

# Recent developments in MXene and MXene/carbon composites for use in biomedical applications

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**Abstract:** MXene is a revolutionary two-dimensional material that has a distinct layer structure and the chemical composition of transition metal carbides. It has special physicochemical characteristics including a large specific surface area, good electrical conductivity, excellent mechanical properties and photothermal behavior, which give it a valuable variety of applications. To endow it a broader range of applications, it is often composited with carbon-based materials. Therefore, MXene and MXene/carbon composites have attracted much attention in applications such as electronics, biosensors and biomedicine over recent years. In this review, the fabrication, modification and biomedical applications of MXene and MXene/carbon composites are introduced, focussing on their biomedical applications, such as biosensors, antibacterial materials, drug delivery, and the diagnosis and treatment of diseases.

**Key words:** MXene/carbon based composites; Biomedical application; Sensor; Antibacterial

## 1 Introduction

With the advancements in material science, a family of novel materials, MXene, with two-dimension structures has emerged, which has drawn increasing attention from researchers owing to the distinct layer structure and excellent physicochemical properties over the past years. MXene is a series of transition metal carbides, nitrides or carbonitrides, whose chemical formula are expressed as  $M_{n+1}X_nT_x$  ( $n=1, 2, 3$ )<sup>[1]</sup>. In this formula, “M” represents the element of transition metal (such as Sc, It, V, Cr, Zr, Nb, Mo, Hf and Ta), X stands for the elements of carbon or nitrogen, while T is the extremity group which is bonded with M layer (such as  $-O$ ,  $-OH$ ,  $-F$ )<sup>[2-3]</sup>. Consequently, the family of MXene is very huge. To date, more than thirty different MXenes with different chemical compositions have been created in labs<sup>[4-6]</sup>. The inherent composition of transition metal carbides enables it exhibit prior conductivity, which makes it possess brilliant prospects in electronic industries<sup>[7-8]</sup>. Of note, the T groups ( $-O$ ,  $-OH$ ,  $-F$ ) were introduced in the surface of MXene during the preparation

process. As a result, MXene is prone to be modified and manifest remarkable biocompatibility and functionality<sup>[9-10]</sup> potential in biomedical fields<sup>[11-12]</sup>.

Even though MXene possesses superior performances in some applications such as sensor, disease treatments and so on, there still exist challenges in the practical application of MXene. For instance, low sensitivity and insufficient therapeutic effect of MXene caused by inadequate conductivity and limited photothermal conversion efficiency are the primary obstacles to be overcome. For solving these problems and broadening the application, MXene is usually composited with carbon-based composites to enhance comprehensive performances over the past years.

Among various carbon materials, carbon nanotubes<sup>[13]</sup> and graphene<sup>[14]</sup> have great potential to construct MXene/carbon based composites due to their unique structure, superior electronic conductivity and mechanical performance. In addition, these carbon materials exhibit admirable biocompatibility and are easily to be modified through chemical processes. The novel characteristics make them have great potential

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in biomedical applications<sup>[15-16]</sup>.

In this regard, the advancements of MXene and MXene/carbon based composites in biomedical applications over the past years are introduced and summarized. On the one hand, a summary of the MXene modification techniques for biomedical applications is discussed. The stability and biofunction classifications of MXenes are explained critically in this section. On the other hand, extensive discussions are given toward the applications of MXene and MXene/carbon based composites in biomedical disciplines. The focus of this section are summarized in the following 4 areas: biosensor domain, antibacterial field, drug delivery domain, diagnosis and treatment of disease (Fig. 1). Eventually, the challenges and outlooks for the further developments of MXene in terms of biomedical applications are critically discussed, in which we expect more excellent breakthroughs of MXene.

## 2 Modification of MXene nanosheets

In general, the universal strategies to obtain MXene are based on eliminating the “A” layer through various etching methods. According to the differences of etching agents, the common strategies for preparing MXenes can be categorized into several methods (Table 1), including hydrofluoric acid (HF)-etching method<sup>[17]</sup>, hydrochloric acid (HCl)/fluoride-etching method<sup>[18]</sup>, Lewis acid molten salt etching method<sup>[19]</sup> and etc<sup>[20-23]</sup>. Among these approaches, HF-etching method and HCl/fluoride-etching method are the most widely utilized methods. These two methods provide active groups ( $-F$ ,  $-OH$ ) on the surface of MXene. Therefore, the further modifications of MXenes could be easily achieved through the modi-

fication of these functional groups.

The surface of MXene nanosheets are endowed with different functional groups owing to different etching methods and etching reagents. The surface chemistries bring about the unique physicochemical characteristics of MXenes. The species and quantity of functional groups have huge impact on the surface properties of MXene.

As a result, it is necessary to modify MXene according to particular purposes. For MXene nanosheets, stability, loading capacity, biocompatibility and hydrophilicity are the main aspects taken into account. In general, the obtained MXene usually possesses  $-O$ ,  $-F$  and  $-OH$  groups on its surface, so MXenes usually exhibit excellent dispersity within aqueous media. As a result, in recent years, an increasingly interest has been focused on the modifications for biocompatibility, stability and loading capacity.

### 2.1 Modification for biocompatibility and stability

In consideration of practical situations, biocom-

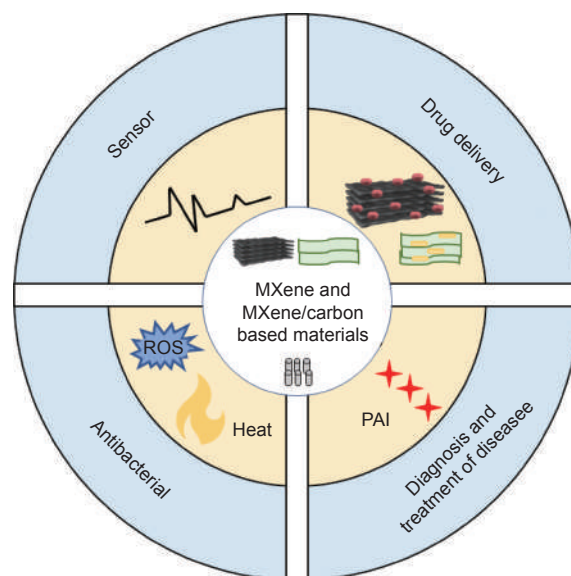


Fig. 1 The applications of MXene and MXene/carbon composites

Table 1 The comparisons of different methods to prepare MXene<sup>[17-19, 22-23]</sup>

Methods	Advantages	Disadvantages	Surface functional groups	Ref.
HF-etching	Simple and stable	Toxic and dangerous	$-F$ , $-OH$ , $-O$	[17]
HCl/fluoride-etching	Mild reaction process and safe	Introduction of hydrophobic group $-Cl$	$-F$ , $-OH$ , $-O$ , $-Cl$	[18]
Lewis acid molten salt etching	Suitable for producing $Ti_nN_{n-1}$	High demand for temperature	$-F$ , $-OH$ , $-O$	[19]
Chemical vapor deposition	Low cost and accurate control during reaction	High demand for temperature	Bare	[22]
Electrochemical corrosion	Mild and safe	Long reaction time	$-OH$ , $-O$	[23]
Alkali-etching	Better surface reactivity	Poor etching effect	$-OH$ , $-O$	[19]

patibility and stability are the prime issues to be solved in the biomedical applications of MXenes. During present explorations, the most commonly used strategy is to modify MXene with polymers. These approaches efficiently ameliorate the drawbacks. Owing to the abundant negative charges on the surface of MXene, a great deal of substances with positive charges could be assembled on the surface of MXenes through electrostatic interactions. For instance, Geng et al.<sup>[24]</sup> modified MXene with polyethylene glycol (PEG) through electrostatic interactions to enhance its stability. Moreover, Chen et al.<sup>[25]</sup> modified MXene with polyvinyl pyrrolidone (PVP) for enhancing its stability and biocompatibility. In fact, modifying MXene with polymers still remains the mainstream. For pursuing MXene with superior behaviors in biomedical fields, more modification strategies need to be investigated in the future.

## 2.2 Modification for biofunction

MXene is regarded as a promising tool for drug loading owing to the huge specific surface areas. Dong et al.<sup>[26]</sup> modified MXene using doxorubicin (Dox) with positive charge through electrostatic interactions. In this study, the results demonstrate that MXene exhibits excellent drug loading capacity, which suggests great potential in the application of tumor treatments.

Apart from drugs, some bioactive substances such as peptides have been utilized to endow the MXene with biofunction. For instance, Deng et al. constructed MXene/MoS<sub>2</sub> bio-heterojunction, which was further decorated with fibroblast growth factor-21 (FGF21) through polydopamine (PDA)-assisted grafting strategy<sup>[27]</sup>. Similarly, they modified MXene-based materials with lactate oxidase (LOx) in the same manner<sup>[28]</sup>. It could efficiently consume lactate to generate hydrogen peroxide (H<sub>2</sub>O<sub>2</sub>). Accordingly, this dedicated MXene-based material possesses great potential in lactate-accumulated infection wound. It provides a novel view in terms of the design of wound dressing.

In addition to the methods discussed above, a variety of methods have been investigated to change MXene nanosheets in order to improve their proper-

ties and enable practical applications.

## 3 Biomedical application of MXene and MXene/carbon based composites

MXene displays distinctive properties due to their special composition and structure. Especially, MXene exhibits good hydrophilia and biocompatibility, which makes it popular in biomedical applications. For example, the inherent composition of transition metal carbides endows MXene with good conductivity, which shows great potential in biosensor applications. Sharp edge and LSPR effect endow MXene with antibacterial property. Except the illustrated applications above, MXene has been extensively studied in bioimaging and treatments of diseases due to the special size effect and excellent photothermal conversion ability of MXene. It prompts the construction on multifunctional platform of diagnosis and treatment towards diseases. Moreover, with the assistance of carbon substrates including graphene and carbon nanotubes, the comprehensive property such as conductivity, composites mechanical property of MXene/carbon based composites could be enhanced, which enables they obtain more achievements in practical applications<sup>[29]</sup>. In this section, the applications of MXene and MXene/carbon composites in biosensor, antibacterial materials, drug delivery, diagnose and treatments toward diseases are discussed.

### 3.1 Biosensor application

Recently, MXene is believed as one of the most powerful candidates in application of biosensor, which is ascribed to its excellent conductivity, flexibility, hydrophilicity and biocompatibility. Among these characteristics, MXene has excellent conductivity owing to the special element composition and structure. It is superior to most of carbon materials. For instance, the multilayered structure and large specific surface area are beneficial to electron transportation, leading to the enhancement of conductivity. During the formation of Ti-O bonds and Ti-F bonds, defects were introduced which act as polarization centers to enhance conductivity. As a result, more and more studies related to MXene as flexible wearable

sensors<sup>[30–31]</sup>, electrochemical sensors<sup>[32–33]</sup> have been published during the past years. Nevertheless, there are shortcomings concerning MXene-based sensors during practical applications. For instance, MXene are prone to be oxidized, leading to instability of MXene-based sensors. Moreover, the stacked layer structure of MXene results in limited sensitivity and narrow detection range. Therefore, MXenes are usually composited with graphene and carbon nanotubes to improve their sensing performances<sup>[34]</sup>. In the following section, flexible wearable sensors and electrochemical sensors based on MXene and MXene/carbon based composites are introduced and discussed.

### 3.1.1 Flexible wearable sensors

Currently, flexible wearable sensors have gained great attentions due to the surface compliance and stretchability. It possesses great potential in health-care monitoring, human motion sensing, and human-machine interaction fields<sup>[35–36]</sup>. MXene has high conductivity, which is the prerequisite for construction of flexible sensors. Meanwhile, it exhibits extraordinary mechanical properties. Therefore, it has been broadly studied in flexible wearable sensors. However, sensors

involving MXene still suffer from thorny issues to be solved such as low sensitivity and narrow sensing range, which is attributed to the stacked adjacent layers. To surmount these obstacles, MXene is usually designed through the introduction of other substances or the regulation of its structures. For instance, Dong et al.<sup>[37]</sup> fabricated sandwich-like MXene/carbon nanotube (CNT) composites-based sensors through layer-by-layer (LBL) spray coating technique for pursuing higher sensitivity (Fig. 2a). In this work, it demonstrates that the loose MXene nanosheets are integrated into a whole by hairy CNT, indicating the formation of an integrated conductive network. The sensitivity (gauge factor up to 772.6) and sensing range (tunable range: 30%-130%) have been significantly enhanced. Moreover, the sensor possesses sensing performances at large and minor strain meantime, which indicates that the sensor has potential in human physiological signals monitoring. Meanwhile, Xiong et al.<sup>[38]</sup> prepared MXene/CNTs composite films as pressure sensors. The introduction of CNTs effectively prevent MXene from stacking and enhance the sensitivity of films. As same as the aforementioned

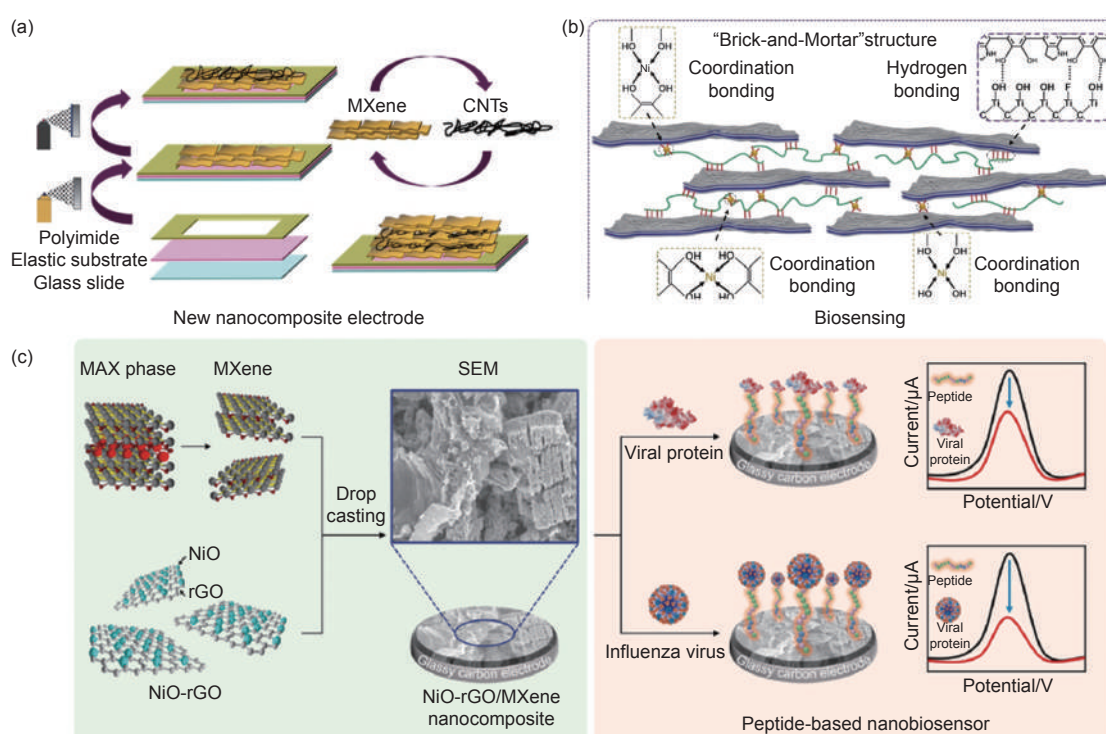


Fig. 2 (a) Preparation of sandwich-like MXene/CNT layer<sup>[37]</sup>. (b) Schematic illustration of the “Brick-and-Mortar” structure  $\text{Ti}_3\text{C}_2\text{T}_x\text{-AgNWs-PDA/Ni}^{2+}$  sensor<sup>[39]</sup>. (c) The principle of NiO-rGO/MXene sensor for detecting influenza viruses<sup>[45]</sup>. Reprinted with permission

strategy, Chen et al.<sup>[39]</sup> prepared bio-inspired  $Ti_3C_2T_x$ -Ag nanowire (AgNW)-PDA/ $Ni^{2+}$  sensor by a “brick-and-mortar” structure (Fig. 2b). In their study, the  $Ti_3C_2T_x$ , AgNW and PDA/ $Ni^{2+}$  were integrated into a whole through hydrogen bonds and coordination bonds. The special structure not only enhances the mechanical strength but also suppresses the crack generation of  $Ti_3C_2T_x$  nanosheets, leading to an ultra-high sensitivity of sensor.

In general, even though great efforts have been made in the design of MXene-based sensor, the narrow sensing range is still considered as an obstacle to be overcome. In order to address this issue, a vast number of researchers have introduced MXene into hydrogels to widen the sensing range. For example, Yu et al.<sup>[40]</sup> fabricated MXene nanocomposite organohydrogel (MNOH) through radical polymerization and hydrogen bonds. The sensor possesses good stretchability (350%) and sensitivity (gauge factor of 44.85). Apart from these characteristics, MNOH exhibits good self-healing property owing to supramolecular interaction and dynamic crosslinking between hydroxyl and tetrahydroxy borate ions, which boosts their practical application values. In addition to the above challenges, the usage convenience and reusability of sensors have been taken into account by researchers gradually. For instance, adhesiveness and self-healing behaviors are the main factors that should be considered in the application of sensor. Chen et al.<sup>[21]</sup> prepared PTCM-Gly organohydrogels with high tissue adhesiveness and self-healing property ascribed to the abundant hydrogen bonds and dynamic borate ester bonds in organohydrogels. It is in favor of the interface connections in practical applications.

In summary, it is difficult to provide high sensitivity and wide sensing range at the same time in MXene-based flexible sensors. As a result, more attentions should be paid in studies to balance the sensitivity and sensing range synchronously in terms of MXene-based sensors.

### 3.1.2 Electrochemical sensors

In electrochemical sensor field, MXene-based sensors occupy an important position attributed to

their large surface areas, outstanding conductivities, biocompatibility and electrochemical activity. During the past years, MXene-based sensors have been extensively applied in the detection of various substances signals including adrenaline, glucose, ascorbic acid and so on<sup>[41-42]</sup>. For instance, Rakhi et al.<sup>[43]</sup> report a study related to MXene/graphite composite paste electrode (MXene/GCPE)-based electrochemical sensor for adrenaline detection. The composite enhances the conductivity of the electrode. It makes adrenaline molecule interact through conductive porous channel onto the electrode easily, which significantly improves the sensitivity and selectivity of the sensor. In addition, MXene also has an excellent performance in cancer detection. For example, Kong et al.<sup>[44]</sup> fabricated a sandwich-structure electrochemical sensor for detection of cytokeratin fragment antigen 21-1 (CYFRA21-1). The sensor exhibits good selectivity and stability. Collectively, the illustrated sensors both confirmed the superiority of MXene in electrochemical sensors domain. It is predictable that MXene-based sensor would acquire profound enhancements with the continuous developments of MXene. Moreover, Jong et al.<sup>[45]</sup> constructed nickel oxide (NiO)-reduced graphene oxide (rGO)/MXene nanocomposite supported on glassy carbon electrodes for detecting influenza viruses. The collaboration of MXene and rGO not only protect MXene from oxidation, but also ameliorate the conductivity and biocompatibility of sensor, which both in favor of increasing the sensitivity of sensor.

In conclusion, benefiting from the superior conductivity, MXene-based composites have made great achievements in sensing field over the past years. Nevertheless, how to improve sensitivity and sensing range still are the primary issues in fabrication and design of MXene-based sensors in future.

## 3.2 Antibacterial application

Over the past years, wound infection has become a major public health concern that not only endangers people's lives but also places a massive burden on society. Among various types of infection,

bacterial infection is a common problem, which is urgent to be solved. In addition to the abuse and misuse of antibiotics, the resistance of bacteria toward these antibiotics has been enhanced. It results in increasing antibacterial difficulties. As a result of their excellent antibacterial effect, many antibacterial substrates have received more attention, including metal ions and antibacterial peptides<sup>[46]</sup>. During the exploration towards antibacterial materials, two dimensional materials such as graphene and MXene have attracted more attention because of the special structure and near-infrared light absorption effect. In this part, the MXene-based antibacterial composite are introduced in detail.

When skin is damaged, haemostasis is the first step in wound healing. The demand for haemostasis materials have been enhanced over the past 5 years. Sheng et al.<sup>[47]</sup> prepared PHBV-GO/MXene composite membranes that possessed hemostatic behaviors and antibacterial performances. Corresponding results demonstrate that the membranes remarkably increased platelet adsorption, blood coagulation time and antimicrobial performance. Therefore, it is an ideal haemostasis material for wound healing.

Meanwhile, wound infection is a huge challenge in medical fields. It impedes wound healing process and even leads to amputation. Consequently, it is vital to kill bacterial to protect human health. In recent years, MXene-based composites have been extensively studied in the field of eliminating wound infection<sup>[48]</sup>. For example, Zhang et al<sup>[49]</sup>. prepared Nb<sub>2</sub>C titanium plate (Nb<sub>2</sub>C@TP) to prevent bacterial infection, which could achieve the objective of synergistic antibacterial function. It includes physical interactions between bacteria membrane and the sharp edge of Nb<sub>2</sub>C MXene and photothermal behaviors. Corresponding *in-vitro* and *in-vivo* antibacterial experiments show that Nb<sub>2</sub>C@TP composites exhibit outstanding antibacterial performances. It can be considered as a potential antibacterial platform for infectious issues. However, with the abuse of antibiotic and evolution of bacterial, single antibacterial modality cannot meet the demands of eliminating bacterial. In present studies, one strategy is to construct antibacterial platform

through introducing multiple antibacterial substrate to achieve the goal of synergistic antibacterial effect. This strategy would enhance the antibacterial effectiveness<sup>[50-51]</sup>. For example, Zhang et al<sup>[52]</sup>. combined traditional antibacterial metal Ag with Ti<sub>3</sub>C<sub>2</sub>T<sub>x</sub> to fabricate Ag/Ti<sub>3</sub>C<sub>2</sub>T<sub>x</sub> composites (Fig. 3a). It manifests good photothermal conversion efficiency and significant antibacterial activity. *In-vitro* wound healing experiments indicate that Ag/Ti<sub>3</sub>C<sub>2</sub>T<sub>x</sub> hydrogel has good antibacterial property, which has a great potential in future wound healing as dressing.

Apart from the combination of MXene with traditional antibacterial metal materials, MXene can be also used in combination with antibiotic to enhance the antibacterial efficiency. Deng et al.<sup>[53]</sup> prepared SP@MX-tobramycin (TOB)/GelMA hydrogel to fight with postoperative infection and guide bone tissue regeneration (Fig. 3b). The composites can exert synergistic antibacterial effect by combining three kinds of antibacterial substrates. Relevant bacterial growth curves and bacterial inhalation experiments demonstrate that the composites SP@MX-TOB/GelMA hydrogel possesses outstanding antibacterial activity. This design offers a new strategy in antibacterial domain.

Except for the above methods, researchers have made great efforts in structure of materials for superior antibacterial effect as well. During the exploration, MXene-based Schottky junction has drawn more attention<sup>[54]</sup>. Schottky junction is a structure formed by the interface of semiconductor and metal. The metal characteristic of MXene enables it to transfer photo-induced electrons easily and then form Schottky junction with semiconductor materials. It facilitates the separation of electrons and holes. The formation of Schottky junction could enhance the photocatalytic activity, which leads to the generation of more reactive oxygen species(ROS). Thus, the Schottky junction can achieve enhanced photothermal therapy effect and photodynamic therapy effect. It significantly enhances the antibacterial effect. For instance, Wu et al<sup>[55]</sup> prepared Bi<sub>2</sub>S<sub>3</sub>/MXene Schottky junction through synthesizing Bi<sub>2</sub>S<sub>3</sub> nanorods *in situ* on the surface of

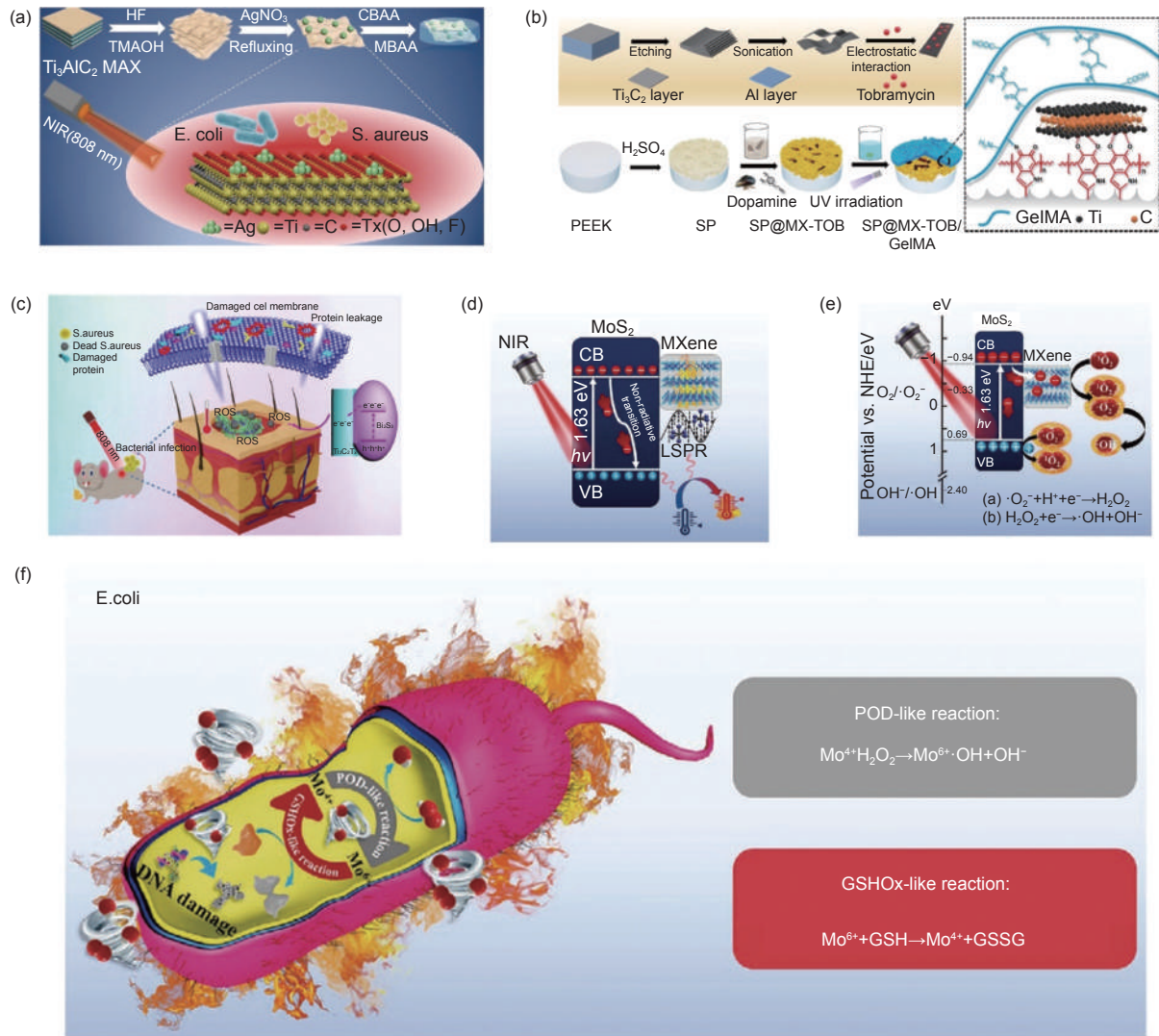


Fig. 3 (a) Fabrication process and photothermal performances of MXene/Ag composites<sup>[52]</sup>. (b) Preparation of SP@MX-TOB/GelMA antibacterial treatment platform<sup>[53]</sup>. (c) Fabrication and antibacterial mechanism of Bi<sub>2</sub>S<sub>3</sub>/MXene Schottky junction<sup>[55]</sup>. (d) Schematic image of photothermal mechanism of MXene/MoS<sub>2</sub> bio-heterojunctions<sup>[27]</sup>. (e) Schematic diagram of photocatalytic mechanism of MXene/MoS<sub>2</sub> bio-heterojunctions<sup>[27]</sup>. (f) Schematic illustrations of POD-like reaction and GSXOx-like reaction mechanism of MXene/MoS<sub>2</sub> bio-heterojunctions<sup>[27]</sup>. Reprinted with permission

MXene (Fig. 3c). The Bi<sub>2</sub>S<sub>3</sub>/MXene Schottky junction is formed due to the contact potential difference of each component, which inhibits the backflows of electrons and accelerate the transfer and separation of charges. Therefore, the photocatalytic ability is obviously enhanced. It leads to the high ROS level and highly antibacterial efficiency. It provides a new insight into designing antibacterial systems based on MXene nanosheets. Meantime, Deng et al.<sup>[27]</sup> fabricated growth factor-decorated Ti<sub>3</sub>C<sub>2</sub> MXene/MoS<sub>2</sub> bio-heterojunctions as a quad-channel synergistic antibacterial platform. The platform exhibits photothermal, photodynamic, peroxidase-like (POD-like) activity

and glutathione oxidase-like characteristic (Fig. 3d-f). Photodynamic properties have been enhanced due to the heterojunction structure. The intracellular ROS level is significantly enhanced. All mentioned above characteristics suggest that MXene/MoS<sub>2</sub> heterojunctions perform outstanding killing bacterial properties.

In summary, the design methodologies for MXene and MXene/carbon based antibacterial materials present a fresh perspective for creating an antibacterial platforms. It would prompt the developments of antibacterial materials exploration. However, the accompanying cytotoxicity should also be considered in its application.

### 3.3 Drug delivery application

The intrinsic characteristics of MXene, including special layer structure, abundant active groups and large specific surface areas, make MXene extremely promising in drug delivery application. Meantime, a number of carbon composites such as graphene, carbon nanotubes possess the ability of loading drugs owing to larger specific area as well. Especially in antitumor drug delivery, they not only work as drug carrier, but also exert photothermal effect against tumors. During the past years, drug release platforms concerning these materials have made great progresses in tumor treatments<sup>[56-57]</sup>. In this section, the design principle and application will be introduced.

Despite great achievements have been made in treatments of disease<sup>[26]</sup>, tumors are still believed as the biggest threats for human health in current society. In present, the most commonly used strategy for tumor treatment is chemotherapy. Nevertheless, chronic usage of chemotherapy drug will result in drug resistance of cancer cells. To solve the thorny issue, some studies related to the combination of chemotherapy and photothermal therapy (PTT) have been developed.

MXene with good photothermal performances and drug loading capacity has been studied in this area. Deng et al.<sup>[58]</sup> prepared MXene/Dox-Cobalt nanowires (CoNWs) heterojunctions for synergetic anticancer of photothermal therapy and chemotherapy. On the one hand, localized heating induced by photothermal conversion ability of heterojunctions leads to fracture between Dox and heterojunctions, and then gives rise to drug releasing. On the other hand, under weak acid environment of tumor, protonation of the amine groups in Dox is enhanced (Fig. 4a-b). Meanwhile, the hydroxyl groups are protonated and then result in repulsive interactions between Dox and MXene/CoNWs. All characters would enhance the target and efficiency of tumor treatment (Fig. 4c). Meanwhile, Liang et al.<sup>[59]</sup> synthesized carbon nanotubes/MXene microspheres loading doxorubicin for cancer treatment. The formation of microspheres offers larger specific area and rough surface, which is beneficial to drug release. According to experiment results, the drug loading capacity can reach 85.6%. With the combination of photothermal therapy, photodynamic therapy and chemotherapy, the anti-cancer efficiency has been sig-

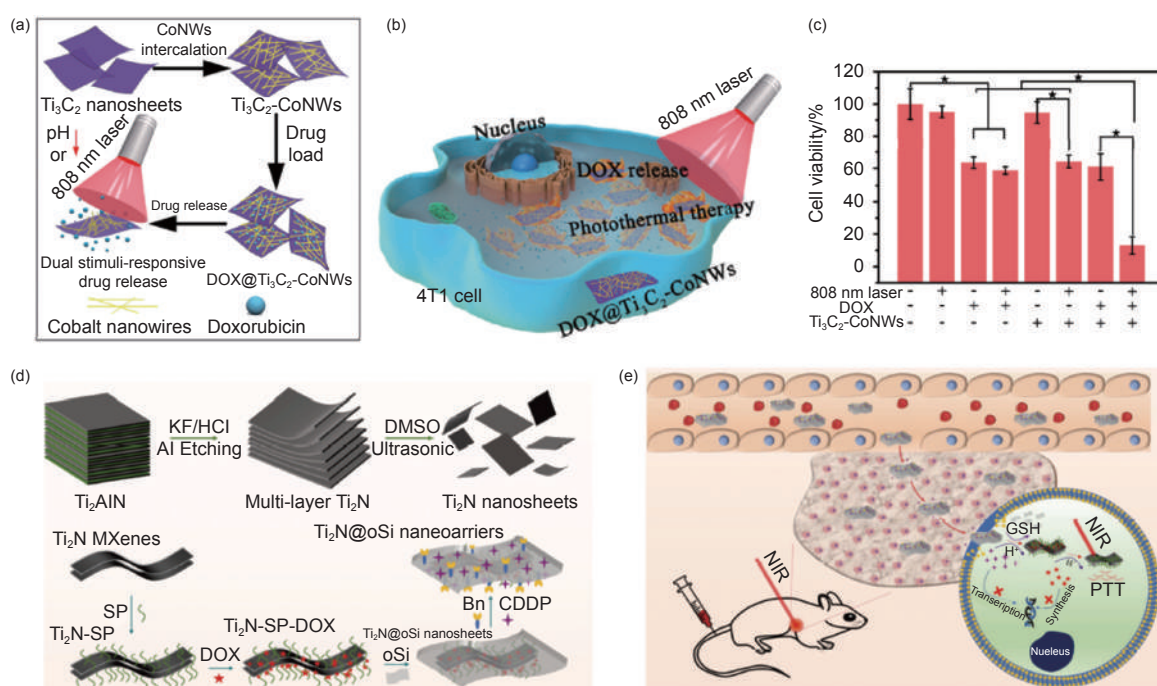


Fig. 4 (a) Fabrication process of Dox@MXene/CoNWs heterojunction<sup>[58]</sup>. (b) Schematic image of chemo-photothermal synergistic anticancer platform Dox@MXene/CoNWs<sup>[58]</sup>. (c) 4T1 cell viability with different treatments<sup>[58]</sup>. (d) Preparation procedure of MXene Ti<sub>2</sub>N@oSi loaded with Dox/CDDP<sup>[60]</sup>. (e) The anticancer mechanism of Ti<sub>2</sub>N@oSi loaded with Dox/CDDP. Reprinted with permission<sup>[60]</sup>

nificantly improved. However, the study is only carried out in cellular level. The real response induced by the *in-vivo* heterojunctions is still unknown. It should be investigated in further study.

In addition, low tumor killing efficiency and poor therapy targeting have been regarded as huge restrictions in antitumor treatments. To enhance the anticancer efficiency, researchers have proposed a view to load multiple drugs for synergistic therapy based on chemo-photothermal therapy platform. In order to improve the targeting of cancer therapy, a strategy that combined multi-stimulus responsive approaches and drug releasing has been proposed. Tumor microenvironment (TME) possesses unique physical and chemical conditions including weak acid environment, high GSH content and so on. It provides opportunities for targeting drug releasing to tumor. Inspired by these viewpoints, Wang et al.<sup>[60]</sup> fabricated MXene  $\text{Ti}_2\text{N}@o\text{Si}$  loading Dox and cisplatin(CDDP) for chemo-photothermal therapy of cancer, which could accomplish pH-responsive, NIR-responsive and GSH-responsive drug releasing at the same time (Fig. 4d, e). Relevant results indicate that the drug loading efficiency reaches 796.3%. *In-vitro* and *in-vivo* anticancer experiment results demonstrate that the composite possesses targeting, triple-stimulus responsive drug releasing ability and great anticancer performances.

To sum up, owing to the large specific surface area and innate negative charge, MXene has become the most charming candidate as drug carrier in tumor treatment. In further investigations, responsive drug release platform based on MXenes should be made more efforts for precise treatment of tumors.

### 3.4 Diagnosis and treatment of disease

Graphene has preminent NIR absorption effect. It not only has broad application in photoacoustic imaging (PAI), but also possesses a great potential in photothermal therapy of tumors<sup>[61]</sup>. For instance, Deng et al. fabricated gallium core with a reduced graphene oxide (RGO) shell ( $\text{Ga}@RGO$ ), which exhibits excellent NIR absorption ability and PAI effect. It could serve as PAI contrast agent *in-vivo*<sup>[62]</sup>.

Similar to graphene, MXene has PAI capacity as well. Additionally, it is susceptible to modification because of the active groups on its surface. There are more possibilities for MXene to combine with other materials for dual-mode imaging and therapy. With the rapid developments of imaging technology and illness progress, single mode imaging cannot meet new requirements of illness diagnosis. As a consequence, supplement information concerning disease are urgent needed. It could significantly enhance the accuracy of diseases diagnosis. MXene with excellent hydrophilicity, biocompatibility and the ability of PAI has become a promising candidate for construction of dual mode imaging platform<sup>[63]</sup>. The inherent photothermal behaviors of MXene endow it with good treatment efficiency of tumor. It could accomplish diagnosis and treatment of disease synchronously<sup>[64-65]</sup>. For instance, Cheng et al.<sup>[66]</sup> fabricated core-shell  $\text{Ti}_3\text{C}_2@Au$  nanocomposites as multifunctional diagnosis and treatment platform. It could achieve CT(Au)/PA ( $\text{Ti}_3\text{C}_2$ ) imaging effect and tumor ablation effect simultaneously (Fig. 5a). Corresponding results demonstrate  $\text{Ti}_3\text{C}_2@Au$  exhibits excellent diagnosis and treatment effects towards tumor. At the same time, Chen et al. prepared  $\text{Ta}_4\text{C}_3$ -iron oxide nanoparticle (IONP) through *in-situ* growth. The system possesses photothermal, CT (Ta) and MRI (IONP) effects simultaneously. *In-vitro* and *in-vivo* results both manifest extraordinary tumor-killing effects with the guidance of CT and MRI. It indicates that  $\text{Ta}_4\text{C}_3$ -IONP could be used in the diagnosis and treatment of tumor successfully. Moreover, in order to enhance the effectiveness of cancer therapy, researchers have also tried to introduce anticancer drugs into the MXene-based platform for diagnostic and treatment. The goal of synergistic anticancer could come true. Chen et al.<sup>[67]</sup> prepared a small planar  $\text{Dox}@Ti_3C_2$ -SP (Fig 5b), which could be easily accumulated into the tumor owing to enhanced permeability and retention (EPR) effects. Corresponding *in-vivo* results manifest that  $\text{Dox}@Ti_3C_2$ -SP possesses a good photothermal ablation ability towards tumor under NIR irradiation with guidance of PAI (Fig. 5c).

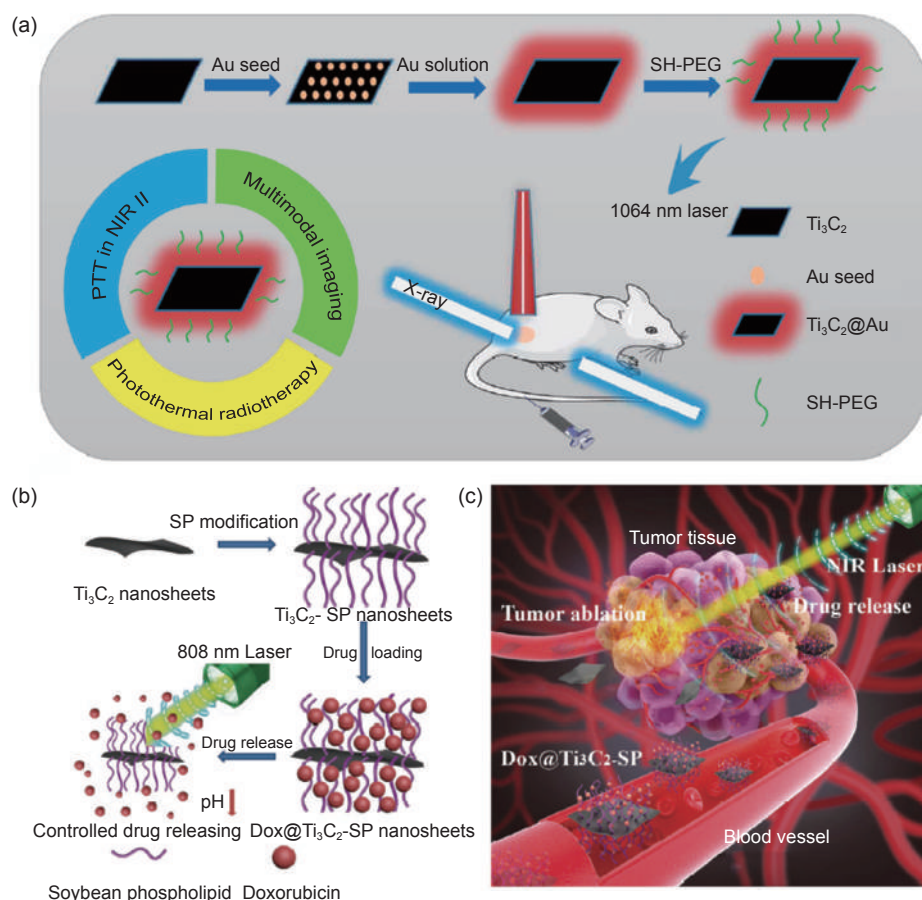


Fig. 5 (a) Preparation procedure and schematic illustration of multifunction diagnosis and treatment platform of  $Ti_3C_2@Au$ <sup>[66]</sup>. (b) Fabrication of  $Dox@Ti_3C_2-SP$  for PA imaging and chemo-photothermal therapy<sup>[67]</sup>. (c) Schematic illustration of diagnosis and treatment mechanism of  $Dox@Ti_3C_2-SP$  against cancer<sup>[67]</sup>.

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## 4 Conclusion and outlook

In summary, MXene, a revolutionary two-dimensional material, has distinctive structure and exceptional properties including conductivity, photothermal conversion ability and so on, which enable them to have a wide application range in various fields. Especially in biomedical fields, MXene has been extensively studied due to its good biocompatibility and the abundance of active groups on the surface. Because of their excellent conductivity, MXene performs admirably in sensor applications. The sharp edge and reductive groups of MXene give it a great potential in antibacterial field. Due to their high specific surface area and active groups, MXenes can load drugs effectively, giving it a bright future in the field of drug delivery. The photothermal characteristics of MXene induced by LSPR effect make it possible to become a

powerful candidate for diagnosis and treatment of disease. Moreover, with the help of carbon materials including graphene and carbon nanotubes, the conductivity, photothermal capacity and mechanical property have been extremely enhanced. It provides more possibilities for a broader range of application. Therefore, MXene and MXene/carbon based composite have made significant advancements in the biomedical fields recently.

The studies of MXene, however, are still in its early stages. There are certainly many issues that need to be resolved. (1) Antibacterial mechanism of MXene should be studied in further studies. Despite the fact that MXene has been widely used to build antibacterial platforms. The accurate antibacterial mechanism is still unknown. It is vital to figure out the antibacterial mechanism for further design of MXene-based antibacterial platform construction. (2) MXene is prone to

be oxidized due to the abundant hydroxyl groups on its surface. It leads to unstable conductivity and influence accuracy of MXene-based sensor. As a result, explorations on the modification techniques of MXene to prevent it from oxidizing is essential in further research. (3) The toxicity of MXene should be systematically analyzed in subsequent studies. If MXene is applied *in vivo*, the investigations about absorption, distribution, metabolism and long-term toxicity towards MXene should be taken into account seriously.

To solve these issues, there are several strategies for references: (1) In terms of the property of being easily oxidized, there are two directions can be concerned. One is to introduce antioxidant substances to prevent MXene from being oxidized. From the point of view of material preparation, the other is to fabricate MXene nanosheets with higher stability. (2) In order to comprehensively investigate the toxicity of MXene nanosheets, corresponding *in vivo* distribution, metabolism and pharmacokinetics assays of MXene-based materials should be carried out in further study.

In conclusion, with the advancements and collaboration of material science, chemistry and biology, MXene and MXene/carbon based composites will make substantial progresses in the biomedical fields in the future.

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