Review Article

Journal of Environmental Nanotechnology

# Roles of MXenes in Biomedical Applications: A Review

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Received: 02.06.2025 Accepted: 20.08.2025 Published: 30.09.2025

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## ABSTRACT

Two-dimensional MXenes have recently gained interest as a new family of materials for biomedical implant purposes because of their exceptional combination of physicochemical and biological properties. This review traces the development of MXenes, highlighting synthesis methods aimed at enhancing biocompatibility and ensuring therapeutic use. Their conducive interactions with biological systems, mechanical stability, and tunable surface chemistry are some of the critical factors in determining implant integration and function. MXenes can improve tissue integration and long-term functionality in a wide range of biological applications, including brain, cardiovascular, and orthopaedic implants, based on recent research. Cumulatively, the research highlights the growing significance of MXenes in future biological implants.

**Keywords:** MXenes; Biomedical implants; Tissue integration; Surface chemistry.

## 1. INTRODUCTION

The evolution of MXenes has been characterised by important discoveries and technical advancements, as their significance in materials research has continuously increased. By the serendipitous formation of first MXene, $Ti_3C_2$, in 2011 by using hydrofluoric acid to selectively etch aluminium from $Ti_3AlC_2$, Barsoum and Gogotsi began their adventure. This opened the eyes on the possibilities of such two-dimensional materials while at the same time introducing a new class of materials. The successful development of these new compositions utilizing various transition metals and surface terminations by 2012 has led researchers to begin to grow the family of MXene materials. This interest began in 2013 with a series of publications detailing the exceptional properties of MXenes, such as their enormous specific surface area, high electrical conductivity, and mechanical strength. These properties paved the way for doing research on MXenes for various applications. Due to significant progress in synthesis and delamination processes in 2014, high quality MXene flakes can be produced and have already begun to be implemented in sectors such as energy storage and catalysis. Researchers started concentrating on scalability in 2016 as interest in the topic increased in order to fulfil the growing demands of both industry and academia. A significant milestone was reached in 2018 when the biocompatibility of MXenes was acknowledged, marking their introduction in the biomedical sector. They can now be used in orthopaedic implants, biosensors, and drug delivery systems. Throughout the 2020s, research has been increasingly focused on developing new compositions, surface modifications, and chemical functionalisation to increase the usability of MXenes. Fig. 1 shows the timeline of development of MXenes. Growing attempts to combine MXenes with cutting-edge fabrication methods such as 3D printing, have made it possible to create implants tailored to each patient and multifunctional biomedical equipment. Their potential for medical use is supported by the analysis of their biodegradability and long-term *in vivo* behaviour. The continuous progress in this field has demonstrated the quick development of material systems and inclusion of several fields, including materials science, chemistry, physics, and biomedical engineering. MXenes will have a big influence on the future development of biomedical technology.

MAX phases are a class of multilayer ceramics with the general formula $M_{n+1}AX_n$. These compounds are made up of carbon and/or nitrogen, an A-group element (like silicon or aluminum), and an early transition metal (like titanium or molybdenum). They are perfect for selective chemical exfoliation because of their naturally layered hexagonal structure, which has comparatively weak metallic bonds between the M and A layers. When these bonds are cleaved, ultrathin, stable nanosheets with surface terminations (shown by $T_x$) that increase their chemical flexibility are obtained. The versatility of MXenes, both in terms of composition and surface chemistry, has enabled their incorporation into a multitude of applications. MXenes continue to show promise as multipurpose materials in a variety of applications, including energy storage, catalysis, and increasingly biomedical sectors. Fig. 2 illustrates their reputation as one of the most promising material systems to emerge in recent years due to its structural tunability, high conductivity, mechanical strength, and surface reactivity.

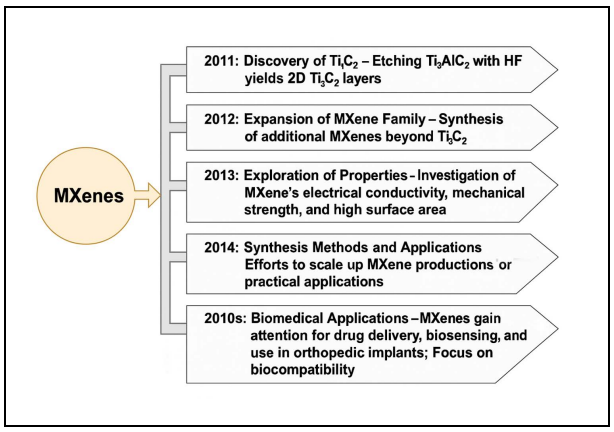



**Fig. 1: Timeline indicating the evolution of mxenes**

The distinctive structural formula of MXenes, where M stands for an early transition metal, X for carbon and/or nitrogen, and $T_x$ for surface terminations like hydroxyl (–OH), oxygen (–O), fluorine (–F), or chlorine (–Cl), is what really sets them apart. These functional groups are introduced throughout the synthesis process and are primarily responsible for the highly changeable surface chemistry and improved water dispersibility of MXenes. Because of their thin, two-dimensional structure, they have a high surface area, remarkable mechanical and thermal resilience, and electrical conductivity, all of which contribute to their broad variety of uses. Computer simulations have predicted over 250 unique compositions since the identification of MXene. Up to 30 have been synthesized to date, each with its own set of distinctive properties suitable to a particular use. The widening diversity of MXenes has been applied in energy storage, water filtration, electromagnetic interference shielding, and catalysis, amongst others. Their electrical conductivity renders them very promising to be used in supercapacitors, batteries, and ultra-sensitive electronic sensors. The large specific surface area of these materials providing numerous active sites for chemical reactions, renders them excellent in the areas of catalysis and energy storage. The strong and flexible nature of MXenes makes them ideal for application in composite materials and load-bearing systems. Their ability to fine-tune their surface properties is one feature that sets them apart. Scientists can modify MXenes to meet diverse performance requirements by modifying the transition metal constituents in their structure or the surface functional groups. Due to their structural flexibility and established biocompatibility in materials such as $TiC_2T_x$, it is possible to explore their utility in medical and technical applications. The development of next-generation wearable and flexible electronics is made possible by the exceptional thermal stability of MXenes. This property qualifies them for high-temperature reactions and their capacity to exfoliate into thin, flexible sheets. When considered collectively, these characteristics show the unique combination of properties that make MXenes one of the most versatile and promising materials in modern STEM fields. In Fig. 3, their primary properties and their applications are summarised.

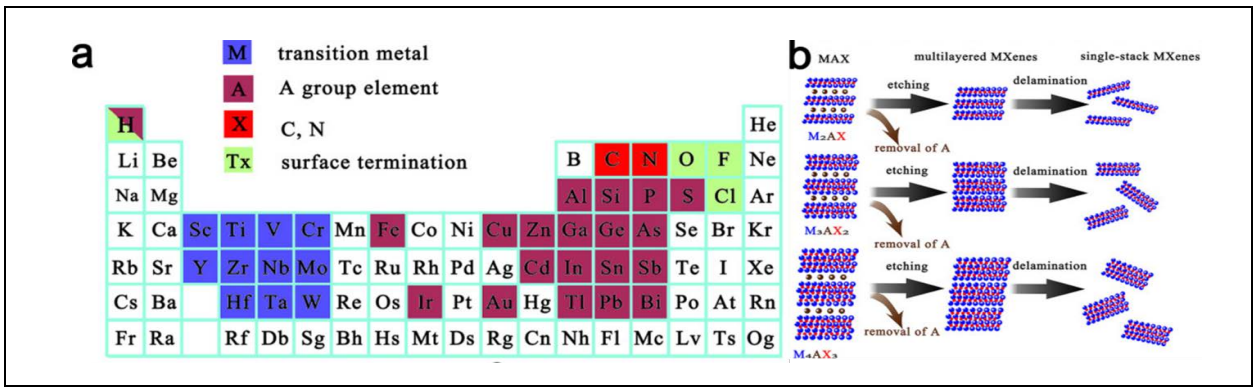



**Fig. 2: (a) Elements in the periodic table that are known to form $M_{n+1}AX_n$ phases and (b) Structure of MAX phases and the corresponding MXenes (Li *et al.* 2023)**

Even though MXenes have many advantages, there are still some significant barriers that keep them from being widely used. One of the main challenges is the synthesis process because dangerous materials like hydrofluoric acid are used so frequently. This causes problems with safety and scalability of large-scale production. Their stability and applicability in real-world situations are restricted by the fact that a number of MXenes are moisture-sensitive and can break down in damp or watery conditions. Another restriction is the limited number of transition metals that can be used to create MXenes. Very little is known about long-term toxicity of MXenes and their behaviour in living things. Though some research indicates that they are biocompatible, there are worries over their potential for usage in biomedical applications. Managing surface terminations precisely is another difficulty (Li *et al.* 2023)

The performance and dependability of MXenes are directly impacted by functional groups, which are crucial for altering the material's characteristics but can be challenging to maintain over time. Also, MXenes are not completely stable in the environment, which under certain conditions can lead to degradation and thus impede them useful in the long term. But, due to their nanoscale dimensions, flexible surfaces, and biocompatibility, MXenes are of particular interest in the biomedical field. These properties make them desirable for a number of applications including cancer therapy and targeted drug delivery. MXenes, like other well-known two-dimensional materials such as graphene and transition metal dichalcogenides, offer unique combinations of high strength, high surface area to bulk ratios, tunable electrical properties, and the ability to tailor size.

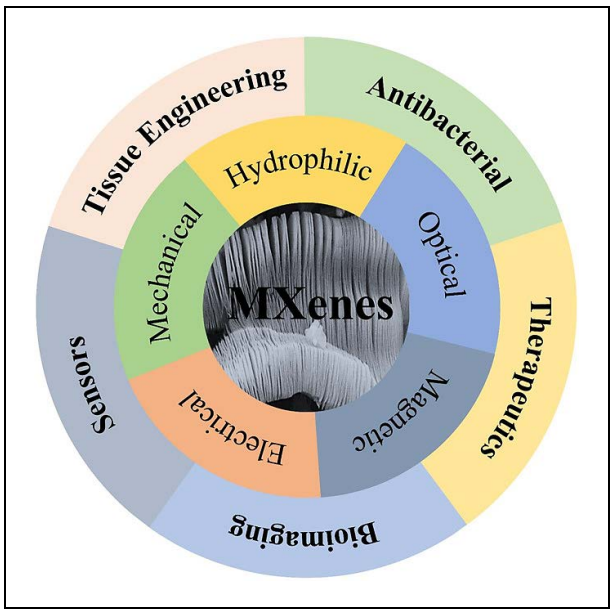



**Fig. 3: Properties and applications of Mxenes (Huang *et al.* 2021)**

Their multitude of functional groups at the surface terminations makes them ideal to bind drugs or imaging agents. This could lead to the development of smart and sensitive drug delivery systems. Due to their outstanding performance as photothermal and photodynamic agents, MXenes have been used to non-invasively treat conditions such as cancer, as they absorb near-infrared light strongly and efficiently convert light to heat. MXenes are also being explored for a wide range of other medical applications, including biosensing as well as tissue engineering and wearable medical technology – such as smart fabrics and electronic tattoos. Among other innovative technologies, these materials are promising for their conductivity, flexibility, and biocompatibility. But long-term toxicity and safety concerns have also highlighted the need for more thorough research and specific regulations. To these issues, scientists are investigating novel surface modifications that can enhance stability and reduce possible toxicity. Among these, the incorporation of biocompatible polymers into MXenes represents one avenue of modification (Vahid *et al.* 2021).

Due to the electrical conductivity and flexible surfaces of MXenes, sensitive, next-generation sensors that can precisely monitor biological signals have been developed. This aligns with other biosensing innovations, such as Ag-Ni-thiol-based hybrid Surface Plasmon Resonance (SPR) biosensors, theoretically designed by Muthumanicam *et al.* (2023) for highly sensitive viral detection. Field-effect transistors and electrochemical detectors are examples of these sensors. MXenes are beneficial and nontoxic, with minimal toxicity in biological systems. This opens up new possibilities for their use in implants, wearable technology, and long-term biological applications. Since MXenes have exceptional versatility, modifiable surfaces, and compatibility with biological tissues, they can be employed in future technologies (Vahid *et al.* 2021).

## 1.1 Other Key Applications of MXenes

Energy storage and conversion due to the growing need for efficient, sustainable energy storage, MXenes have recently gained attention. Batteries, supercapacitors, and hybrid energy devices can all benefit from their high conductivity and tunable chemistry. They have also shown promise in catalysing reactions like the hydrogen evolution reaction (HER) and the oxygen evolution reaction (OER), which are essential to renewable energy systems.

MXenes hold great promise in environmental and sensing technologies such gas sensing, heavy metal removal, microwave absorption, and electromagnetic interference (EMI) shielding. Their distinct layered structure and functional surface groups improve their capacity to precisely block electromagnetic noise, filter impurities, and detect gases. Despite the great potential they hold, there is still opportunity to enhance their selectivity and guarantee steady, sustained performance across a range of applications (Fig. 4).

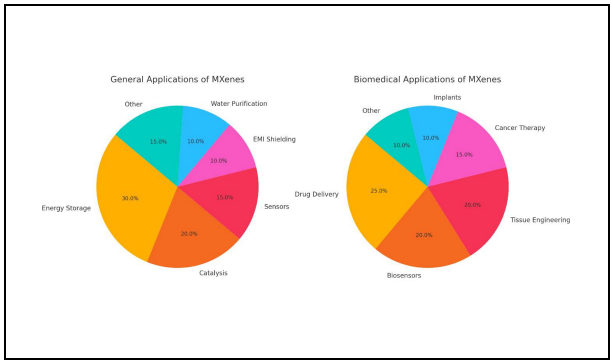



**Fig. 4: (a) General uses of MXenes (b) Usage of MXenes in biomedicine**

### 1.2 Classifications of MXenes

MXenes are a fascinating class of two-dimensional materials that feature distinctive structural properties, making them ideal for various uses in electronics and medical technologies. Altering the chemistry and structure of MXenes enables their capabilities to broaden across various domains based on particular requirements. Ti-based MXenes like $Ti_3C_2$ and $Ti_2CT_x$ are prominent as the most studied and acknowledged substances in the MXene family, despite the fact that researchers have explored and examined numerous other MXene varieties. Besides Ti-based MXenes, various other types of MXenes exist, including Nb-based MXenes (e.g., $Nb_2CT_x$, $Nb_4CT_x$), V-based MXenes (e.g., $V_2CT_x$, $V_4CT_x$), Ta-based MXenes (e.g., $Ta_4CT_x$), Mo-based MXenes (e.g., $Mo_2CT_x$, $Mo_2N_2T_x$), and W-based MXenes (e.g., $W_2CT_x$, $W_2N_2T_x$). Table 1 shows classification of MXenes.

**Table 1. Common classification of MXenes**

| S. No. | MXene Type | Transition Metal | Elements in Structure | Surface Termination | Layer Count | Suitable Applications |
|---|---|---|---|---|---|---|
| 1 | $Ti_3C_2T_z$ | Titanium (Ti) | Carbon (C) | -OH, -F, -O | Multi layered | Energy storage (batteries, supercapacitors), Catalysis, Biomedical applications (drug delivery) |
| 2 | $V_2CT_x$ | Vanadium (V) | Carbon (C) | Variable ($T_x$) | Multi layered | Energy storage, Catalysis, Sensors |
| 3 | $Nb_4CT_x$ | Niobium (Nb) | Carbon (C) | Variable ($T_x$) | Multi layered | Biomedical applications (biosensing, drug delivery), Energy storage, Catalysis |
| 4 | $Mo_2Ti_3C_2T_x$ | Molybdenum (Mo) | Carbon (C) | Variable ($T_x$) | Multi layered | Energy storage, Catalysis, Electronics |

## 2. Methods of MXene Synthesis

There are many different types of MXenes due to the tremendous advancements in MXene synthesis in recent years. The three primary types of these synthesis methods are top-down, bottom-up, and surface engineering. Top-down methods form MXene nanosheets by delaminating or exfoliating precursor materials, typically MAX phases. This approach usually uses methods like selective etching and mechanical exfoliation. Mechanical exfoliation transforms bulk MAX phases into nanoscale MXene layers using mechanical force, and selective etching separates specific layers from the MAX phases to form the necessary MXene structure. But bottom-up methods focus on building MXene structures from atomic or molecular components. The structure and composition of the final MXenes can be precisely controlled because to these methods. Atomic layer deposition (ALD) and chemical vapor deposition (CVD) are two bottom-up techniques used to create MXenes with precise characteristics.

The third strategy, surface engineering, focuses on improving the functionality of current MXenes for particular applications by altering their surface characteristics. Adding functional groups or molecules to the MXene surface can enhance its performance in a variety of applications or its ability to interact with other materials. Fig. 5 summarizes common synthesis techniques of MXenes.

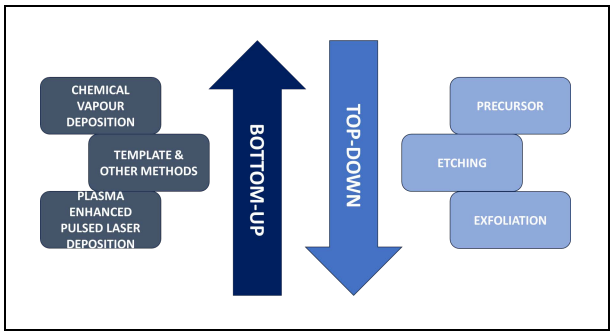



**Fig. 5: Synthesis methods involved in producing MXenes**

### 2.1 Top-down Method

Top-down strategies have long been established as effective methods for the synthesis and design of nanomaterials, particularly in the transformation of bulky precursors into essential quantum particles. Various three-dimensional and two-dimensional bulk materials, such as graphite, carbon nanotubes, graphene, $MoS_2$ crystals, $WS_2$ powder, black phosphorus, and g-CN, have been successfully converted into quantum dots through

top-down techniques. These methods, including ball-milling, liquid exfoliation, chemical etching, electrochemical processes, intercalation, hydrothermal/solvothermal treatments, ultra-sonication, and microwave irradiation, play a crucial role in establishing initial oxygen-containing functionalities on catalyst surfaces, leading to the formation of defects that serve as reactive sites for breaking down bulk molecules into smaller quantum particles (Gogotsi, 2023).While these techniques offer advantages such as operation at low temperatures and the use of abundant raw materials, challenges like low yield and specific treatment requirements exist. Notably, ultrasonication, ball-milling, intercalation, hydrothermal, solvothermal, micro-explosion, and acid reflux are among the most widely employed top-down approaches for MXene fabrication, and their details are explored in this section.

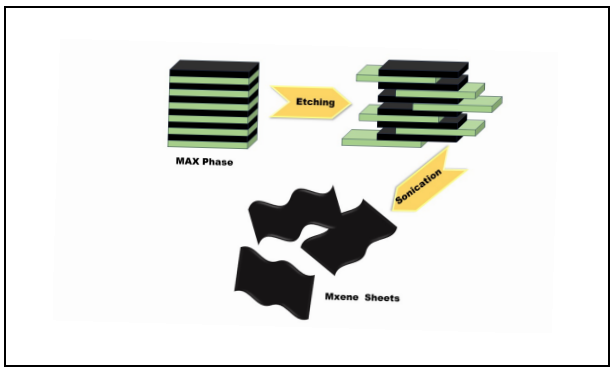



**Fig. 6: Top-down synthesis method for MXenes**

As shown in Fig. 6, MXenes are produced top-down by carefully extracting layers from a bulk MAX phase precursor, often a ternary metal carbide or nitride. It is normal practice to use the precursor $TiAlC_2$. Following the selection of the MAX phase, the A-layers are selectively etched utilising techniques such as acid treatment or fluoride-based etching. Following mechanical forces or intercalation that delaminate or exfoliate the MAX layers, MXene nanosheets are obtained. Washing to eliminate contaminants and drying to achieve the correct MXene content are the last stages. MXenes with specific properties can be produced in a scalable and regulated manner using this top-down approach, making them suitable for applications in energy storage, biomedical engineering, and catalysis. Since its launch in 2011, the top-down synthesis of two-dimensional transition metal carbides, nitrides, and carbonitrides has been the primary method for producing MXenes. This method has accelerated the synthesis of several MXene compositions, each with distinct surface terminations, properties, and potential applications, by employing wet chemical etching to selectively remove precursor components. Researchers can optimize MXenes for specific applications by adjusting the synthesis conditions for each one. To form highly conductive, free-standing, or thin films for use in devices such transistors, transparent conductors, saturable absorbers, photonic diodes, lasers, detectors, and electromagnetic interference shielding, softer etching techniques are favored in electronic applications. Comparatively, MXenes with nanoscale flakes, lower lateral diameters, and more exposed edges are perfect for gas sensing, light-to-heat materials, gas catalysis, surface-enhanced Raman spectroscopy (SERS) substrates, and biological photothermal therapy. These diverse applications demonstrate how crucial surface terminations, morphology, structure, composition, and synthesis techniques are in defining the characteristics and possible applications of MXenes. The development of MXenes as a flexible material family with wide-ranging applications in many different industries will be enabled by current investigations.

## 2.2 Bottom-up Method

To form MXene nanosheets, the material is assembled from atoms or tiny molecules using a bottom-up synthesis method. The size distribution, geometric shape, and surface termination of MXenes can be precisely controlled through bottom-up synthesis, in contrast to the top-down method, which involves selectively removing layers from a bulk precursor. Usually, the procedure begins with the assembly of atoms or tiny molecules to build 2D structured structures, which can then be converted into MXene nanosheets. As shown in Fig. 7, bottom-up approaches have the potential to improve the stability and compatibility of MXenes and offer advantages in terms of size distribution controllability, although they are less studied at the moment than top-down methods. The challenge lies in optimizing these methods for scalability and cost-effectiveness to make them more widely applicable for MXene synthesis (Dong *et al.* 2020). This method can be applied to produce MXene quantum dots (MQDs) from small precursors of both organic and inorganic molecules. Although previous investigations have laid a solid foundation for bottom-up MXene preparation, addressing challenges like large-scale fabrication, highly efficient precursors with low toxicity, gentle reaction conditions, excellent crystallinity, monodispersity, and high yields is crucial. One-pot bottom-up methodologies, with their relatively simple operating conditions compared to top-down methods, are likely to be employed for MXene fabrication in the future to meet increasing application demands. While there is limited research on bottom-up methodologies for MQD fabrication, the promising nature of the study warrants significant attention and emphasis on these strategies (Thakur *et al.* 2023).

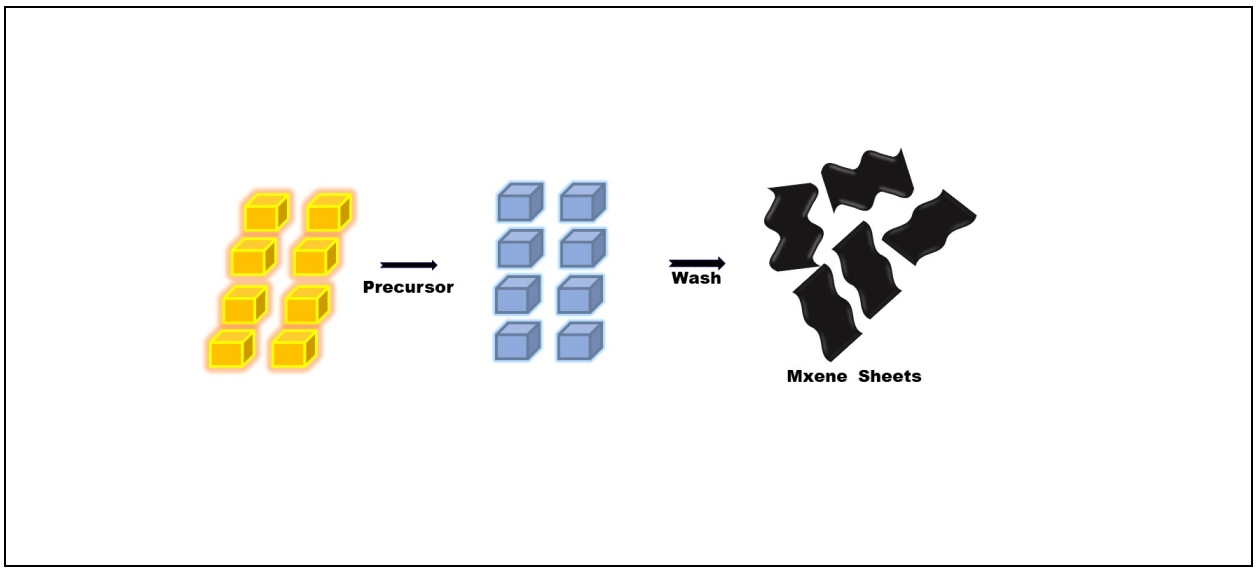



**Fig. 7: Bottom-up synthesis approach of MXene**

In recent years, various bottom-up synthesis methods, including chemical vapor deposition (CVD), plasma-enhanced pulsed laser deposition (PEPLD), and the template method, have been developed for the synthesis of 2D transition metal carbides (TMCs) and nitrides (TMNs). These methods have proven effective in producing high-crystalline-quality materials, distinguishing them from MXenes. Importantly, bottom-up methods enable the synthesis of 2D TMCs and TMNs that are challenging to achieve through top-down methods, expanding the family to include materials like WC, TaC, TaN, MoN, and heterostructures. The high-quality samples obtained allow in-depth investigations into the intrinsic structure and properties of these materials, particularly in the context of superconductivity. Additionally, these 2D TMCs and TMNs exhibit promising potential for applications in electrocatalysis, Li-ion batteries, and supercapacitors (Khazaei *et al.* 2019). While the bottom-up synthesis methods offer the prospect of further enlarging the family of 2D TMCs and TMNs, certain challenges remain. Achieving large-area uniform films and producing atomically thin samples, down to one unit cell thick, poses ongoing difficulties. Further research efforts are needed to explore the properties and applications of these high-quality 2D TMCs and TMNs.

The bottom-up synthesis approach for MXenes involves atomic-scale control, starting from small organic or inorganic molecules or atoms, leading to the organized growth of 2D-ordered layers. One common method for this approach is chemical vapor deposition (CVD), which yields high-quality thin films on various substrates (Lim *et al.* 2022). However, the films produced are often multi-layered. An example is the synthesis of ultrathin $Mo_2C$ MXene using methane gas as the carbon source and a Cu/Mo foil substrate at temperatures above 1085°C. Despite achieving defect-free and highly crystalline films with lateral sizes between 10 and 100 µm, the lack of surface functional groups and the relatively large size make them less ideal for biomedical applications. Other methods explored for MXene synthesis include the template method and plasma-enhanced pulsed laser deposition (PELPD). $Mo_2C$ films synthesized by PELPD demonstrated high quality, controllable thickness. Scalable salt-template synthesis has been applied to produce 2D nitrides. However, limited information is available on the bottom-up synthesis of biocompatible MXenes, leaving room for improvement in this area (Salim *et al.* 2019; Oyehan *et al.* 2023; Soman *et al.* 2023).

## 2.3 Surface Engineering

Despite the remarkable electronic, optical, hydrophilic, biocompatible, and mechanical properties of MXenes, their inherent instability and propensity for aggregation in physiological environments necessitate surface modification to optimize their properties for broader applications without compromising their original 2D morphology. Synthetic MXenes feature functional groups, high-density charges, and a large surface area, making them amenable to various modification techniques, including electrostatic adsorption, hydrogen bonding, and van der Waals forces. There are three distinct surface modification methods, namely, compound-based strategies in surface chemistry, inorganic nanoparticle-based surface chemistry, and metal nanoparticle-based surface chemistry. These approaches aim to enhance the stability and functionality of MXenes for tailored applications while preserving their unique 2D structure (Huang *et al.* 2020).

Engineering certain molecules or polymers, such as polyethylene glycol (PEG), soybean phospholipid (SP), hyaluronic acid (HA), polyvinyl

pyrrolidone (PVP), and their mixtures, is the basis of polymer-based surface modification techniques for MXenes. A variety of methods such as, aryl diazonium salt method, self-initiated photo-grafting and photopolymerization (SIPGP), and non-covalent physical adsorption interactions are employed to effectively construct these polymers onto the surface of MXenes. Among these, non-covalent interactions and simple physical adsorption are frequently utilized, particularly in drug loading applications. This method enhances the stability, utility, and compatibility of MXenes for targeted applications and provides a versatile base for developing drug delivery systems and various biological uses (Oyehan *et al.* 2023). Mesoporous silica nanoparticles (MSN) offer an intriguing inorganic nanoparticle approach for modifying the surface of MXene, serving as an alternative to polymers. $TiC_2$ MXene combined with MSN serves as an example of effective surface nanopore engineering in drug delivery systems, achieved through a straightforward sol-gel chemical method.

Tetraethyl orthosilicate (TEOS) is used as a precursor of silica in an alkaline environment, while cetyltrimethylammonium chloride (CTAC) is a mesopore-directing agent. The process yields a composite with well-ordered mesopores, improved hydrophilicity, and better surface chemistry. Through improved dispersion and controlled release, the modification enhances the capability of MXenes to be used in drug delivery. The $TiO_2$-$TiC_2$ nanocomposite biosensor opens up biomedical possibilities by demonstrating how combining MXenes with nanoparticles provides flexible platforms that are more stable, bioactive, and biocompatible (Huang *et al.* 2020).

Another effective strategy for enhancing the properties of MXenes and diversifying their uses is the incorporation of noble metals such as platinum, silver, and gold. These modifications can enhance resistance to electrochemical signals and biofouling, thus doubling the signal up to four times.

MXene flake electrochemical activity is improved by the presence of 5 nm gold nanoparticles (AuNPs), which have unique thiol-Au bond interactions. The modification retains the exceptional antifouling activity and sensitivity of the biosensor while reducing the analysis time. Additionally, by promoting DNA adsorption, aromatic hydrophobic groups help palladium (Pd) nanoparticles and Pd/Pt composites develop uniformly. These modifications, particularly enhancing electrocatalytic activity, illustrate the wide range of applications for which noble metal-modified MXenes can be utilized, including photoelectric catalysis, improved charge transfer, and enhanced sensing capabilities (Verger *et al.* 2019). Table 2 presents a general overview of the main objectives, raw materials, synthesis processes, applications, and examples of the top-down, bottom-up, and surface engineering methods used in MXene synthesis.

**Table 2. Essential elements of surface engineering, bottom-up, and top-down approaches in MXene synthesis**

| S. No. | Aspect | Top-down Approach | Bottom-up Approach | Surface Engineering |
|---|---|---|---|---|
| 1 | Main Objective | Selective removal of layers from bulk precursor (MAX phase) | Building up material from atoms or molecules to form MXene | Modifying surface properties for enhanced functionality |
| 2 | Starting Material | Bulk MAX phase precursor | Atoms or small molecules | Synthesized MXene nanosheets |
| 3 | Synthesis Steps | • Selection of MAX phase precursor<br>• Etching A layer<br>• Washing and delamination<br>• Drying and powder formation<br>• Surface Modification | • Building from atoms or molecules<br>• Precise control of structure<br>• Challenges inscalability and cost<br>• Hybrid approaches | • Introduction of functional groups, intercalation, coating, doping, etc.<br>• Tailoring surface chemistry<br>• Enhancing stability and compatibility |
| 4 | Applications | Various applications like energy storage, catalysis, sensing | Limited scalability, potential for precise control over properties | Tailoring MXene for specific uses, improving compatibility |
| 5 | Examples | MXene nanosheets | $TiC_2T_x$ and $Mo_2TiC_2T_x$ (Limited examples due to challenges) | Functionalization with -OH, -COOH, $-NH_2$, etc.<br>Intercalation of ions, Surface coating with polymers or oxides |

## 3. BIOMEDICAL APPLICATIONS

Research into a range of biological domains, including implant materials, diagnostics, biosensing, bioimaging, and antibacterial therapies, has been stimulated by the physicochemical properties of MXenes. MXenes are highly versatile and offer solutions for a range of biomedical applications due to their enormous surface area, electrical conductivity, mechanical strength, and changeable surface chemistry (Su *et al.* 2022). Among the several MXenes, $Ti_3C_2T_x$ has emerged as a preferred choice, especially for applications involving biomedical implants. Its unique combination of high conductivity, strong mechanical properties, and customisable surface terminations enables improved performance and biocompatibility in implantable devices. Poor electrical performance and poor biological tissue integration are two issues with conventional implant materials that are solved by these characteristics (Singh and Santhosh, 2021). The integration of MXenes in cutting-edge medical technology is predicted to advance with further research into their behaviour in biological systems. Manufacturing, biology, energy, and optics are only some of the sectors in which applications for MXenes are increasing rapidly. The excellent electrical conductivity, high surface-to-volume ratio, and strong near-infrared absorption of these nanoplatforms make them ideal for drug delivery, cancer therapy, bioimaging, and biosensing (Singh and Santhosh, 2021).

In addition, colloidal stability can be improved, circulation time prolonged, and *in vivo* toxicity reduced by merely polymer-nanoparticle functionalisation of MXenes (Heo *et al.* 2022). Intrinsic antibacterial activity of MXenes can be applied in targeted drug delivery of medication, photothermal treatment, improved biomedical implants, and photoacoustic and optical imaging. Surface modification makes their interactions with biological systems exactly customisable and therefore more efficient (Heo *et al*. 2022; Garg and Flavia, 2023; Yan *et al.* 2021). Regenerative medicine, cancer treatment, infection prevention, and biosensing are just a few of the biomedical engineering applications where MXenes have demonstrated great potential. Their performance can be enhanced by combining or hybridising them with other materials. In soft robotics, wearable medical gadgets, and tissue engineering, MXene-reinforced hydrogels provide significant benefits because of their superior mechanical qualities and biocompatibility. Current challenges include the lack of standardized safety testing protocols (consistent use of cell lines, dosages, and animal models) and limited comprehensive studies linking material properties to biological responses and toxicity (Yan *et al.* 2021). Further research on the biosafety of MXene formulations is necessary due to concerns about their biodegradability, especially for medicinal and regenerative applications. To assess both acute and long-term impacts on organs and biological systems, systematic *in vivo* research using both small and large animal models is crucial. Understanding the underlying molecular mechanisms of MXenes in tissue regeneration, infection prevention, and cancer treatment also requires cooperative research with molecular biologists. Another exciting avenue for applications in responsive nanomedicine, regenerative therapies, and diagnostics is the synthesis of ultrasmall MXene-based quantum dots. Notably, MXene nanocomposites that react to NIR-II light provide a fresh approach to deep-tissue therapies like infection therapy and cancer ablation. Incorporating other elements during synthesis opens up possibilities for novel hybrid materials with a wide range of enhanced properties (Garg *et al*. 2023; Yang *et al.* 2019a; Guo *et al.* 2022). Furthermore, the influence of MXenes on stem-cell engineering, especially *via* processes like electrical stimulation and thermomodulation, is less understood while having enormous potential. These processes have the potential to transform regenerative tissue platforms and 3D cell cultures based on hydrogel. Additionally, MXene-based composites exhibit significant potential as biosensing devices, multi-modal imaging agents, antimicrobial formulations, and sensitizers for photothermal cancer therapy. Future challenges include creating novel surface engineering approaches to improve biocompatibility and functionality, enhancing synthesis methods, and scaling up manufacturing in a cost-effective manner. To enable the clinical translation of MXene technologies and make MXenes prominent materials in contemporary biomedicine, these problems must be resolved (Peng *et al.* 2018).

## 4 BIOMEDICAL IMPLANTS

Biomedical implants have revolutionized contemporary healthcare by providing novel treatments for a variety of illnesses. These implants have been vital in regaining mobility, reducing pain, and enhancing general quality of life in anything from knee replacements to cardiovascular devices. Advances in technology and the development of biocompatible materials have significantly enhanced implant life and reduced immunological rejection risks, thus resulting in more reliable and long-lasting outcomes (Guo *et al.* 2022). Despite such advances, biomedical implants remain challenging. Infection is still a risk, and adverse effects consist of tissue rejection and failure of the implant. Additionally, the importance of constant evaluation is underscored by the lack of certainty when it comes to the long-term influence of some implant materials on human health. The need possible post-surgery complications underscore the importance of developing more sophisticated materials that ensure patient safety and improve implant performance. MXenes are one promising class of two-dimensional nanomaterials that possess special features that make them amenable to biomedical applications, especially in orthopaedic implants. Their unique properties, such as excellent mechanical strength, electrical conductivity,

and dynamic surface chemistry, make them the ideal choice to enhance implant integration and function (Wang *et al.* 2018). In orthopaedic applications, MXenes actively stimulate bone tissue remodelling and regeneration. The surface modification of MXenes creates a bioactive interface that fosters osteoblast adhesion and proliferation. MXenes can also promote osteogenic differentiation of mesenchymal stem cells, speeding up new bone formation around the implant. Since they are biodegradable, they can gradually incorporate into the surrounding tissue, reflecting the body's own healing processes. Antimicrobial activity of MXenes is yet another major benefit. Infection is a major concern in orthopaedic surgery, and it helps lower the risk of infection. Furthermore, doctors can monitor implant integration and bone healing in real time because of their capacity to act as contrast agents in medical imaging. Due to its adaptability, MXenes have become next-generation orthopaedic implant materials that enhance implant success and durability by combining structural support and biological activity (Zhang *et al.* 2020). Beyond orthopaedics, MXenes show great promise in a range of biological applications. Their high surface area, conductivity, and ease of functionalisation make them suitable for application in drug delivery, biosensing, and diagnostic platforms. MXenes offer the ability to deliver medications with a controlled and targeted release, improving therapeutic efficacy while lowering side effects. The highly sensitive and selective detection of biological markers, made possible by their usage in biosensors, is essential for early sickness diagnosis and surveillance. Furthermore, preliminary studies on MXenes have demonstrated strong biocompatibility, supporting their use in tissue engineering and regenerative medicine.MXene-reinforced hydrogels, for instance, are being researched for applications in wearable medicine, bionic devices, and 3D cell cultures, where their mechanical properties and conductivity can regulate tissue growth and cell behaviour (Han *et al.* 2019).The biosafety and long-term effects of MXenes on the human body remain serious issues despite their many benefits. Numerous elements have a significant impact on cytotoxicity and biocompatibility, including flake size, surface functional groups, and oxidation states. To evaluate the acute and long-term impacts of MXene–cell interactions *in vivo*, more research is required to completely understand the exact processes behind these interactions. To get thorough conclusions regarding their safety, standardized testing procedures, including uniform cell lines, doses, and animal models, are required. The practical use of MXenes in biomedical applications also requires addressing issues with large-scale synthesis, economical production, and environmental sustainability (Guo *et al.* 2022; Wang *et al.* 2018; Zhang *et al.* 2020; Han *et al.* 2019). In future, MXenes will likely play a significant role in the creation of smart orthopaedic implants by serving as platforms that are bioactive, antimicrobial, and imaging-enabled in addition to being structural materials. Because of their adjustable characteristics, they are perfect for drug-delivering structures, implant scaffolds, and surface coatings that promote osseointegration, lower inflammation, and facilitate real-time tissue healing monitoring. Potential orthopedic uses for MXenes are compiled in Table 3, which also emphasizes how their multifunctional qualities can improve implant durability, functionality, and patient outcomes.

**Table 3. MXenes with potential applications in implants and potential orthopedic implant applications**

| S. No. | MXene Type | Transition Metal | Elements in Structure | Surface Termination | Layer Count | Potential Orthopedic Implant Applications |
|---|---|---|---|---|---|---|
| 1 | $Ti_3C_2T_z$ | Titanium (Ti) | Carbon (C) | -OH, -F, -O | Multi layered | Implant coatings, Biocompatible scaffolds, Drug delivery systems |
| 2 | $Nb_4C_3T_x$ | Niobium (Nb) | Carbon (C) | Variable (Tx) | Multi layered | Biocompatible coatings, Tissue engineering, Orthopedic implants |
| 3 | $Mo_2TiC_2T_x$ | Molybdenum (Mo) | Carbon (C) | Variable (Tx) | Multi layered | Orthopedic implant materials, Biocompatible coatings |

## 4.1 MXenes in Orthopedic and Neural Applications: Advancing Implant Technology and Regenerative Medicine

Despite their widespread use, medical implants still confront problems such tumor recurrence, infections, immunological rejection, and poor tissue integration. MXenes offer a promising solution because of their superior biocompatibility, biodegradability, and intrinsic antimicrobial qualities. They work as surface coatings on implants to improve bioactivity and dramatically lower problems like bacterial infection and tumor regeneration (Yang *et al.* 2019b; Khan *et al.* 2022). Multifunctional MXene-integrated implants have been produced for the

treatment of osteosarcoma, showing improved osseointegration, promote osteogenic differentiation, and have increased cytocompatibility. Interestingly, 2D niobium carbide ($Nb_2C$) nanosheets attached to 3D-printed scaffolds have demonstrated efficient photothermal therapy ablation of bone cancer cells while concurrently encouraging angiogenesis and bone regeneration (Alli *et al*. 2024). Like graphene, MXenes promote osteogenic differentiation in mesenchymal stem cells, which speeds up the creation of new bone. Among these, $Ti_3C_2T_x$ has drawn interest due to its function in neural tissue engineering, where it promotes neurite outgrowth and synaptic activity by boosting voltage-gated calcium currents, which in turn supports the maturation and differentiation of neural stem cells (Vasyukova *et al*. 2022; Mallakpour *et al*. 2021). These characteristics, which include advantageous electrical conductivity and mechanical strength, make MXenes ideal for guided bone regeneration (GBR) and bone tissue engineering applications. *In vitro* and *in vivo* investigations, such as ALP and qRT-PCR assays, demonstrate their capacity to promote early osteogenic differentiation in preosteoblast cells. The biocompatibility and non-toxic nature of $Ti_3C_2T_x$'s was confirmed (Rabiee *et al*. 2023; Iravani and Rabiee, 2023; Garg and Flavia, 2023). With multifunctional properties spanning from bone regeneration and antimicrobial activity to neurological repair and cancer therapy, previous findings highlight their use in next-generation orthopedic implants (Guo *et al*. 2020).

## 5. ORTHOPAEDIC IMPLANTS

Traditionally, organic materials, which frequently have limited chemical and thermal stability as well as single-function capabilities, have been used to make biodegradable orthopedic implants. In response, because of their better physicochemical properties, inorganic two-dimensional (2D) nanomaterials, in particular, MXenes, have become potential alternatives (Koyappayil *et al.* 2022). MXenes are the perfect materials for improving the performance of orthopedic implants because of their important characteristics, which include easy functionalization, customizable morphology, great biocompatibility, selective biodegradability, multifunctionality, and high physiological stability (Koyappayil *et al.* 2022). They promote early cell proliferation and bone formation by facilitating osteogenic differentiation of bone marrow mesenchymal stem cells through their graphene-like structure (Maleki *et al*. 2022). Additionally, MXenes like $TiC_2T_x$ have improved synaptic transmission and neurite outgrowth in neural stem cells, suggesting their wider use in regenerative medicine (Maleki *et al*. 2022). Studies conducted *in vivo* have confirmed MXenes' good biocompatibility, demonstrating that at safe concentrations, there are little negative effects on neurotoxicity, movement, and general health (Chouhan *et al*. 2023). They are appropriate for implantable applications due to their low cytotoxicity and successful integration into biological systems, which have been further validated by *in vitro* testing (Chouhan *et al*. 2023). They also help lower the incidence of post-surgical infections, which are frequent problems in orthopedic treatments, thanks to their natural antibacterial qualities (Mostafavi and Siavash, 2022). MXenes also strengthen implants mechanically, which makes them appropriate for load-bearing applications like knee and hip replacements (Du *et al*. 2022). Their large surface area facilitates drug loading for targeted administration, which may improve treatment results (Du *et al*. 2022). Controlled bioactivity is further made possible by surface changes, which allow MXene composites to be tailored to certain medical purposes. In order to achieve clinical preparedness, more study is required to assess long-term biosafety, including genotoxicity and reproductive toxicity, even though MXenes exhibit great promise (Chouhan *et al*. 2023; Iravani and Rajender, 2022; Das *et al*. 2023). When it comes to biodegradable orthopedic implants and other biomedical innovations, MXenes is an all-around versatile platform with revolutionary possibilities.

**Table 4. Different types of orthopedic implants reinforced with MXenes and their potential applications**

| S. No. | Type of Implant | MXene Reinforcement | Potential Applications |
|---|---|---|---|
| 1 | Hip Joint Replacements | $Ti_3C_2T_x$ MXene Coating | Enhanced mechanical properties, improved osseointegration |
| 2 | Knee Joint Replacements | $Nb_2C$-PVP MXene Nanosheets | Biocompatible, potential for drug delivery, improved durability |
| 3 | Bone Plates and Screws | $Ti_3C_2$MXene Composite | Increased strength, tailored biodegradability, potential for drug delivery |
| 4 | Dental Implants | MXene-Modified Surfaces | Improved bioactivity, enhanced osseointegration |

A brief overview of several orthopedic implants augmented with various MXene reinforcing types and their associated medical uses is provided in Table 4. MXenes, such as $Ti_3C_2T_x$ and $Nb_2C$-PVP, have attracted a lot of attention as reinforcing materials for orthopedic devices such dental implants, bone plates, screws, and hip and knee joint replacements. For example, it has been demonstrated that covering hip joint replacements with $TiC_2T_x$MXene enhances mechanical strength and encourages osseointegration, both of which are essential for long-term implant durability. In a similar vein, $Nb_2C$-PVPMXene nanosheets applied to knee joint implants enhance biocompatibility and wear resistance while offering chances for localised medicine delivery to lower the risk of inflammation or infection after surgery. MXenes can be used in a variety of ways to improve implant performance, including enhanced biological response, durability, and therapeutic potential, as these reinforced systems demonstrate. Additionally, MXene-treated dental implant surfaces have shown enhanced bioactivity, supporting early bone integration and the long-term sustainability of dental prostheses (Yin *et al*. 2020). As research progresses, it is anticipated that MXene-reinforced implant optimisation will improve clinical outcomes and support customised treatment programs in orthopaedic and dental care.

## 6. BIOSAFETY EVOLUTION

A novel category of two-dimensional (2D) nanomaterials known as MXenes has demonstrated significant potential in various biological areas, including biosensing, cancer therapy, infection control, and regenerative medicine. Their exceptional performance and versatility across different domains can be ascribed to their distinctive blend of mechanical, electrical, chemical, and physical characteristics (Zhong *et al*. 2022). For instance, hydrogels reinforced with MXene have demonstrated significant potential in tissue engineering and wearable healthcare due to their superior conductivity, mechanical strength, and compatibility with cells (Chakraborty *et al*. 2019; Kang *et al*. 2023). To enhance their biocompatibility, biopolymers like collagen, silk fibroin, polyethylene glycol (PEG), poly(lactic-co-glycolic acid) (PLGA), chitosan, and poly-L-lysine have been employed in surface modifications. These modifications have demonstrated an enhancement in cellular connectivity and a reduction in negative effects (Iravani and Rajender, 2021). Additionally, the cytotoxicity profiles of MXenes have been anticipated by utilizing recent advancements in computer modeling, such as machine learning, which have expedited safety assessments and enabled more targeted biological applications (Chen *et al*. 2021). Despite recent improvements, there is still concern about MXenes' possible cytotoxicity. Numerous elements, such as size, surface functional groups, oxidation states, manufacturing processes, and exposure duration, have been shown to significantly affect cytotoxic behaviour (George and Balasubramanian, 2020). Specifically, cells can readily absorb MXene particles with sizes ranging from 1 to 100 nm through endocytosis, which could lead to adverse biological responses. Experimental data have shown that at concentrations as high as 250 mg/L, cell viability can decrease to less than 70% (Alhussain *et al*. 2020). Additional mechanistic research is necessary because it is still unclear exactly how MXenes harm cell membranes and impede intracellular signalling (Lim *et al*. 2021). Factors like particle size, shape, surface charge, and hydrophilicity that affect biological reactions must be taken into account when assessing the biocompatibility of nanomaterials, particularly MXenes. Potential damage routes include oxidative stress, genotoxicity, haemolysis, and organ-specific toxicity, particularly in the reproductive and neurological systems (Zhang *et al*. 2023). Stronger alternatives are sought for biodegradable orthopaedic implants because of the shortcomings of traditional organic materials. In this sense, MXene-based inorganic nanostructures offer a number of benefits, including intrinsic biocompatibility, programmable form, and controlled biodegradability and simple surface functionalisation. These features, along with MXenes' excellent physiological stability and multifunctionality, make it a strong candidate for orthopedic implant technologies (Das *et al.* 2020; Jatoi *et al.* 2023). Important factors such as solubility, dispersibility, long-term degradation, and systemic toxicity are still being studied to ensure their clinical safety and efficacy (Li *et al.* 2023). However, subsequent *in vivo* investigations have revealed little adverse effects on neurotoxicity, motility, and systemic health, even at dosages deemed safe for orthopedic usage (Sivasankarapillai *et al.* 2022). According to complementing *in vitro* studies, MXenes have the potential to be used in biomedical implant design and have shown comparable low cytotoxicity (Gogotsi, 2023). Continuous evaluations of genotoxic and reproductive toxicity are still required to guarantee their safe application in clinical practice.

## 7. CONCLUSION

MXenes, a rising class of two-dimensional transition metal carbides, nitrides, and carbonitrides, have garnered biomedical interest due to their high surface area, conductivity, tunable biocompatibility, and structural flexibility (Das *et al*. 2020; Jatoi *et al*. 2023). Their layered architecture allows modification via top-down or bottom-up methods, with fluorine-free etching offering safer, more biocompatible routes (Li *et al.* 2023). These properties make MXenes attractive for drug delivery, antimicrobial therapy, biosensing, cancer treatment, and tissue engineering. Their inherent antibacterial activity supports use in coatings for masks, catheters, and surgical gloves (Huang *et al*. 2021), while their mechanical flexibility favors implanted electronics and wearables (Vahid *et al.* 2021). In oncology,

photothermal and photodynamic activity enables precise, non-invasive therapies (Gogotsi and Babak, 2019).

Despite promise, in vivo interactions remain underexplored. Cytotoxicity varies with size, charge, oxidation, and functionalization, with smaller particles (<100 nm) linked to reduced cell viability (Dong et al. 2020). Biopolymer coatings (PEG, PLGA, chitosan, silk fibroin) improve compatibility (Khazaei *et al.* 2019). Machine learning approaches are advancing toxicity prediction (Lim *et al.* 2022). In orthopedics, MXenes offer tunable biodegradability, stability, and osseointegration, enabling composites with antibacterial, drug-delivery, and mechanical reinforcement benefits (Salim *et al.* 2019; Oyehan *et al.* 2023). Overall, while challenges remain in toxicity evaluation and clinical translation, MXenes' multifunctionality positions them as next-generation biomaterials with transformative potential. Future directions include scalable, eco-friendly synthesis, combinatorial surface engineering, and regulatory frameworks to ensure safe clinical use. With optimization, MXenes can redefine diagnostics, implants, and regenerative medicine (Verger *et al.* 2019).

## FUNDING

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

## CONFLICTS OF INTEREST

The authors declare that there is no conflict of interest.

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