stage. For instance, etoposide binds and stabilizes the temporary DNA break caused by the enzyme, disrupts the reparation of the break through which the double-stranded DNA passes, and consequently stops

DNA unwinding and replication. Mutants resistant to either podophyllotoxin, or to its topoisomerase II inhibitory derivatives such as etoposide (VP-16), have been described in Chinese hamster cells. The mutually exclusive cross-resistance patterns of these mutants provide a highly specific means to distinguish the two kinds of podophyllotoxin derivatives. Mutant Chinese hamster cells resistant to podophyllotoxin are affected in a protein P1 that was later identified as the mammalian HSP60 or chaperonin protein. Furthermore, podophyllotoxin is classified as an arytetralin lignan for its ability to bind and deactivate DNA. It and its derivates bind Topo II and prevent its ability to catalyze rejoining of DNA that has been broken for replication. Lastly, experimental evidence has shown that these arytetralin lignans can interact with cellular factors to create chemical DNA adducts, thus further deactivating DNA.

Chemistry

Structural characteristic

The structure of podophyllotoxin was first elucidated in the 1930s. Podophyllotoxin bears four consecutive chiral centers, labelled C-1 through C-4 in the following image. The molecule also contains four almost planar fused rings. The podophyllotoxin molecule includes a number of oxygen containing functional groups: an alcohol, a lactone, three methoxy groups, and an acetal.

Biosynthesis

The biosynthetic route of podophyllotoxin was not completely eludicidated for many years; however, in September 2015, the identity of the six missing enzymes in podophyllotoxin biosynthesis were reported for the first time. Several prior studies have suggested a common pathway starting from coniferyl alcohol being converted to (+)-pinoresinol in the presence of a one-electron oxidant through dimerization of stereospecific radical intermediate. Pinoresinol is subsequently reduced in the presence of co-factor NADPH to first lariciresinol, and ultimately secoisolariciresinol. Lactonization on secoisolariciresinol gives rise to matairesinol.
A sequence of enzymes involved has been reported to be dirigent protein (DIR), to convert coniferyl alcohol to (+)-pinocresol, which is converted by pinocresol-lariciresinol reductase (PLR) to (-)-secoisolariciresinol, which is converted by sericoisolariciresinol dehydrogenase (SDH) to (-)-matairesinol, which is converted by CYP719A23 to (-)-pluviatolide, which is likely converted by Phex13114 (OMT1) to (-)-yatein, which is converted by Phex30848 (2-ODD) to (-)-deoxypodophyllotoxin. Though not proceeding through the last step of producing podophyllotoxin itself, a combination of six genes from the mayapple enabled production of the etoposide aglycone in tobacco plants.

Chemical synthesis

Podophyllotoxin has been successfully synthesized in a laboratory; however, synthesis mechanisms require many steps, resulting resulted in low overall yield. It therefore remains more efficient to obtain podophyllotoxin from natural sources.
Four routes have been used to synthesize podophyllotoxin with varying success: an oxo ester route, lactonization of a dihydroxy acid,cyclization of a conjugate addition product, and a Diels-Alder reaction.

Natural abundance

Podophyllotoxin is present at concentrations of 0.3% to 1.0% by mass in the rhizome of the American mayapple (Podophyllum peltatum). Another common source is the rhizome of Sinopodophyllum hexandrum Royle (Berberidaceae).
It is biosynthesized from two molecules of coniferyl alcohol by phenolic oxidative coupling and a series of oxidations, reductions and methylations.

2. Results And Discussion

Characterization
The chemical structure of the Uio-67-Podophyllotoxin was characterized with different analytical methods such as XRD, SEM & TEM.

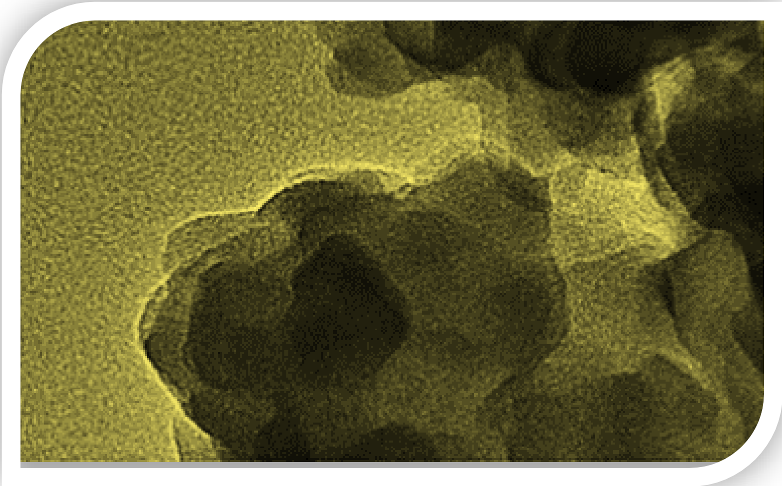

Fig7. TEM image of Uio-67- Podophyllotoxin

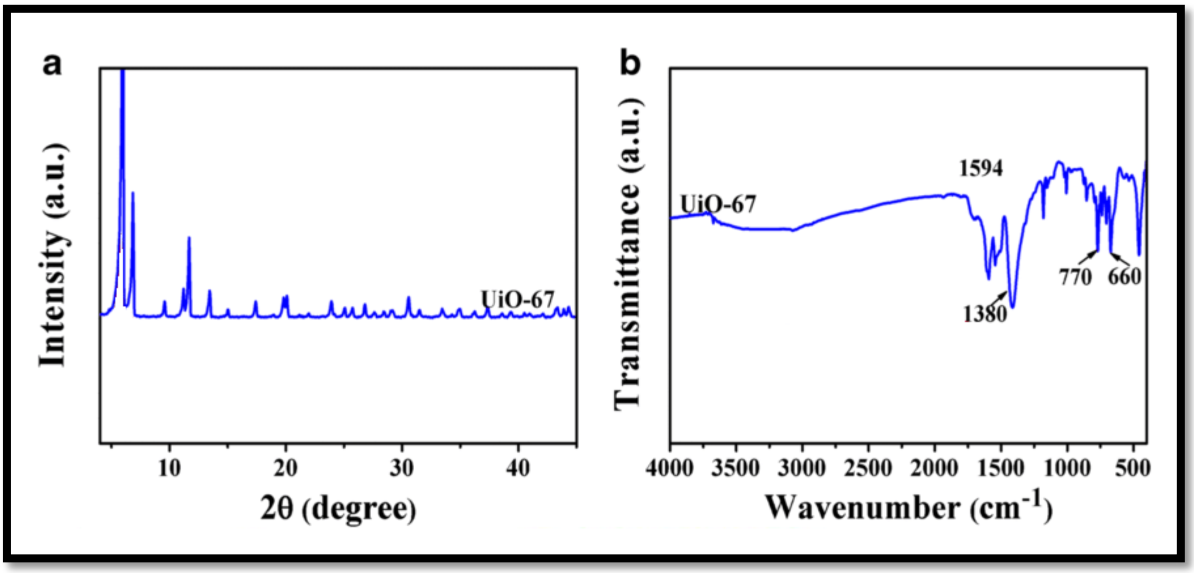

Fig8. (a) XRD and (b) FT-IR patterns for UiO-67.

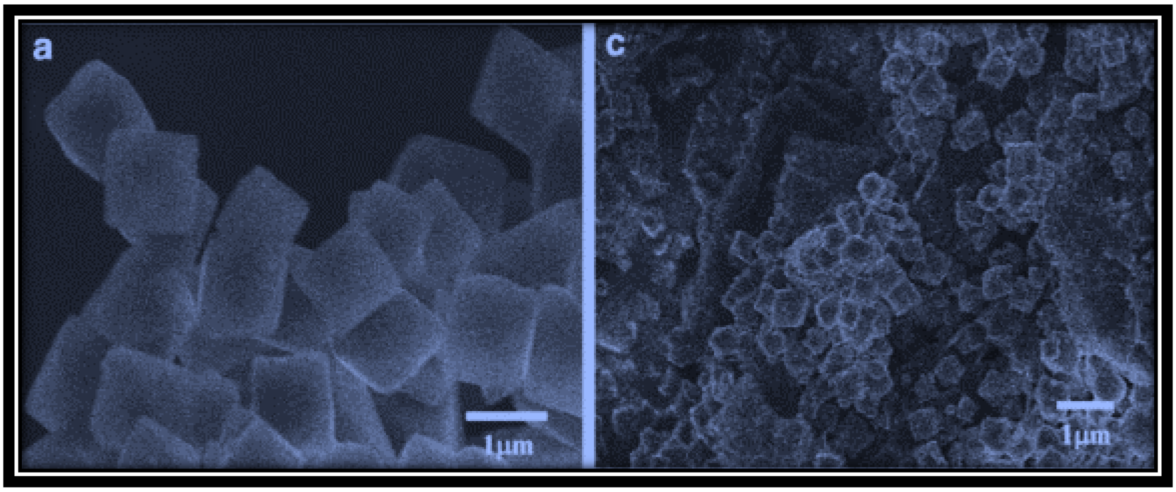

Fig9. SEM images of Uio-67 samples obtained podophyllotoxin: (a)Uio-67, (c) Uio-67-podophyllotoxin.

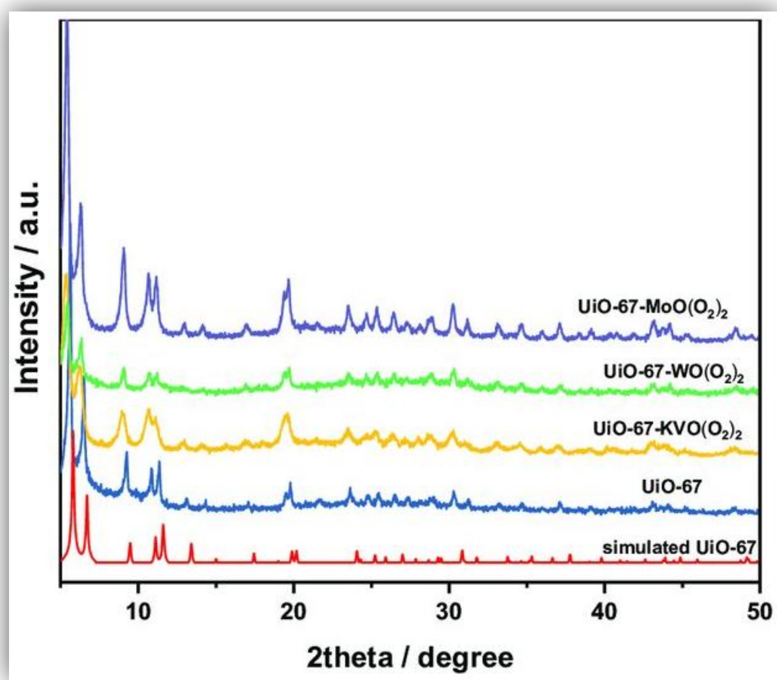

Fig 10.XRD patterns of the simulated UiO-67 and the synthesized UiO-67, UiO-67-$MoO(O_2)_2$, UiO-67-$WO(O_2)_2$, and UiO-67-$KVO(O_2)_2$. [29]

3. Conclusion

In this study, UIO-67as a drug carrier was applied for delivery ofPodophyllotoxin. The obtained nanostructure poses spherical morphology with an average diameter of 39-52 nm. The results showed the high loading capacity (73%) and sustained drug release behavior for Podophyllotoxin after 48h. In addition, upon exposure by UIO-67 —Podophyllotoxin, the growth inhibition was increased compared to those for UIO-67 and Podophyllotoxin drug against HT-29 cells. Collectively, UIO-67 may could beused asa promising drug deliverysystem for Podophyllotoxin.

Outlook for MOFs

The numerous advantages of MOFs, foremost their high surface area and modular composition, place them at a multidisciplinary crossroads. For good reason, MOFs are one of the most active research fields today, with aspects of their fundamental and applied properties permeating into disciplines as varied as electronics, chemical engineering, and optics. Whereas this Outlook does not attempt to delineate the developments and potential in all these areas, we have introduced some of the exciting prospects related to continued synthetic advances in the field. We further elaborated on three applied areas where MOFs are primed to excel: in challenging gas separations, as porous electrical conductors, and in heterogeneous catalysis. These examples are not exhaustive, but present subtleties that are applicable and relevant to many other applications of MOFs. The challenges and opportunities in these select applications, which span both the traditional and the modern aspects of the field, are illustrative of the continually expanding interest and bright future for MOF chemistry.

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