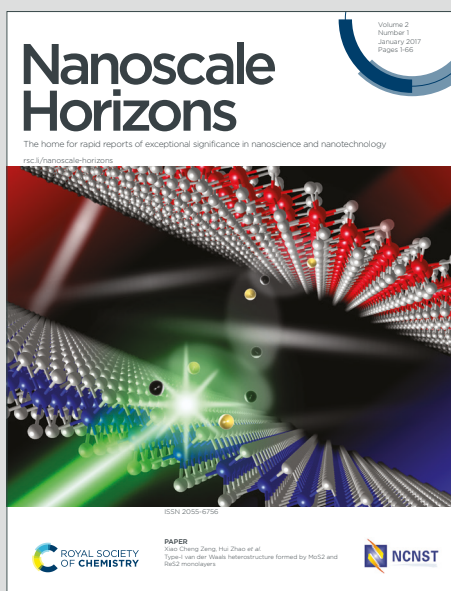


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View Article Online  
DOI: 10.1039/D4NH00209A

No new data were generated or analyzed in this study. All data supporting the findings of this study are available from the referenced articles within the review.



# Synergistic Integration of MXene Nanostructures into Electrospun Fibers for Advanced Biomedical Engineering Applications

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## Abstract

MXene-based architectures have paved the way in various fields, particularly in the healthcare area, owing to remarkable physiochemical and electromagnetic characteristics. The modification of MXene structures, along with their combination with polymeric networks, have also gained considerable prominence to further progress their features. The combination of electrospun fibers with MXene faces would be promising in this era since electrospinning has been declared a mature technique that is now being spun out into commercial biomedical applications. The introduction of MXene into the electrospun fibrous frameworks has highlighted outcomes in various biomedical usages, including cancer therapy, controlled drug delivery, antimicrobial targets, sensors, and tissue engineering. Correspondingly, this review describes the employed strategies for the preparation of electrospun configurations in tandem with the MXene nanostructures with fabulous characteristics. Then, the advantages of MXene-decorated electrospun fibers for use in biomedical applications are comprehensively enlightened. According to the investigations, rich surface functional groups, hydrophilicity, large surface area, photothermal features, and antimicrobial and antibacterial activities of the MXene could synergize the performance of electrospun layers to engineer versatile biomedical targets. Also, the future of this path is clarified to combat the challenges related to the electrospun fibers decorated with MXene nanosheets.

**Keywords:** MXene; Electrospinning; Nanofiber; Biomedical application; Drug delivery; Tissue engineering.

## 1. Introduction

In recent decades, nanofibrous configurations have emerged as valuable constraints toward approaching a diverse range of biomedical applications, specifically biomedical targets [1, 2].



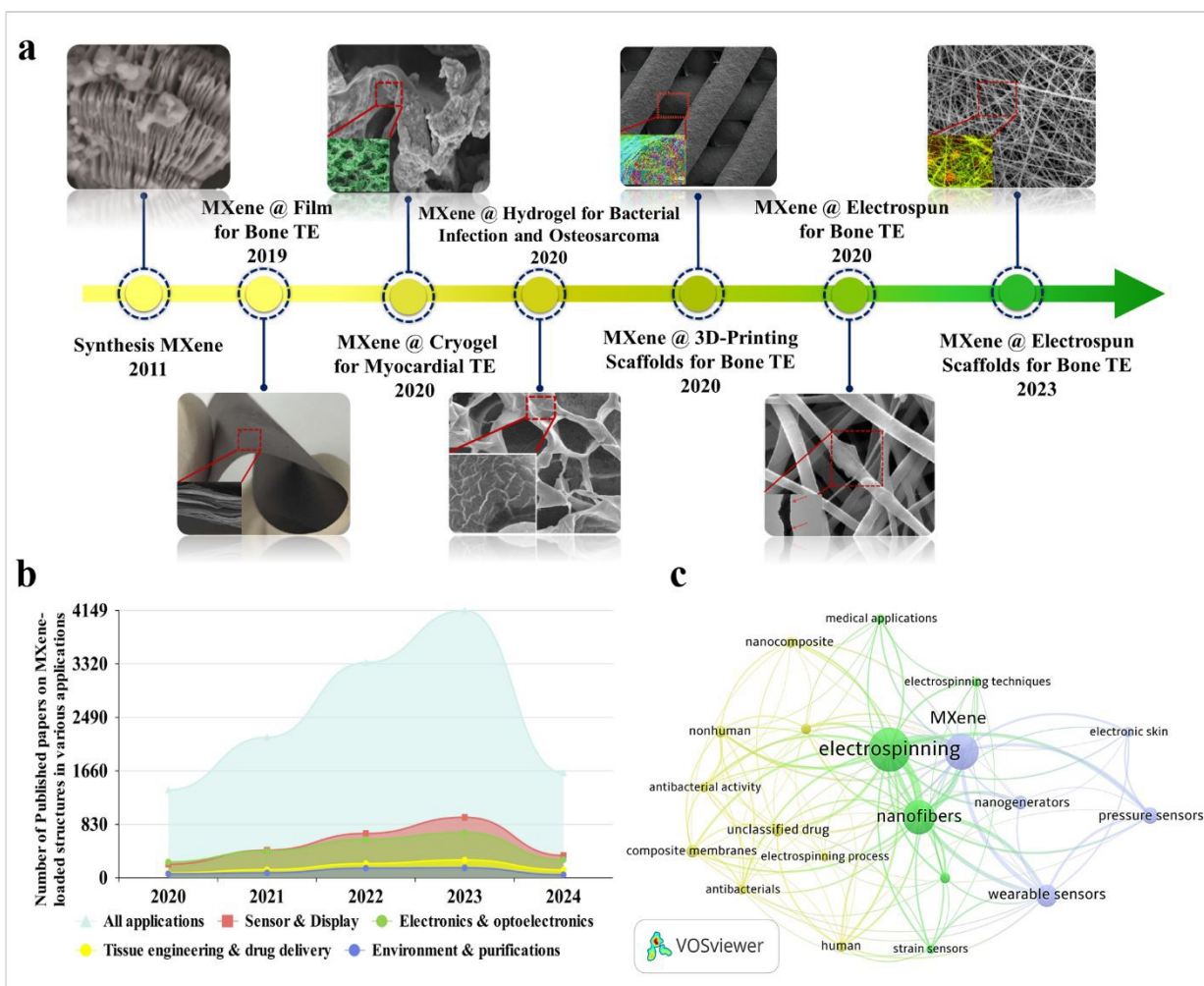
36 Electrospinning is a well-known and scalable technique extensively declared to fabricate  
37 flexible fibers in the range of nano to micro diameters with tunable mechanical strength. The  
38 electrospun fibers could be feasibly synthesized from numerous polymeric materials in  
39 adjustable alignment ratios [3, 4]. Highly porous structure, tiny and interconnected pores, and  
40 large surface-to-volume ratio are remarkable characteristics that make the electrospun carrier  
41 media a promising candidate for biomedical and tissue engineering applications [5-7].  
42 Meanwhile, several parameters have limited their practical usage, including the challenges  
43 linked with the electrospinning procedure in tandem with the defects in the final deployed  
44 structures. As an example, several polymers could not be easily fabricated due to improper  
45 electric conductivity, low viscosity, or non-electrospinnability department. Additionally,  
46 inhomogeneous structure, poor dimensional stability, inadequate cell infiltration, and  
47 cytotoxicity are other unfavorable traits declared for some electrospun compositions [8-10].

48 As a representational strategy, the addition of nanoparticulate architectures into the  
49 electrospun fibers could effectively combat these blocks [11, 12]. The size and distribution of  
50 nanoparticles can be effectively modified by adopting appropriate methods of fabrication and  
51 carefully adjusting key process parameters [13]. It's crucial to select the right additive with the  
52 appropriate morphology and dimensions based on the influencing parameters. In this era,  
53 MXene has been broadly investigated for assorted applications, resulting from remarkable  
54 features such as electrical conductivity, hydrophilicity, mechanical strength, chemical stability,  
55 and high surface-to-volume ratio [14-16]. Besides, photothermal activity, biological features,  
56 antimicrobial and antibacterial properties, and formidable adhesiveness to natural organs have  
57 caused outstanding outcomes for the MXene-decorated electrospun fibers in biomedical end-  
58 users [17, 18].

59 **Fig. 1a** shows the timeline relating to applying MXene nanosheets in various forms and  
60 configurations for tissue engineering targets in the biomedical era. As can be seen, MXene was  
61 introduced in 2011 and modified through the years. In 2019, MXene-decorated film was  
62 declared as an efficient nanocomposite for bone regeneration [19]. Additionally, loading  
63 MXene into the hydrogel [20], 3D printed [21], cryogel [22], and nanofibrous [23]  
64 architectures were reported to regenerate bone and heart tissues in 2020. **Fig. 1b** displays the  
65 number of Scopus-indexed publications on employing the MXene configurations in various  
66 fields, showing the increasing focus on the usage of MXene-loaded structures in different  
67 applications. Among various integrated tissue configurations, the electrospun structures have  
68 revealed favorable results benefiting the pros of both electrospun media, as well as MXene  
69 nanosheets. According to the literature, the MXene nanosheets are commonly embedded into  
70 the electrospinning solutions to decorate the electrospun fibers. Based on the polymer chain  
71 groups, the MXene galleries could be located inside, on the surface, or in both regions,  
72 changing characteristics of the electrospun fibers. **Fig. 1c** exhibits the visualization  
73 bibliographic map of the Scopus-indexed papers relating to employing MXene in electrospun  
74 structures, highlighting the application of MXene-loaded electrospun structures in a wide range  
75 of biomedical usages.



76



**Figure 1.** Evolution history of the MXene-decorated tissue scaffolds; (a) MXene structure: Reproduced from reference [24] with permission from Wiley, Copyright 2011, MXene-loaded film for bone tissue: Reproduced from reference [19] with permission from Dove press, Copyright 2019, cryogen containing MXene for heart tissue: Reproduced from reference [22] with permission from Ivyspring International Publisher, Copyright 2020, hydrogel-based tissue loaded with MXene: Reproduced from reference [20] with permission from the American Chemical Society, Copyright 2020, bone tissue developed by embedding MXene into a 3D-printed layer: Reproduced from reference [21] with permission from Wiley, Copyright 2020, and integrated electrospun fibers fabricated in 2020 and 2023: Reproduced from references [23, 25] with permissions from the American Chemical Society, Copyright 2020 and 2023. (b) the number of Scopus-indexed publications related to the MXene-loaded compositions for various end usages, and (c) visualization of a bibliographic map of the Scopus-indexed papers relating to the usage of MXene in electrospun architectures.

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93 As a two-in-one strategy, the electrospun architectures integrated with MXene nanosheets  
94 have resulted in remarkable compositions applicable to medical-related usages. The synergetic  
95 effect of integrating MXene in the electrospun nanofibers for biomedical applications has been  
96 overviewed in some studies [26, 27]. Meanwhile, few papers have comprehensively  
97 demystified the intriguing behavior of MXene nanosheets, bare electrospun fibers, and  
98 MXene-loaded nanofibrous architectures in all biomedical sub-categories. Accordingly, this  
99 review has provided an in-depth investigation of the synthesis and characterizing of the MXene  
100 nanostructures. Then, the beneficial role of pristine electrospun fibers for biomedical targets is  
101 remarked. Additionally, the electrospun scaffolds embedded with MXene nanosheets are  
102 overviewed, throwing up many knowledge gaps and novel ideas for exploring versatile  
103 electrospun composite networks applicable in cancer therapy, drug delivery, antimicrobial  
104 activities, sensor devices, and tissues. Besides, the biomedical usages of the MXene-loaded  
105 hybridized structures, obtained through combining the electrospun nanofibers with hydrogels,  
106 films, and other polymeric architectures, are pointed out in this review.

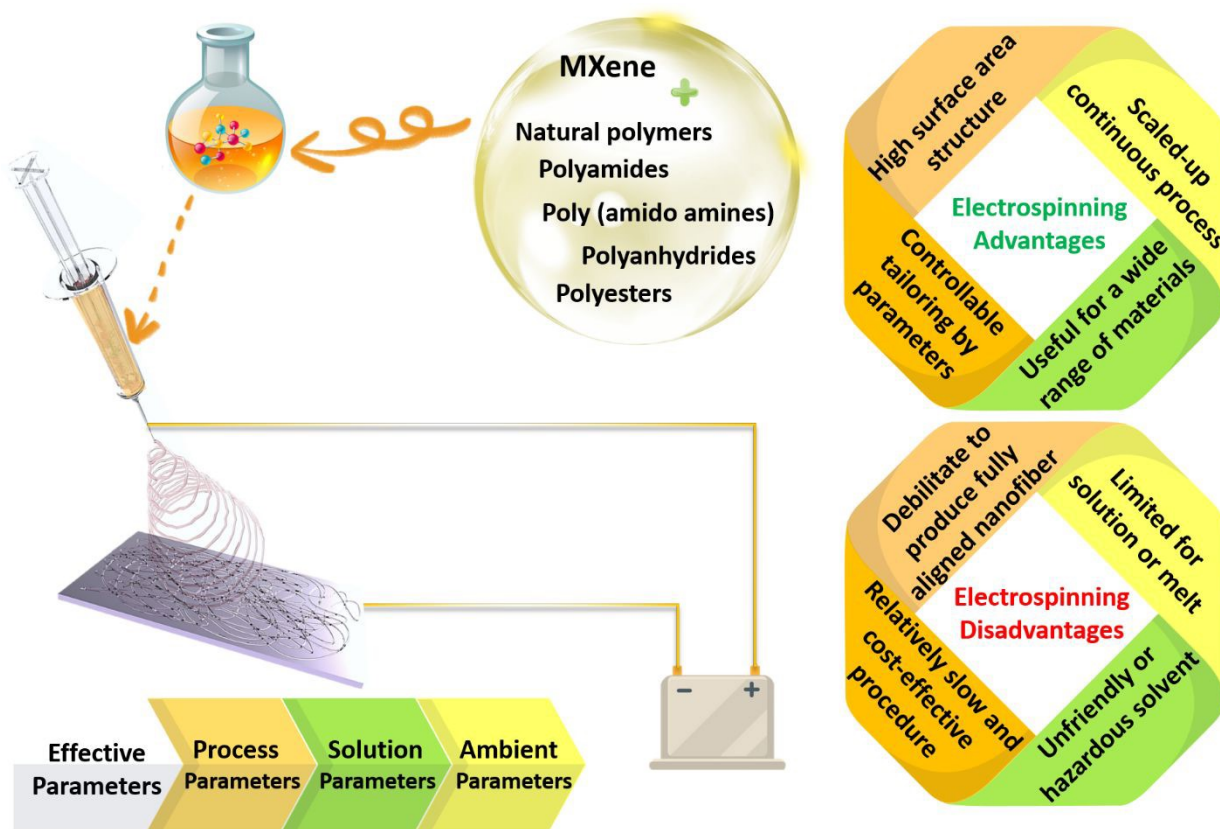
## 107 108 **2. Electrospun fibers for biomedical targets**

109 Polymeric architectures have been extensively declared for various targets in clinical  
110 management. To design a fabulous polymeric structure for biomedical applications, the  
111 physical features of the polymeric element, in tandem with the geometrical properties, play  
112 crucial roles. Chemistry, composition, biodegradation rate, and biocompatibility are  
113 categorized as well-documented physical characteristics, while shape and size are critical  
114 morphological parameters. In this regard, the selection of polymer type is a significant factor  
115 to be noticed. Based on the literature, biopolymers (collagen, gelatin, alginate, chitosan, etc.),  
116 polyesters (e.g., polycaprolactone (PCL)), polyamides (e.g., silk and nylon), poly (ortho esters)  
117 (e.g., polyglycolic acid (PGA) and poly-lactic acids (PLA)), poly (amido amines),  
118 polyanhydrides, and poly ( $\beta$ -amino esters) could be appropriate choices, which are also called  
119 bio- and smart-polymers. The polymers, as mentioned above, are hydrolytically degradable  
120 and serve prompt physical and chemical changes. The degradability of the polymeric  
121 compositions should be customized based on the final usage to prevent the accumulation of  
122 materials and so toxicity. Additionally, such polymers are normally selected as they represent  
123 proper compatibility with the body. Besides, solubility, thermal stability, mechanical strength,  
124 and other inherent features are major properties which are considered depending on the end  
125 usage of the designed product [28, 29].

126 Regarding the geometrical properties, the fabrication of polymeric compositions in the  
127 form of thin nanofibers could endow remarkable properties for a wide range of biomedical  
128 targets. So far, different mechanical, chemical, thermal, and electrostatic methods have been  
129 introduced to generate fine and homogenous fibers in the nanoscale region. Among them,  
130 electrospinning has been known as the most employed method as a result of the straightforward  
131 setup, which is schematically shown in **Fig. 2**. Electrospinning involves electrohydrodynamic  
132 force to form nanoscale threads from polymeric droplets using a high-voltage power supply, a



133 spinneret, a syringe pump, and a conductive collector. This procedure could be divided into  
 134 several main steps. In the first phase, the liquid droplet is charged, generating a cone-shaped  
 135 jet called a Taylor cone. The electric field applied to the droplet induces a charge separation,  
 136 creating a positive charge at the surface and a negative charge at the center of the droplet.  
 137 Afterwards, the charged jet is extended along a straight line, forming thin, continuous fibers.  
 138 The speed and direction of the jet depend on the applied voltage, the distance between the  
 139 spinneret and the collector, and the solution properties, such as viscosity and surface tension.  
 140 Then, the jet thins out due to the presence of an electric field and grows the electrical bending  
 141 instability, which arises from the competition between the electrostatic repulsion and the  
 142 surface tension of the jet. As a result, the jet meanders and forms a series of loops and coils,  
 143 leading to an increase in the surface area of the fibers. Finally, the jet solidifies and forms  
 144 nanoscaled fibers, which are gathered on a collector. The collected fibers can be further  
 145 processed by annealing, crosslinking, or functionalization to enhance their mechanical,  
 146 chemical, and biological properties [30-32].



147  
 148 **Figure 2.** Schematic illustration of the electrospinning setup, along with the pros and cons of  
 149 the electrospinning method for the fabrication of nanofibrous structures.

150 The electrospinning process could be modified by playing with electrospinning parameters,  
 151 such as the solution factors, in tandem with the electrospinning conditions, leading to  
 152 fabricating fibrous structures with various morphologies. For example, the critical voltage  
 153 employed during the electrospinning is identified based on the polymer solution. Changes in  
 154 the critical voltage of a specific electrospinning solution could lead to fibers with different



155 morphological structures being obtained. In this era, a proper voltage range of 10-20 kV was  
156 exhibited for electrospinning the PAN nanofibers. According to this study, a rise in the voltage  
157 from 10 to 20 kV could cause the formation of finer fibers due to the amplified repulsive forces,  
158 thereby inducing more stretching [33]. However, increasing the voltage might fabricate fibers  
159 with larger diameters in some cases. For example, Matabola et al. [34] declared an increment  
160 in the average PVDF fiber diameters from 100 to 180 nm by enhancing the voltage from 10 to  
161 16 kV. There is also a critical flow rate for electrospinning the polymer solutions, varying  
162 based on the polymer type, in tandem with solution concentration. Generally, the flow rate  
163 differs from a hundred microliters to a thousand microliters per minute in standard polymer  
164 solutions. A rise in the optimized range of the feeding rate could lead to generating thicker  
165 fibers, resulting from the ejection of more solution. For example, a shift from 1 to 2  $\mu\text{l}\cdot\text{min}^{-1}$   
166 in the feeding rate increased the fiber diameters from 18.9 to 36  $\mu\text{m}$ . It is worth noting that an  
167 asymmetrical Taylor cone is developed below the optimized threshold, causing instability of  
168 the electrospinning jet and the fabrication of fibers in a wide-diameter distribution [35]. As  
169 another variable, the working distance should be set based on the polymer system to attain  
170 homogenous electrospun fibers. In short working distances, solvent evaporation is limited,  
171 leading to defects and beading in the nanofibers. Also, the electrical field is weakened above  
172 the threshold, increasing the jet instability. In a study conducted by Jabur et al. [36], it was  
173 displayed that a rise in the working distance from 4 to 22 cm could lead to an increase in the  
174 PVA fiber diameters from 875 to 600 nm. Therefore, it is vital to determine the optimized  
175 parameters based on the required morphological factors of the electrospun fibers.

176  
177 Electrospun fibers have shown several advantages, including a high surface-to-volume  
178 ratio, consistent structure, tunable porosity, and malleability to conform to diverse sizes and  
179 forms. These characteristics make electrospun fibrous membranes particularly attractive for  
180 biomedical applications, such as cancer therapy, drug delivery, sensor devices, and tissue  
181 engineering. In drug delivery systems, high surface area is beneficial as it allows for loading  
182 diverse amounts of drugs. Additionally, loading larger therapeutic agents into the system  
183 becomes more accessible with an expandable pore size. It is important to note that the specific  
184 surface area of a drug delivery system has a significant impact on the rate of drug release. This  
185 is because the surface area determines the amount of drug that is exposed to the surrounding  
186 environment and thus controls the rate at which the drug is released [37, 38].

187 Also, electrospun membranes have established specific attention in generating biosensors  
188 due to showing a high surface area, modification simplicity, and fabricability. Additionally,  
189 nanosized structures have proven effective as membranes that immobilize bioanalytics. This  
190 creates a favorable microenvironment for physiologically active molecules, enhancing  
191 biosensing efficiency [39-42]. In the case of tissue engineering, the high surface-to-volume  
192 ratio allows for increased cell attachment and proliferation, while the consistent structure  
193 provides a uniform environment for tissue growth. Furthermore, electrospun fibers' tunable  
194 porosity and malleability permit customization to match specific application requirements.





195 However, this technique still faces two main limitations: insufficient tiny pores and porosity  
196 and poor mechanical properties, which are significant features that cover the requirements  
197 essential for biomedical applications [31]. To overcome the challenges, researchers have come  
198 up with some innovative solutions. One approach is to adjust the electrospinning parameters,  
199 such as the solution concentration, flow rate, applied voltage, and the collector. Accordingly,  
200 numerous attempts have been devoted to optimizing the fiber diameter, pore size, and porosity  
201 of the electrospun fibers. As an example, McCann et al. [43] utilized a cryogenic liquid to  
202 collect the fibers. In the proposed procedure, a phase separation was induced between the  
203 solvent and the polymer, forming highly porous structures and revealing a promising  
204 architecture for various biomedical applications. Another approach is to use a sacrificial  
205 component during electrospinning, which can be removed to create a more open and  
206 interconnected network for cell migration. Considering this strategy, Huang and Thomas  
207 combine chloroform with ethanol and dimethyl sulphoxide as low and high boiling point  
208 liquids to create surface and internal porosity in the electrospun PLA nanofibers, respectively  
209 [44].

210 Poor mechanical strength is another challenge related to the electrospun networks for load-  
211 bearing applications. Therefore, post-processing modification techniques, such as cross-  
212 linking, annealing, or heat treatment, have enhanced the structural and mechanical strength of  
213 electrospun fibers. These approaches could create fibrous membranes that are more suitable  
214 for biomedical applications and tissue engineering targets [45-47]. For example, Lee et al. [48]  
215 Utilized a simple freezing/thawing process to increase the crystallinity of the PVA electrospun  
216 fibers from 23.5 to 43.6%, thereby raising the mechanical strength to 65% compared to the  
217 untreated PVA nanofibers.

218 Additionally, integrating particulate fillers into the electrospun structures has been  
219 extensively recommended as an efficient modification [49, 50]. For example, carbon nanotubes  
220 (CNTs) and graphene are documented as appropriate fillers for the polymeric membranes,  
221 which could be evenly distributed in the developed architectures. The high mechanical strength  
222 of the CNT filler could provide incomparable superb specific strength for the electrospun fibers  
223 [51]. The enhancement of mechanical strength in the CNT-loaded electrospun fibers could be  
224 attributed to the increased interconnections between the polymer chains by the presence of  
225 CNT filler. Also, the mediated CNT could decrease the contact angle and improve cell viability  
226 in the electrospun tissues [52]. However, graphene has been known as a more interesting filler  
227 for promoting the characteristics of electrospun fibers due to its abundance and lower cost [53].  
228 Reduced graphene oxide (rGO), a substantial graphene derivative, has been widely employed  
229 to engineer potential bioactive electrospun architectures. While GO possesses frequent  
230 functional groups, and so proper hydrophilicity, rGO provides superior electrical conductivity  
231 [54]. Accordingly, Ivanoska-Dacicj et al. [55] declared that the incorporation of 20 wt. % rGO  
232 into the PEO-based nanofibers could effectively reduce the electrical resistance, leading to an  
233 approach of 96% cell viability. In another attempt, Gozutok et al. [56] displayed that the  
234 incorporation of 1 wt.% rGO into the PVA nanofibers could serve 23 and 30% higher elastic



235 modulus and tensile strength values than those of the neat PVA nanofibers, resulting from the  
236 created strong interaction between the PVA polymer chains and rGO nanogalleries. Moreover,  
237 TGA analysis confirmed the thermal degradation of rGO-filled PVA structure at 450°C, while  
238 the pure PVA fibers degraded at 345°C. Furthermore, the filler incorporation led to an  
239 increment in the electrical conductivity from 0.1 to 11  $\mu\text{S}\cdot\text{cm}^{-1}$ .

240 As a new emerging filler, MXene nanosheets have also reaped much attention by boosting  
241 the mechanical properties, along with enhancing the physiological and biological features,  
242 widening their applications in various biomedical fields. MXene nanosheets could be easily  
243 embedded into the electrospinning solutions and form thin nanofibers, benefiting from their  
244 outstanding rheological characteristics. These structures endow excellent electrical  
245 conductivity with no need to perform reduction procedures. MXene-loaded solutions could be  
246 generated in various cylindrical, ribbon, aerogel, or core-shell structures, depending on the  
247 polymer matrix. The defects and loose stacking states of the MXene-integrated electrospun  
248 fibers could be enhanced by the axial MXene orientation in the electrospun networks. By  
249 tuning the spinning condition, MXene size, and filler concentration, different physical,  
250 chemical, mechanical, and electrical conductivity could be tailored depending on the  
251 considered application. Correspondingly, the MXene-polymer nanofibers composite has  
252 convincingly shown tremendous potential in promising areas, such as antibacterial treatments,  
253 wound healing, cellular differentiation, bone tissue regeneration, neural tissue guidance, and  
254 health monitoring systems. In the following section, the role of MXene in biomedical  
255 applications is described based on its noteworthy properties.

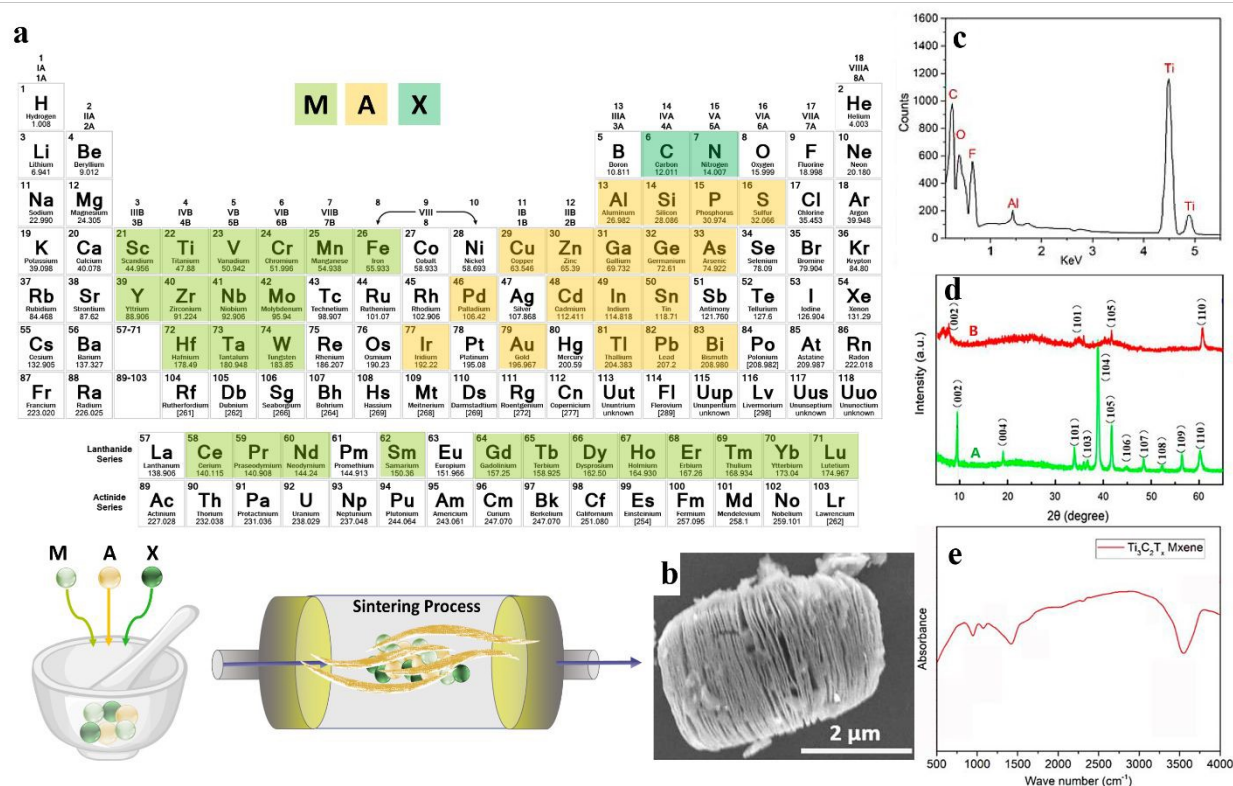
### 256 3. Synthesis methods and biomedical applications of MXene

#### 257 3.1 Synthesis and Characteristics of MXene

260 Over the last two decades, two-dimensional (2D) nanomaterials have been an attractive  
261 field of study due to their outstanding physical and chemical properties. Carbides and nitrides  
262 of early transition metals are considered significant materials, resulting from their unique  
263 features consisting of superior chemical stability, excellent hardness, and high metallic  
264 electrical conductivity [57]. MXenes are 2D inorganic compounds with few atoms thickness,  
265 comprising nitrides, carbides, and carbonitrides layers of early transition metals [58]. MXenes  
266 are usually obtained by chemical etching of a MAX phase with a general formula of  $\text{M}_{n+1}\text{AX}_n$ ,  
267 where M represents an early transition d-metal (Mo, Ti, Zr, Cr, etc.), A is mostly referred to as  
268 an element of group 13 to 16 (e.g., Al, Ga, Ge, Si, etc.), X represents carbon and/or nitrogen,  
269 and n is equal to 1 to 3 (see **Fig. 3a**). The MAX phase possesses a layered hexagonal structure,  
270 including densely packed M layers and X atoms occupied octahedral positions. After selective  
271 etching of A layers in the MAX phase, the chemical formula of resulting MXene would be  
272  $\text{M}_{n+1}\text{X}_n\text{T}_z$ , where  $\text{T}_z$  is the surface terminations group ( $-\text{F}$ ,  $-\text{O}$ ,  $-\text{OH}$ , etc.) bonded to M, and z  
273 is the number of the interfacial functional groups [59].



274



**Figure 3.** The structure and synthesis of the MXene nanosheets; (a) schematic illustration of the MXene structure and synthesis procedure. (b) SEM, (c) EDX, (d) XRD, and (e) FTIR results of the  $Ti_3AlC_2$  and  $Ti_3C_2T_x$  powders, Reproduced from reference [60] with permission from MDPI, Copyright 2020.

To date, several attempts have been devoted to developing the etching methods. In general, these approaches could be divided into three different methods, including wet chemical, molten salt, and electrochemical methods [61]. Among them, the wet chemical etching route is the most conventional and mature etching technique, consisting of HF-containing and HF-free approaches. Although it is reported that HF-containing methods possess high-risk operation conditions and require extra caution, it is still the most efficient etching technique [62]. Accordingly, studies over wet chemical routes to minimize or even avoid using HF resulted in valuable outcomes. As an example, Dirscoll's group reported using a small portion of HF along with other acids. They successfully fabricated  $Ti_3C_2$  MXene using a volumetric ratio of 6:3:1 of HCl: water: HF [63]. Comparing the conventional use of HF as the etchant, the proposed method reduced the usage of this hazardous acid by 90%. Additionally, the authors reported fewer structural defects, large lateral sizes, and high yield for the developed MXene nanosheets. In another approach,  $Ti_3C_2T_x$  was synthesized by immersing the  $Ti_3AlC_2$  powders in a LiF/HCL solution. SEM illustration of the synthesized nanosheet is displayed in **Fig. 3b**. Additionally, the elemental mapping of the generated nanostructure is represented in **Fig. 3c**, showing strong peaks of C, Ti, O, and F components, along with a weak peak regarding the Al



297 element. Accordingly, the etching procedure was almost completed in the obtained MXene  
298 nanostructures. Also, the presence of  $-F$ ,  $-OH$ , and  $-COOH$  functional groups could be  
299 corroborated by the appeared peaks. **Fig. 3d** examines the XRD patterns of the  $Ti_3AlC_2$  and  
300  $Ti_3C_2T_x$  powders. As can be seen, the  $Ti_3AlC_2$  revealed about eleven peaks, showing its  
301 crystalline structure. Meanwhile, the crystalline regions were reduced to 4 phases after the  
302 etching procedure, which could be linked to the removal of Al layers. The 002 crystalline plane  
303 was also shifted to a lower value in a broadened peak, proving a rise in c-spacing by replacing  
304 the Al atoms with  $-F$  and  $-OH$  functional groups. **Fig. 3e** shows the FTIR spectrum of the  
305  $Ti_3C_2T_x$  nanosheets, displaying the  $-OH$  and  $C-F$  vibrations at 3490 and 1216  $cm^{-1}$ ,  
306 respectively [60].

307 The molten salt etching is based on the selective removal of A elements through a redox  
308 reaction of molten salts and A elements. Consequently, it can be used to install and remove  
309 surface functional groups. Moreover, applying molten salts as etchant enables synthesizing  
310 MXenes with  $-O$ ,  $-S$ ,  $-NH$ ,  $-Se$ ,  $-Cl$ , and  $-Br$  termination, as well as bare MXenes with no  
311 surface group [64]. As an example, Urbankowski et al. [65] employed this method to  
312 synthesize the first nitride MXene  $Ti_4N_3T_z$ . Additionally, Huang et al. [66] applied molten  
313  $ZnCl_2$  for the etching of new Zn-MAX phases, such as  $Ti_2ZnN$ ,  $Ti_2ZnC$ ,  $Ti_3ZnC_2$ , and  $V_2ZnC$ ,  
314 reporting the substitution of Zn and resulting Cl-terminated MXenes.

315 The electrochemical etching method has also been used as an effective route to fabricate  
316 MXenes in an HF-free way [64].  $Ti_2CT_z$  and  $Ti_3C_3T_z$  can be obtained through electrochemical  
317 etching of A elements from  $Ti_2AlC$  and  $Ti_3AlC_2$  MAX phases using HCl,  $NH_4Cl$ , and  
318 tetramethylammonium hydroxide as an electrolyte. However, extreme etching would change  
319 the MAX phase to carbon as a result of the simultaneous dissolution of A and M fundamentals  
320 [67]. Apart from the aforementioned etching methods, some other infrequent approaches have  
321 been used. A promising study by Yang et al. [68] reported the anodic corrosion of  $Ti_3AlC_2$  as  
322 a fluoride-free etching process. The authors claimed that the method successfully transforms  
323  $Ti_3AlC_2$  to  $Ti_3C_2T_x$  with a sufficient yield.

324 In the generated multilayered MXene structures, the layers are held together through van  
325 der Waals and hydrogen bonding. Nevertheless, these secondary bonds make the intercalation  
326 between layers possible to produce delaminated MXene [69]. Generally, inorganic cations and  
327 organic or ionic compounds are utilized for the intercalation and, thereafter, an ultrasonication  
328 step. Due to the negatively charged surface of the as-obtained flakes, they are able to make a  
329 stable suspension in organic solvents or water without any surfactant addition. Based on the  
330 literature, several cations, such as  $Na(1+)$ ,  $K(1+)$ ,  $Mg(2+)$ , and  $Al(3+)$ , have been successfully  
331 applied to intercalate the MXenes [70]. As a result, MXenes can be obtained in different forms  
332 of multilayer powders to delaminated flakes, which can be employed in several applications  
333 via various techniques, including printing, spraying, fiber forming, electrospinning, and many  
334 more [58].

335 MXene structures could be feasibly functionalized with covalent and non-covalent bond  
336 interactions to combat the MXene weak points, such as poor oxidation stability. Non-covalent



functionalization is commonly carried out through weak intermolecular or interatomic bonding, such as van der Waals forces, hydrogen bondings, or electrostatic interactions in a fast and mild procedure. Meanwhile, the covalent functionalization method creates strong interactions via equal sharing of electron pairs, offering surface modification with superior stability. Unlike the non-covalent modification method, covalent functionalization requires a complex synthetic procedure, lasts long, and might lead to oxidative degradation [71, 72]. Overall, far from synthesizing other 2D materials with similar applications that yield small amounts under challenging conditions, MXenes can be produced on a large scale through a straightforward procedure, making it more potential to meet industry measurements. MXenes have become one of the most favorable groups of 2D nanomaterials because of their outstanding properties. The easy functionalization of MXenes renders them extremely auspicious material for laboratory studies, as well as practical usage in various industries.

### 3.2 The role of MXene and MXene-loaded nanofibers in biomedical applications

According to the literature, the MXene family is a promising candidate to boost versatile structures for a wide range of applications, such as environment and purification, electronics, sensors and displays, and biomedical targets. In the biomedicine category, MXene has been utilized to optimize the efficiency of cancer treatment, drug delivery, bioimaging, and biosensors in the developed architectures. The highlighted potentials could be referred to as proven fascinating features of the MXene-based configurations, such as proper elastic mechanical strength, electronic conductivity, hydrophilicity, chemical stability, and many more [73]. Incorporating MXene nanosheets into the electrospun fibers creates a synergetic effect for biomedical applications due to their complementary features. The combination of MXene layered structure and high porosity of electrospun fibers endow a large surface area. The mechanical strength of the electrospun fibers could be reinforced by embedding the MXene nanosheets into the nanoarchitecture, attesting to better performance in various biomedical applications. The layered structure of the MXene, in tandem with appropriate morphological characteristics of the electrospun fibers, serves great capacity for loading drugs, providing sustained and controlled drug release. The electrical conductivity could also be escalated by incorporating the MXene into the conductive electrospun fibers, which is favorable for tissue engineering and sensors.

#### 3.2.1 Cancer Therapy

In recent years, the MXene family has been introduced to achieve therapeutic, imaging, and drug delivery precise abilities in photothermal tumor treatments (PTT) and photodynamic therapy (PDT). High light-to-heat conversion efficiency and strong absorption in both the first and second NIR bio windows in comparison with conventional photosensitizers, have remarked the advantages of MXene nanostructures toward PTT and PDT. Also, the highlighted capabilities of MXenes in anti-cancer therapy could be linked with the proper atomic number, paramagnetic behavior, and high surface-to-volume ratio. Common cancer therapies lead to unwanted side effects and drawbacks, resulting in direct biological targeting for the local cancer treatment requiring signal transduction and actuation, which could be carried out via radical oxygen, heat, and irradiation. Among the introduced methods, PTT is assumed to be a fresh and efficient



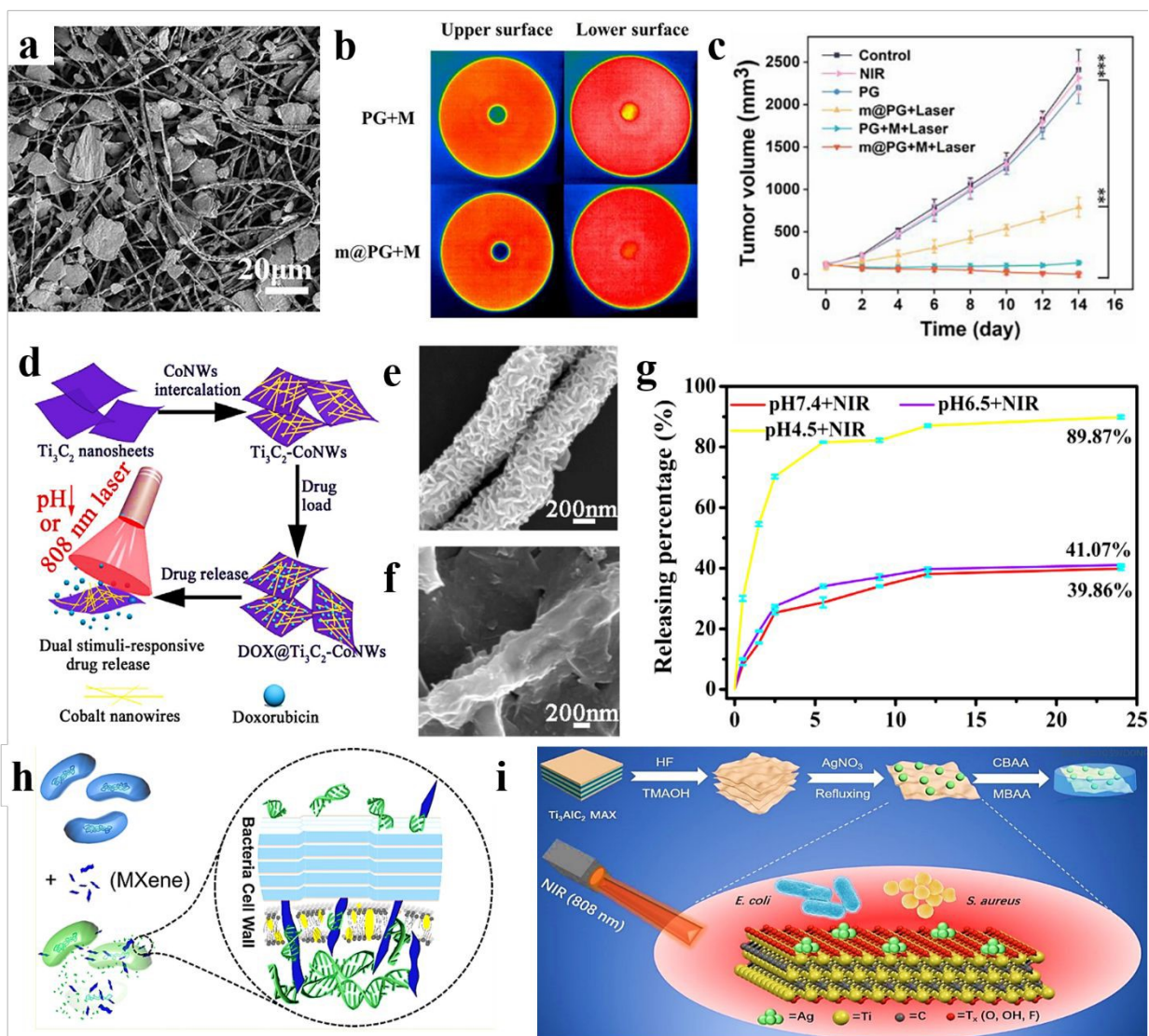
378 treatment for cancer curing. In this technique, the light is converted to heat, causing cell death  
379 without influencing the surrounding tissues. Also, the precise location of the cancer cells could  
380 be detected and monitored through the PTT agent inflation in tumors in a remotely controlled  
381 manner.

382 Li et al. [74] utilized a droplet light heating system to estimate the light-to-heat photothermal  
383 activity of the  $Ti_3C_2$  MXene nanostructure. A wide spectrum laser beam was irradiated to the  
384 droplets containing  $Ti_3C_2$  and CNT, implying a higher temperature for the  $Ti_3C_2$  than that of the  
385 CNT, possibly due to the superior light absorption of the MXene. According to the obtained data,  
386 excellent light absorption capability was represented by the employed  $Ti_3C_2$  compared to that of  
387 the carbon nanotubes. Accordingly, the CNT structure did not reveal any absorption peak from  
388 300 to 1300 nm, while  $Ti_3C_2$  showed a higher absorption and an observable peak around 800 nm.  
389 In addition, the internal light-to-heat conversion efficiency of 100% was approached. Despite the  
390 great advantages of MXene, its non-stable structure in buffer saline, poor oxidation stability, and  
391 agglomeration behavior have motivated researchers toward modifying the MXene family through  
392 combination with other structures. Gao et al. [75] designed a 3D honeycomb structure comprising  
393  $Ti_3C_2$ /CNT to approach the anti-aggregation property, displaying proper photothermal activity  
394 and stability in the NIR region.

395 It is also worth noting that among various 2D materials, MXene nanosheets are ideal for use  
396 in PDT as photosensitizers. PDT is a safer and more targeted cancer treatment than chemotherapy  
397 and radiotherapy, reducing the risk of side effects [76]. This is because photosensitizer drugs only  
398 become toxic when activated by external light. In this era, Liu et al. [77] confirmed the excellent  
399 drug release profile of MXene-based structure, due to its efficient NIR laser-induced and pH-  
400 responsive behavior. The attempts in the area of MXene modification in cancer therapy have  
401 resulted in the evaluation of MXene photothermal activity in different configurations, including  
402  $Ti_3C_2$  quantum dots [78],  $Ti_2C$  nanosheets [79],  $Ti_3C_2$ /Co nanowires [80], MXene/Doxjade  
403 platform [81], Au/ $Fe_3O_4$ / $Ti_3C_2$  nanocomposite [82], MXene/PVA hydrogel [83],  
404 collagen/silk/hydroxyapatite/MXene 3Dprinted scaffold [84], MXene/borneol-poly(N,N-  
405 dimethyl ethyl methacrylate) [85], and many more. Furthermore, MXene-based  
406 nano/microarchitectures could be employed in targeted anti-cancer drug delivery systems or  
407 therapeutic agents after modifying with biocompatible activated agents. Considering the  
408 beneficial characteristics of the electrospun fibers in biomedical engineering, as well as the  
409 prominent role of MXene in designing versatile architectures, several studies have been devoted  
410 to analyzing the properties of the MXene-loaded electrospun compositions. For example, Ding et  
411 al. [86] declared that simultaneous  $Ti_3C_2T_x$  electrospay on the  $Ti_3C_2T_x$ -loaded PLA nanofibers  
412 could generate a highly efficient membrane with the ability to kill tumor cells, in tandem with  
413 bacteria after surgical melanoma excision, decreasing the tumor recurrence. **Fig. 4a** shows the  
414 SEM image of the electrospun fibers decorated with MXene nanocoating. **Fig. 4b** exhibits the  
415 upper and lower surfaces of the provided films attached to the hot plate. When the hot plate was  
416 applied to the upper surface, the lower surface of the sample containing MXene nanosheets  
417 represented higher temperature compared with that of the free-filler film, corroborating the better



418 conductivity of the MXene-loaded film. Resulting from the  $Ti_3C_2T_x$  presence both inside and on  
 419 the surface of the electrospun fibers, and so an excellent unidirectional thermal conductivity, a  
 420 high temperature of about  $70^\circ C$ , could be achieved in 1 min with proper photothermal cycling  
 421 stability. As a result, reaching a certain temperature in the developed structures could result in  
 422 killing the B16F10 cancer cells. **Fig. 4c** shows the tumor growth curve relating to the application  
 423 of various films. Based on the results, the tumor recurrence was effectively prevented from  
 424 MXene-loaded structure. Additionally, an antimicrobial ring diameter of 1.3 cm was approached  
 425 in the mentioned membrane under 808 nm laser NIR light, mighty resulting from the enhanced  
 426 thermal distribution in the lower surface of the fibrous structure.



427  
 428 **Figure 4.** Characteristics of the PLA nanofibers decorated with electrospayed MXene for cancer  
 429 treatment; (a) SEM image of the film, (b) temperature distribution in the MXene-free and MXene-  
 430 loaded films, and (c) the growth curve of tumor volume in different provided films. Reproduced  
 431 from reference [86] with permission from Elsevier, Copyright 2023. Properties of the  
 432  $Ti_3C_2$ /cobalt nanowire heterostructure; (d) the designed procedure, (e&f) SEM images of the

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433 *Ti<sub>3</sub>C<sub>2</sub> and Ti<sub>3</sub>C<sub>2</sub>/cobalt nanostructures, and (g) drug delivery rate. Reproduced from reference*  
434 *[80] with permission from Elsevier, Copyright 2020. (h) Mechanism of the MXene antimicrobial*  
435 *activity. Reproduced from reference [87] with permission from the American Chemical Society,*  
436 *Copyright 2018. (i) Simultaneous use of antimicrobial and NIR photothermal activities of*  
437 *MXene/Ag nanocomposite. Reproduced from reference [88] with permission from the Royal*  
438 *Society of Chemistry, Copyright 2020.*

439

### 440 3.2.2 Drug delivery

441 Ultra-thin 2D planar structure, NIR responsiveness, photothermal conversion capability,  
442 and chemically adjustable surface functionalities of the MXene family caught the interest of  
443 researchers for developing efficient controlled drug release systems. MXene structures could more  
444 freely migrate through the body than the large particles. In addition, a lower drug amount is  
445 required to be loaded on the MXene due to its outstanding surface area. Notably, the pH sensitivity  
446 and photothermal activity of MXene structures have made them a great candidate in cancer therapy.  
447 Therefore, these unique materials could reveal a dual-stimuli response for drug release, as well as  
448 ablation of malignant cells.

449 Although the MXene family has revealed remarkable characteristics, their inadequate  
450 control ability and poor drug loading capability lead to continuous drug detaching and injuring  
451 normal tissues. In addition, non-stable structure in the physiological conditions causes the  
452 limitation toward efficient treatment of cancer diseases. To address the highlighted downsides,  
453 adding magnetic nanoparticles to the MXene structure has been considered a prominent strategy  
454 [89, 90]. Accordingly, the drug could be effectively confined to the targeted tissue by applying an  
455 external magnetic field. For example, Liu et al. [80] designed a heterostructure Ti<sub>3</sub>C<sub>2</sub>  
456 MXene/cobalt nanowire, noticing the ferromagnetic properties of the cobalt. In this study, the  
457 cobalt is intercalated on the Ti<sub>3</sub>C<sub>2</sub> nanosheets, and the doxorubicin was loaded on the prepared  
458 structure. Then, the loaded drug was released under an 808 nm laser beam in three pH levels, which  
459 is schematically summarized in **Fig. 4d**. SEM images of Ti<sub>3</sub>C<sub>2</sub> and Ti<sub>3</sub>C<sub>2</sub>/cobalt nanocarriers are  
460 illustrated in **Figs. 4e&f**, respectively. The provided structure showed excellent photothermal  
461 conversion activity at the wavelength of 808 nm. The doxorubicin loading increased up to 225%,  
462 corresponding to the electrostatic interaction between the negative surface of the Ti<sub>3</sub>C<sub>2</sub>-cobalt  
463 nanocarriers and the positive charge of the employed drug. In addition, the drug release of the  
464 prepared material in various pHs is shown in **Fig. 4g**, declaring 89.3% release at a pH of 4.5 after  
465 illuminating NIR for 24h. Overall, chemo photothermal therapy could be enhanced resulting from  
466 the synergetic effects of the composite elements, which is beneficial in cancer therapy.

467 MXene properties could also be modified by various polymers. For example, hydrophobic  
468 biocompatible polymers, such as PLGA, can tune the hydrophilicity inherent feature of the  
469 MXene and ease its interaction with hydrophobic drugs [91]. In addition, the combination of  
470 photothermal polymers, such as polypyrrole and polydopamine, can cause a synergetic effect and





471 boost the MXene performance. Moreover, polymer matrixes could provide a desirable  
472 accommodation for the MXene nanoparticles, impeding the leakage in the body [92]. In this era,  
473 the enhanced drug delivery performance of MXene combined with nanoscaled polyacrylamide  
474 [89], polyethylene glycol (PEG) [93], Chitosan/hyaluronic acid/gold [94], agarose [95],  
475 polydopamine/gold [96], and PEG/gold [97] compositions are reported.

476 To escalate the efficiency of drug delivery systems, temperature-responsive MXene nanobelt  
477 fibers were generated through electrospinning the PAN/PVP/MXene solution, followed by  
478 coating with polyacrylonitrile and polyvinylpyrrolidone composition. In a 3 min time, the  
479 developed structure could reach from 23 to 39°C under NIR exposure. Accordingly, the coating  
480 layer could be opened and the loaded vitamin E could be released in a favorable profile over a  
481 longer period, resulting in good wound healing. According to the obtained data, proper surface  
482 area, high mass loading, and the mass production capability of the suggested structure could  
483 facilitate the application of this architecture in a diverse range of biomedical applications, from  
484 drug delivery and wound dressing to biosensors and tissue engineering [98]. In another research  
485 study, a hybrid system was designed comprising MXene nanofibers and hydrogel components  
486 embedded with deferoxamine mesylate (DFOM) and acetylsalicylic acid (AC) to develop a highly  
487 efficient wound dressing. Based on the results, the photothermal activity of the MXene nanofibers  
488 could regulate the release of DFOM to prevent excessive angiogenesis. The immune micro-  
489 environment around the wound region could be controlled by favorable release of AC, assisting  
490 in approaching appropriate anti-inflammatory activity [99].

### 491 3.2.3 Antimicrobial activity

492 Today, medication overuse has caused microorganism resistance against drugs' antimicrobial  
493 activity, requiring the development of materials with superior efficiency. MXene family possess a  
494 remarkable antibacterial property, linked with appropriate semiconductor features, hydrophilicity,  
495 electrical conductivity, functional groups on the surface, the thickness of the atomic layer, and  
496 optical behavior (see **Fig. 4h**). Based on the literature, these materials are able to inhibit Gram-  
497 negative (*E. coli*) and Gram-positive (*B. subtilis*) growth, depending on the employed MXene  
498 concentration. This could be attributed to the interfacial interaction between the MXene-based  
499 structures and the cells. In fact, this direct contact destroys the cell membranes, followed by cell  
500 death. The active surface, as well as the small size of the MXene nanosheets, ease their penetration  
501 into the cells, resulting in their significant interaction with the specific molecules placed in the  
502 microbial cell walls and cytoplasm, and eventually, cell disruption and death. Moreover, a  
503 conductive bridge could be created on the lipid layers due to the anionic surface of the MXene  
504 nanostructures, boosting the electron transduction from bacteria to the environment and so the cell  
505 death [100, 101]. Furthermore, the hydrogen bonding between MXene's surface functional groups  
506 lipopolysaccharide string in the cells might hinder bacterial growth. As an example, better  
507 antimicrobial behavior was reported by reducing  $Ti_3C_2T_x$  nanosheet size against both *E. coli* and  
508 *B. subtilis* [102]. In another attempt, the application of  $Ti_3C_2T_x$  was proposed to attain both  
509 photothermal and antibacterial activities, which is schematically depicted in **Fig. 4i**. [103].  
510



511 Benefitting the favorable characteristics of the electrospun fibers, a core-shell structure was  
512 generated comprising PCL/Ti<sub>3</sub>C<sub>2</sub>T<sub>x</sub> and PCL/gelatin/Ti<sub>3</sub>C<sub>2</sub>T<sub>x</sub>, respectively, as the core and shell  
513 to develop an antibacterial and electroactive wound dressing. Based on the results, the presence of  
514 Ti<sub>3</sub>C<sub>2</sub>T<sub>x</sub> led to an increment in the mechanical stability, antibacterial behavior, proliferation  
515 activity, and wound healing procedure. Additionally, the electrospun matrix acted as a barrier  
516 against bacterial infiltration through the formation of a dense structure, revealing a promising  
517 architecture applicable in bioactive dressings for cutaneous wound healing [104].

### 518 3.2.4 Smart sensors

519 The large surface area and easy surface modification ability of the MXene groups potentiate them  
520 for application in the design of various sensors, such as gas, humidity, stress-strain, and optical  
521 devices. In addition, the ideal MXene properties, such as biocompatibility, conductivity, surface  
522 chemistry, and shaping, have made it an exceptional platform for electrochemical sensors [41, 105].  
523 Besides, MXene nanosheets have illustrated a wide band gap. For instance, the band gap of some  
524 MXenes Oxides, such as Zr<sub>2</sub>CO<sub>2</sub> and Ti<sub>2</sub>CO<sub>2</sub> is found to be 2.13 and 1.15 eV, respectively.  
525 Moreover, when compared to other established 2D nanomaterials like graphene, MXenes propose  
526 superior hydrophilicity and superior electrical conductivity [106, 107]. Furthermore, studies have  
527 shown higher electrical conductivity of MXene nanosheets compared with CNTs and reduced  
528 graphene oxide (rGO) materials, which could be attributed to their layered structure, allowing for  
529 efficient electron transport along the layers [74, 108]. Accordingly, such structures could be  
530 employed in chronoamperometric biosensors due to its unique characteristics, including  
531 electrocatalytic activity and fast response in the 50 to 750 μm region, which is beneficial for  
532 glucose detection. Meanwhile, van der Waals bondings between the MXene sheets cause the  
533 synthesis of thin layers and nanosheet aggregations, requiring further modification methods to  
534 address the block as mentioned above [109-111]. As an example, Rakhi et al. [112] developed a  
535 Ti<sub>3</sub>C<sub>2</sub>T<sub>x</sub>/Au composite for glucose biosensors, showing proper stability and reproducibility  
536 behaviors. MXene-based materials have also illustrated a prominent role in fabricating wearable  
537 electrochemical sensors, applicable in health- and sport-related devices. Accordingly, a porous  
538 sandwiched structure was fabricated comprising Ti<sub>3</sub>C<sub>2</sub>T<sub>x</sub> and PLA to produce a pressure-flexible  
539 and degradable sensor, representing a great sensitivity even in a wide range from 10.2 Pa to 30  
540 kPa and great cyclability over 10000 cycles. So, it could be utilized in monitoring the patient's  
541 health effectually and in real-time clinical diagnosis [113]. In an attempt carried out by Sohel Rana  
542 [114], it was declared that loading Ti<sub>3</sub>C<sub>2</sub>T<sub>x</sub> nanosheets into the PVDF-TrFE nanofibers could  
543 generate a sensor motion with outstanding low-pressure performance (power 4.02 W/m<sup>2</sup>) as well  
544 as proper mechanical response sensitivity (1.1 V/kPa). According to the results, embedding  
545 Ti<sub>3</sub>C<sub>2</sub>T<sub>x</sub> could cause a rise in the electronegativity, dielectric property, and biocompatibility of the  
546 provided architecture, resulting from the formation of microscopic dipoles and microscopic  
547 networks. Hence, the integration of electrospun fibers with MXene-based galleries could open a  
548 viable new avenue to tackle challenges in sensor fabrication and approach the desirable  
549 performances.



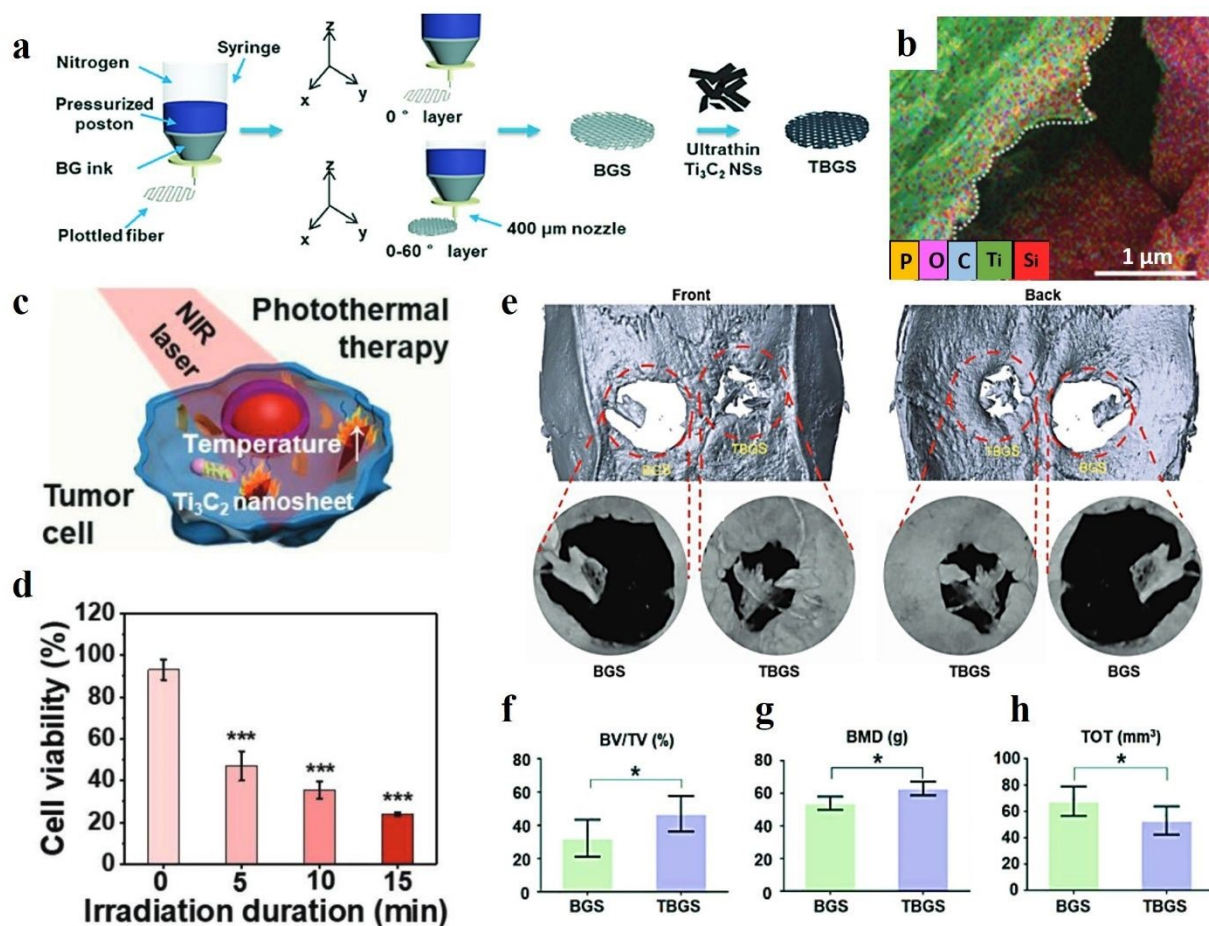
### 550 3.2.5 Tissue engineering

551 The organs' injuries and fractures could result in traumas, diseases, paralysis, and mortality of  
552 many people every year. The multifaceted tissue engineering field has utilized biomaterials,  
553 biological molecules, cells, and scaffolds to efficiently recover and reconstruct damaged organs.  
554 Accordingly, numerous attempts have been made to design tissues with the ability to mimic natural  
555 matrixes. Therefore, novel composite scaffolds have been developed, comprising synthetic and  
556 natural polymers, as well as ceramics and 2D materials. MXene is a considered 2D geometry  
557 substance, endowing notable characteristics to the scaffolds due to its large surface area, proper  
558 hydrophilicity, 2D structure, conductivity, and particle size regulation. The hydrophilic surfaces  
559 of MXenes, with high metallic conductivities, distinguish them from most 2D materials such as  
560 graphene. Moreover, their high metallic conductivity allows them to efficiently transport electrical  
561 signals, which is crucial for many tissue engineering applications [115]. Meanwhile, more attempts  
562 are required to optimize and adjust the prepared composite according to the targeted native matrix,  
563 such as oxidative stability, biodegradability, biocompatibility, physiological condition stability,  
564 etc. Correspondingly, surface functionalizing of the MXene by organic and inorganic materials  
565 has been extensively suggested as a result of its high surface area. Also, the formation of MXene  
566 in various composite architectures, such as membranes, layers, porous structures, particles, 3D  
567 printed composites, and specifically nanofibrous configurations, could integrate its features.

568 MXene-based structures have been employed to boost the regrowth and reconstruction of  
569 various tissues. For example, it is a good choice for designing and regeneration of bone defects.  
570 The MXene-based materials easily interact with water and oxygen, causing their degradation and  
571 subsequent release of Ti-based materials. Such species are appropriate for the promotion of bone  
572 cell growth. Therefore, they could be applied in bone cancers to simultaneously ablate the tumor  
573 cells and reconstruct the bone. Pan et al. [17] synthesized a 3D-printed  $\text{Ti}_3\text{C}_2$ /bioactive glass bone  
574 scaffold (TBGS) and compared it with a bioactive glass 3D-printed membrane (BGS), which is a  
575 common and beneficial material for bone scaffolds. The fabrication route of both BGS and TBGS  
576 layers are schematically provided in **Fig. 5a**. A desirable element distribution was also shown by  
577 the element-mapping analysis (See **Fig. 5b**). As is depicted in **Fig. 5c**, triggering photothermal  
578 ablation was examined by irradiating the osteosarcoma cells by 808 nm laser. **Fig. 5d** confirmed  
579 much fewer living cells with increasing the laser-irradiation duration. 3D reconstruction of the  
580 tissue was analyzed after 24 weeks of implantation of the composite scaffolds, representing more  
581 calcified tissues and better regeneration outcome with the presence of TBGS, compared with that  
582 of applying BGS (**Figs. 5e**). The values of BV/TV, BMD, and TOT in newborn osseous tissues  
583 collectively exhibited a superior osteogenic performance of TBGS than the BGS layer, displaying  
584 in **Figs. 5f-h**.

585





**Figure 5.** Characteristics of a 3D-printed  $Ti_3C_2$ /bioactive glass bone scaffold; (a) schematic design of the synthesis methods, (b) EDS mapping, (c&d) schematic illustration of the photothermal therapy and its outcome, (e) evaluating the 3D reconstruction of the tissue after 24 weeks implantation of the composite tissues, and the value of (f) BV/TV, (g) BMD, and (h) TOT in newborn osseous tissues. Reproduced from reference [17] with permission from Wiley, Copyright 2020.

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593

594 MXene films have also illustrated promising features, such as planar structure for regenerating  
595 the skin tissue. In a study, a multifunctional crumpled  $Ti_3C_2T_x$  MXene-based membrane was  
596 designed as a skin tissue scaffold. In this research, various MXene ratios were coated on the  
597 polycarbonate membrane using a vacuum filtration technique. According to the results, the  
598 mechanical features were enhanced to 30.48% strain, 28.63 MPa tensile strength, and 77.0 dB  
599 shielding performance for the membrane containing 70 mg  $Ti_3C_2T_x$ . This could be attributed to  
600 the interfacial interaction between the MXene nanosheets and the 3D fibrous network. So,  
601 increasing the MXene ratio up to 70 mg provides more hydrogen bonds and higher mechanical  
602 features. The fracture morphology of the MT70 membrane also revealed the tighter attachment of  
603 the fibers inside the layer, which could be the reason for attaining superior mechanical properties.  
604 Moreover, thermal conductivity was improved by loading more MXene ratio in the membrane.



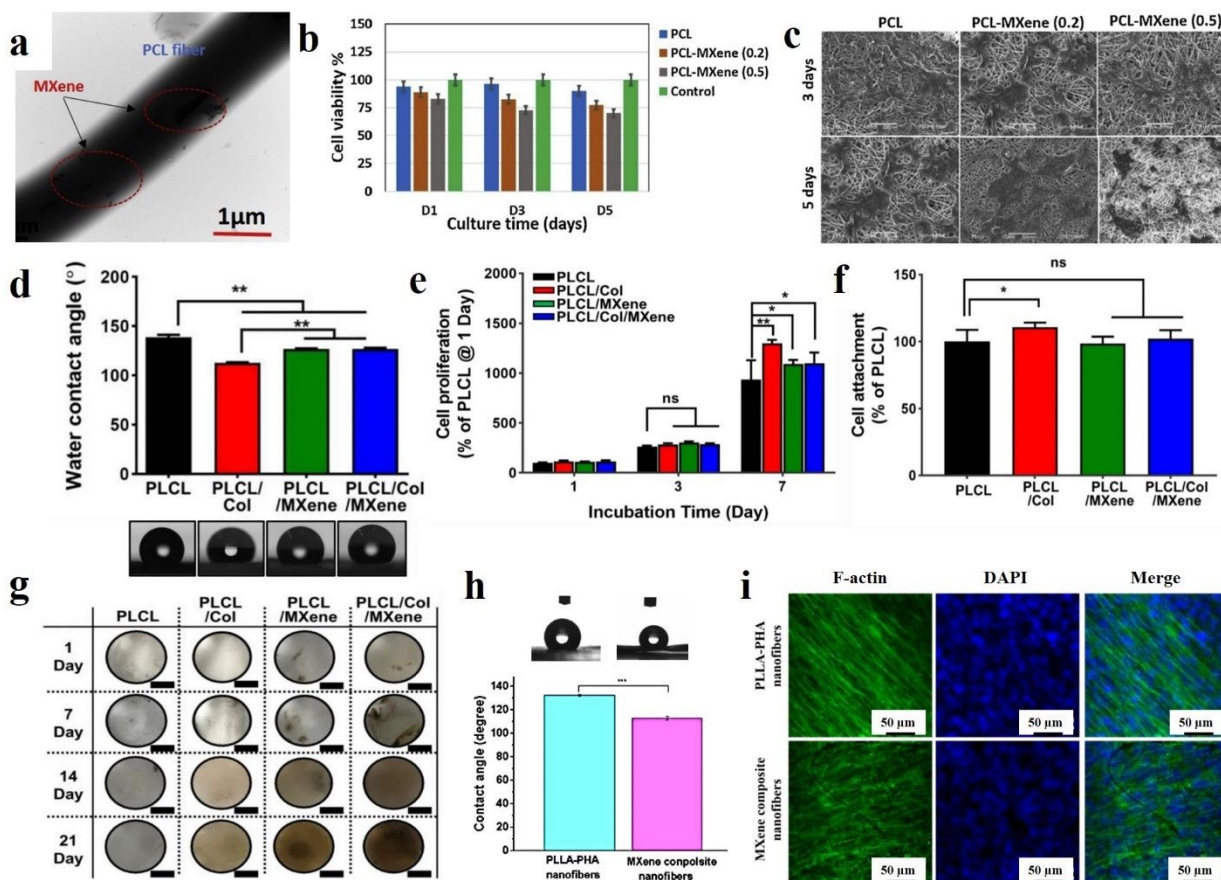
605 The through-plane conductivity enhancement refers to the vertical arrangement of the MXene  
606 nanosheet on both sides of wrinkles [15].

607 MXene has also exhibited a fabulous structure as a cardiac patch by mimicking the native tissue  
608 regarding its excellent electrical conductivity and topography cues. As an example, Basara et al.  
609 [116] designed a 3D-printed  $Ti_3C_3T_x$  MXene/PEG composite for cardiac tissue engineering. They  
610 confirmed the non-cytotoxicity of the prepared tissue for the human-induced cardiomyocytes. Also,  
611 the 3D-printed layer provided a great condition for cell alignment, resulting in the improvement  
612 of the synchronous beating and conduction velocity. A similar outcome was also obtained by using  
613  $Ti_2C$  cryogel as a conductive bifunctional cardiac patch. The results illustrated the formation of a  
614 3D vessel network after culturing the aortic endothelial cells. Moreover, this membrane  
615 represented rapid calcium transient, enhanced cardiac function, and great synchronous heart-like  
616 beating. Although the biocompatibility of the MXene-based compositions has been declared by  
617 many attempts, long-term biocompatibility assessments seem to be scarce in this era. Accordingly,  
618 incorporating systemic toxicity evaluations, immunogenicity assessments, and detailed  
619 histopathological analyses of major organs following implantation could substantiate the safety  
620 profile of these materials [117].

621 With the emerging nanotechnology science and the outstanding aptitudes of nanomaterials,  
622 they caught a huge interest in tissue regenerating and biomedical applications. These arrays could  
623 assist in approaching minimal side effects, passive and active targeting of damaged tissues, time-  
624 dependent drug release, and controllable degradation. Considering the vital role of MXene and  
625 various electrospun fibers in the progress of tissues, their combination could lead to eliminating  
626 their downsides and obtaining a synergetic effect. Accordingly, Awasthi et al. [118] fabricated an  
627 electrospun PCL/ $Ti_3C_2T_x$  composite and verified its potential for tissue engineering applications.  
628 To prepare the specimens,  $Ti_3C_2T_x$  with various concentrations of 0.2, 0.5, 1, and 2 wt.% was  
629 added into the electrospinning solutions. The electrospinning procedure was carried out using a  
630 12 ml syringe with a nozzle diameter of 0.51 mm under a spinning distance of 15 cm, voltage of  
631 15 kV, and feeding rate of 1 ml/h. **Fig. 6a** shows the TEM illustration of the  $Ti_3C_2T_x$ -loaded  
632 nanofibers. The presence of MXene in the electrospun scaffolds was confirmed by XPS data. The  
633 electrospun fibers containing 0.2, 0.5, 1, and 2 wt.% MXene showed average diameters of 0.69,  
634 0.83, 1.32, 1.35, and 1.6  $\mu m$ , respectively. The increment in the diameter could be due to the  
635 presence of interconnected pieces of MXene. The mentioned membranes also exhibited a rise in  
636 the contact angle from 100.7 to 37.2<sup>o</sup> with increasing the MXene concentration, which is  
637 fascinating for improving the cell adhesion and proliferation on the surface of scaffolds (see **Fig.**  
638 **6b&c**). A laboratory biomineralization test was used to evaluate the hydroxyapatite nucleation  
639 performance of the generated fibers. The EDS results obtained from the treatment of MXene-  
640 reinforced scaffolds with SBF confirmed the sufficient deposition of calcium and phosphorus on  
641 the surface of fibers for osseointegration according to the standard values reported for the HA  
642 crystals, which could be assigned to the proper wettability of the MXene nanosheets.  
643 Biocompatibility was investigated by fibroblast (NIH-3T3) and pre-osteoblast (MC3T3-E1) cells.



644 According to the results, PCL nanofibers loaded by MXene (up to 0.5 wt.%) represented more  
645 biocompatibility compared to the structures embedded with higher MXene ratios. This could be  
646 related to incrementing the fibers' diameter, leading to a reduction in protein adsorption, cell  
647 viability, and cell adhesion. Therefore, the biological activity of scaffold or bone graft could be  
648 boosted resulting from the MXene presence in the electrospun fibers due to its osteogenic  
649 properties.  
650



651  
652 **Figure 6.** Various characteristics of the MXene-decorated electrospun scaffolds; (a) TEM, (b)  
653 cell viability, and (c) cell attachment of the PCL nanofibers loaded by 0.2 and 0.5% MXene.  
654 Reproduced from reference [118] with permission from Elsevier, Copyright 2020. (d) water  
655 contact angle, (e) cell proliferation, (f) cell attachment, and (g) digital photographs of von  
656 Kossa-stained scaffolds of MXene-loaded PCL/Col nanofibers. Reproduced from reference [119]  
657 with permission from Springer, Copyright 2022. (h) water contact angle and (i) fluorescent  
658 images of the cultured BMSCs after 5 days of the PLLA-based nanocomposite. Reproduced from  
659 reference [23] with permission from the American Chemical Society, Copyright 2020.

660 Considering hybrid techniques of film casting and electrospinning, Yan et al. [120] fabricated a  
661 highly sensitive bionic MXene-based pressure sensor using the microstructure of the ginkgo leaf.  
662 The core deformation part of the sensor possessed microscopic shapes imprinted from the ginkgo



663 leaves. MXene was sprayed onto a PDMS model film with the ginkgo leaf structure. Also, the  
664 PVA nanofibers were synthesized by the electrospinning technique between the MXene  
665 component to approach a high-pressure sensitivity of up to  $03.46 \text{ kPa}^{-1}$ . The proposed pressure  
666 sensor was durable and displayed a short response time of 99.3 ms, representing the promising  
667 potential for application in physiological signal testing and human-computer interaction. Focusing  
668 on combining the structures, a triboelectric nanogenerator (TENG) was developed using  $\text{Ti}_3\text{C}_2$   
669 MXene supported by cotton fabric as an electrode layer for self-powered flexible sensors. The  
670 MXene was mixed with cellulose nanofibers to create the electrode layer, providing electrical  
671 conductivity and negativity, while the cotton fabric boosted strength and flexibility. The generated  
672 TENG could produce open-circuit voltage up to 400 V in single-electrode mode and sense the  
673 mass of touched steel objects ranging from 2 to 200 g with good repeatability and a linear  
674 relationship. The proposed TENG was highly flexible and could be stretched up to 100% of its  
675 original length, producing different voltage signals depending on the bending and folding angles.  
676 Therefore, the designed structure could be used as a self-powered flexible sensor to monitor  
677 various physiological movements of the human body [121].

678 In 2022, Lee et al. [119] developed nanofibrous matrices of poly(L-lactide-co- $\epsilon$ -  
679 caprolactone)/collagen (PLCL/Col) nanofibers loaded by  $\text{Ti}_3\text{C}_2$  nanosheets for bone tissue  
680 engineering. First, PLCL (75:25) and Col with concentrations of 5 and 0.5% (w/v) were dissolved  
681 in 1, 1, 1, 3, 3, 3-hexafluoroisopropanol.  $\text{Ti}_3\text{C}_2$  was dispersed in deionized water and mixed with  
682 PLCL/Col solution to approach the final solution concentration of  $400 \mu\text{g/ml}$ . The electrospinning  
683 distance was adjusted to 9 cm. The electrospinning process was carried out with a feeding rate of  
684 0.2 ml/h under a voltage of 16 kV. According to FESEM images, the mean diameter of PLCL,  
685 PLCL/Col, PLCL/ $\text{Ti}_3\text{C}_2$ , and PLCL/Col/ $\text{Ti}_3\text{C}_2$  nanofibers were  $908 \pm 68$ ,  $449 \pm 44$ ,  $368 \pm 22$ , and  
686  $357 \pm 3$  nm, respectively. The observed reduction in fiber diameters could be related to the changes  
687 in the viscosity of the solutions. Additionally, the surface roughness of the scaffolds also showed  
688 a downward trend, possibly due to the formation of finer fibers. As is displayed in **Fig. 6d**, the  
689 hydrophilicity of the PLCL scaffold increased with the addition of Col,  $\text{Ti}_3\text{C}_2$ , and Col/ $\text{Ti}_3\text{C}_2$   
690 combination. Cell attachment and proliferation of MC3T3-E1 preosteoblasts on the scaffolds were  
691 also investigated, implying a significant increase in the cell attachment through the addition of Col  
692 into the PLCL matrix compared with that of the PLCL (**Figs. 6e&f**). Meanwhile, there was no  
693 significant difference in the cell attachment between the PLCL/ $\text{Ti}_3\text{C}_2$  or PLCL/Col/ $\text{Ti}_3\text{C}_2$  and  
694 PLCL. At 7 days of incubation, PLCL/Col and PLCL/Col/ $\text{Ti}_3\text{C}_2$  nanofibrous matrices showed  
695 significantly increased cell proliferation,  $p < 0.01$  and  $p < 0.05$ , respectively. The obtained data  
696 suggested the synergistic impact of increased initial attachment, as well as hydrophilicity  
697 enhancement, in the improvement of cell proliferation. The results of exposure of the scaffolds to  
698 cells stained with von Kossa exhibited that the MXene-loaded scaffolds exceptionally increased  
699 osteogenesis activity and caused spontaneous differentiation from pre-osteoblasts (see **Fig. 6g**).  
700 After cell incubation for 14 days, the mineralized bone nodules appeared on the provided MXene  
701 loaded scaffolds, which are stained in a dark-brown color, while the MXene-free membranes did  
702 not show any color changes. Therefore, the MXene presence in the structure could lead to stronger



703 attractive cell interactions, accelerating the  $\text{Ca}^{2+}$  ions adsorption and so boosting the late-stage  
704 osteogenic differentiation.

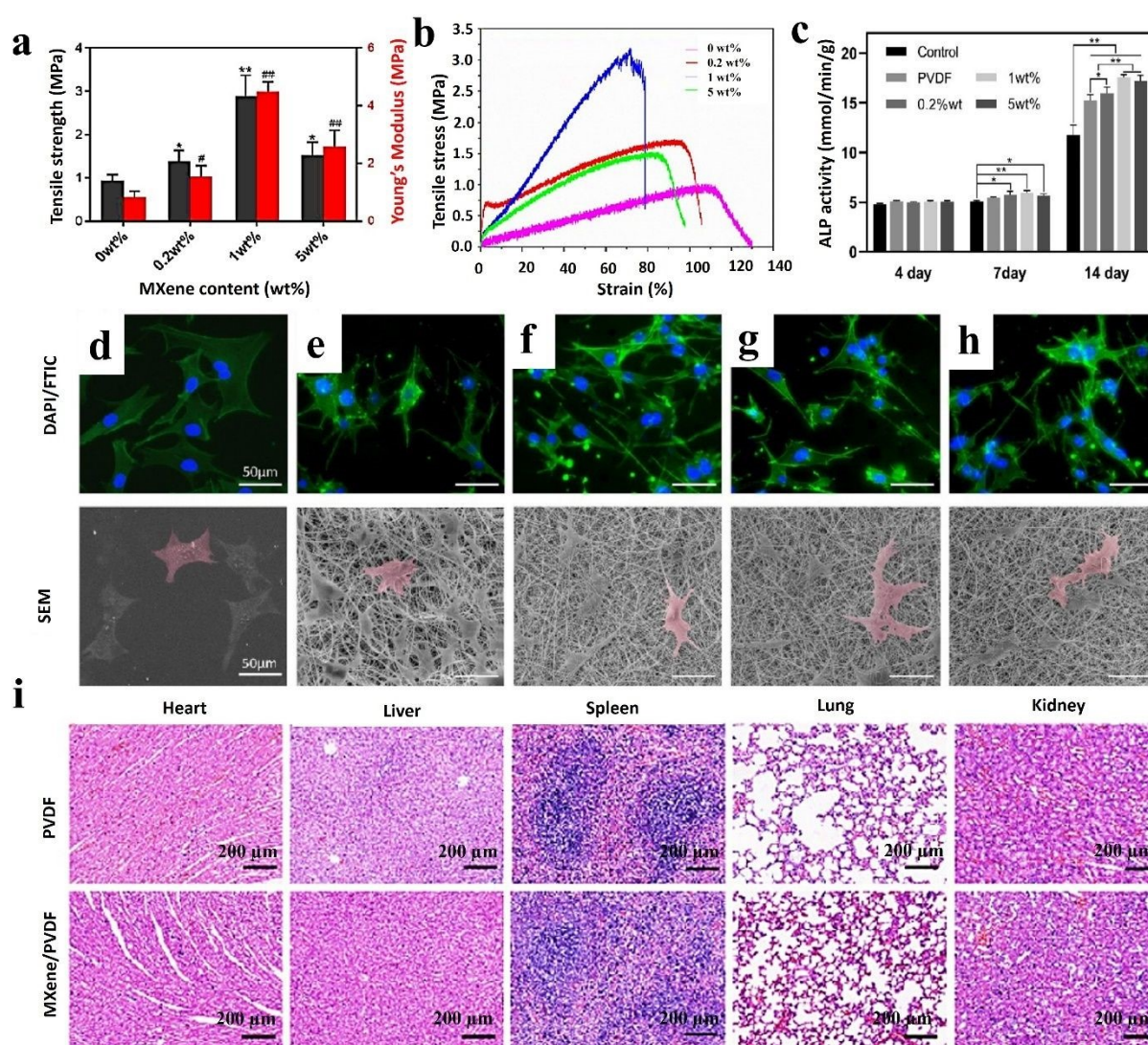
705 Huang et al. [23] also fabricated poly-l-lactic acid/Polyhydroxyalkanoates (PLLA/PHA)  
706 nanofibers filled with  $\text{Ti}_3\text{C}_2$  for bone tissue engineering. First, 40 mg of  $\text{Ti}_3\text{C}_2$  was added to 4 ml  
707 dichloromethane/dimethylformamide (DCM/DMF) and sonicated for 2 hours in an ice bath. Then,  
708 0.16 mg of PLLA and 0.16 g of PHA were introduced into the mixture and stirred for 24h. The  
709 electrospinning process was conducted using a 1 ml syringe under a voltage of 15 kV and a feeding  
710 rate of 0.6 ml/h. According to the obtained data, fine and homogenous fibers with an average  
711 diameter of 850 nm ranging from 600 nm to 1.5  $\mu\text{m}$ . were obtained. The XPS data revealed the  
712 creation of a large number of -OH and -O- terminal groups on the nanofibers' surfaces. The contact  
713 angle of the electrospun composites decreased from 132.27 to 112.76° after the incorporation of  
714  $\text{Ti}_3\text{C}_2$  into the PLLA/PHA nanofibers, resulting from the MXene functional groups (see **Fig. 6h**).  
715 Bone marrow-derived mesenchymal stem cells (BMSCs) were seeded on the scaffolds for 1, 3, 7,  
716 and 14 days. The results confirmed the cell adhesion enhancement on the MXene-loaded scaffolds  
717 after day 1, which could be attributed to the rise in the hydrophilicity ratio. On day 3, a similar  
718 trend was observed in the cell adhesion between the samples with and without MXene nanosheets.  
719 Meanwhile, it was again enhanced in the filled membrane after day 7, which could be linked with  
720 the formation of a desirable microenvironment for cell adhesion and proliferation. SEM images of  
721 cell culture on the scaffolds showed the spreading of the BMSCs cells along the nanofibrous  
722 pattern and the formation of a fiber-cell network (see **Fig. 6i**). The results of the PCR test displayed  
723 that the scaffolds reinforced with MXene had better osteogenesis functions than the filler-free  
724 scaffold after 14 days.

725 In 2023, Fu et al. [25] produced  $\text{Ti}_3\text{C}_2\text{T}_x$ /PVDF nanofibers through a standard electrospinning  
726 process for bone scaffolds. PVDF was first dissolved in a mixture of N, N-dimethylformamide/  
727 acetone (3:2), and the solution with a concentration of 20 wt./v% was obtained after 2h stirring at  
728 50°C. Then, 0.2, 1, and 5%  $\text{Ti}_3\text{C}_2\text{T}_x$  were sonicated in the obtained polymer solution at 4°C for 30  
729 min, followed by a stirring step of 8h at ambient temperature. The prepared solution was  
730 transferred to a syringe with a 20-gauge nozzle and electrospun with a feeding rate of 0.8 ml/min  
731 under a voltage of 13 kV and a spinning distance of 15 cm. The filler-free PVDF, as well as the  
732 loaded samples with 0.2, 1, and 5%  $\text{Ti}_3\text{C}_2\text{T}_x$ , represented average diameters of  $854.6 \pm 300.4$ ,  $803.4$   
733  $\pm 245.9$ ,  $648.9 \pm 215.5$ , and  $538.8 \pm 171.1$  nm, respectively. The destruction examination  
734 confirmed the high stability of the provided scaffold structures and corroborated the role of the  
735 PVDF shell in hindering MXene oxidation. According to the results, the PVDF scaffold is a  
736 hydrophobic layer ( $116.47 \pm 0.99^\circ$ ), and its contact angle and hydrophobicity was increased to  
737  $125.45 \pm 1.88$ ,  $123.72 \pm 2.20$ , and  $124.85 \pm 1.87^\circ$  by adding 0.2, 1, and 5 wt % MXene, respectively.  
738 These results are in contrast with previous studies, which can be stated that the PVDF leaf layer  
739 prevents the contact of MXene with water droplets, and it is also speculated that the addition of  
740 MXene increases the hydrophobicity of the structure due to the reduction of the surface free energy  
741 and the increase of the pore structure. The pure PVDF scaffold showed a tensile strength of 0.94





742  $\pm 0.12$  MPa and Young's modulus of  $0.82 \pm 0.22$  MPa. Embedding up to 1% MXene into the PVDF  
 743 structure caused an increase in the tensile strength ( $4.49 \pm 0.33$  MPa), while loading 5% led to a  
 744 reduction in the tensile value ( $1.52 \pm 0.29$  MPa) (see **Figs. 7a&b**). Accordingly, a small amount  
 745 of MXene could raise the modulus, possibly due to the strong interaction force between PVDF  
 746 molecular chains and MXene functional groups. However, exceeding a specific loading ratio led  
 747 to filler agglomeration and so a reduction in the scaffold modulus.



748  
 749 **Figure 7.** Features of the MXene/PVDF nanofibrous bone scaffolds; (a&b) mechanical  
 750 properties, (c) ALP activity, morphology, and adhesion of MC3T3-E1 cells on (d) glass, (e)  
 751 pristine PVDF, (f) 0.2 wt % MXene/PVDF, (g) 1 wt. % MXene/PVDF, and (h) 5 wt %  
 752 MXene/PVDF, and (i) H&E staining images after employing different treatments for 8 weeks in  
 753 various organs, including heart, liver, spleen, lung, and kidney stained with hematoxylin–eosin.  
 754 Reproduced from reference [25] with permission from the American Chemical Society, Copyright  
 755 2023.



756 Staining of dead cells was performed by inoculating MC3T3-E1 on the scaffolds for 24h, showing  
 757 acceptable cell viability by incorporating up to 1% MXene while increasing the dead cells through  
 758 loading 5% MXene (see **Figs. 7c-h**). The fluorescence microscope proved the spreading of the  
 759 MC3T3-E1 cells after 3 days on the surface of the scaffolds, which could be attributed to the 3D  
 760 topographical structure of the electrospun fibers. To investigate the effective substances on the  
 761 biological behavior of cells, a scratch test was conducted, showing similar migration of cells into  
 762 the gaps in all samples after 24 and 48h. This phenomenon confirms the hypothesis of MXene  
 763 placement in the PVDF shell, which does not affect the external cellular environment. The cell  
 764 viability assay confirmed the suitability of the scaffolds for cell growth. The results of cell culture  
 765 after 4 days were the same in all samples, but after 7 days scaffolds, containing 0.2% and 1%  
 766 MXene showed the highest cell viability. This could be attributed to the difference in surface  
 767 potential and topography of fibers, resulting from loading various amounts of MXene. The ALP  
 768 activity of cells after 14 days in samples containing MXene was higher than that in the pristine  
 769 PVDF, linking with the increase in surface potential and the fibers' topography. To evaluate the  
 770 osteogenic activity of camels, the relative expression of the MC3T3-E1 bone gene, including OCN,  
 771 OPN, ALP, Runx2, and Col I, was cultured and investigated. Accordingly, incorporating 1%  
 772 MXene mainly regulates the expression level of osteogenic genes in both early and late periods,  
 773 representing the great ability to improve osteogenic differentiation with a potential of  $69.34 \pm 2.64$   
 774 mV.

775 Finally, animal tests exhibited the appearance of normal branched muscle fibers in heart tissue,  
 776 radially scattered cells in liver tissue, ideal splenic nodules in the spleen, proper alveoli and  
 777 epithelial lining of bronchioles in lung tissue, and glomeruli and tubules for 8 weeks (see **Fig. 7i**).  
 778 No significant difference was observed in the pathological results of the PVDF and PDF/MXene  
 779 scaffolds on different organs, which indicates their outstanding biocompatibility. Also, new tissues  
 780 were formed at the site of the bone defect after 4 and 8 weeks of treatment. The surface potential  
 781 of the scaffold enhanced the differentiation of bone-forming cells and the absorption of osteogenic  
 782 cells on the surface of the scaffold, allowing the bone defect to be filled after 8 weeks. Other recent  
 783 attempts toward integrating the nanofibers via embedding MXene nanosheets toward approaching  
 784 efficient tissues, as well as versatile healthcare devices, are summarized in Table 1.

785 **Table 1.** MXene-loaded electrospun fibers applicable as various biomedical devices and tissue  
 786 engineering membranes.

Material contents	Application	Mechanism and Results	Ref.
MXene/Amoxicillin/PVA	Antimicrobial and photothermal platform for wound infection	-PVA matrix could control the Amoxicillin release. -MXene presented local Hyperthermia due to transforming the NIR laser into heat in battling bacterial infection.	Xu et al. [122]



		-The nanomembrane exhibited an antibacterial and accelerated wound healing capacity in the in vivo and in vitro models.	
<b>TiC/zeolite imidazole framework-8 (MZ-8)/PLA</b>	Wound healing	-MZ-8 could show hyperthermia PPT activity with a bactericidal rate of more than 99.0% and remarkable antitumor efficiency relying on photodynamic/photothermal therapy. -MXene/zeolite/PLA could boost infected wound healing without any bacteria resistance.	Zhang et al. [123]
Ti <sub>3</sub> C <sub>2</sub> T <sub>x</sub> /chitosan	Antibacterial wound dressing	-In vitro, antibacterial activity was depicted via crosslinked chitosan nanofibers integrated with MXene. -Direct bacterial membrane destruction was observed by contacting and penetrating bacteria in MXene flakes, with a 95% to 62% reduction in colony-forming units. -The features were synergized with intrinsic chitosan antimicrobial activity.	Mayerberger et al. [124]
Ti <sub>3</sub> AlC <sub>2</sub> MAX phase/PLA	Curcumin delivery system with antibacterial behavior	-PLA electrospun membranes decorated with MAX phase exhibited significantly higher toughness than the plasticized PLA membrane with low cytotoxicity, supporting the proliferation of mouse fibroblast L929 cells, as well as higher antibacterial properties against E. coli and S. aureus. -Due to the curcumin diffusion from the polymer fibers and the MAX phase surface contributing to the overall increased curcumin adsorption and release sites, 7-day curcumin release was increased from 45 to 67%.	Krasian et al. [125]
PVA/ Ti <sub>3</sub> C <sub>2</sub> T <sub>x</sub> / Molybdenum Diselenide (MoSe <sub>2</sub> )/ polyethylene terephthalate	Human skin moisture/Energy harvesting sensor	-Self-powered sensing device was fabricated by PVA/MXene nanolayer and integrated with a single layer of MoSe <sub>2</sub> to decipher humidity by commuting mechanical energy to electric energy. -The excellent metallic conductivity and hydrophilicity of PVA/MXene, concomitant with the piezoelectric properties of MoSe <sub>2</sub> generated the flexible, fast response humidity sensor (0.9/6.3 s, about 40-fold higher than pure MXene).	Wang et al. [126]
Ti <sub>3</sub> C <sub>2</sub> T <sub>x</sub> /PVDF	Aptasensors	-The designed nanocomposite detected secondary fungal metabolite mycotoxin due to their electroactive sites and covalent biofunctionalization of the redox probe with aptamer. -The designed sensor was useful for OTA trace determination in the food safety analysis in the concentration range from 1 fg.mL <sup>-1</sup> to 1 ng.mL <sup>-1</sup> .	Al-Dhahebi et al. [127]
Ti <sub>3</sub> C <sub>2</sub> T <sub>x</sub> /dopamine/polyurethane	Wearable sensor	-The inclusion of thermoplastic polyurethane in the composition offered enhanced flexibility and breathability.	Zhang et al. [128]



		<p>-The presence of a poly-dopamine coating facilitated adhesion between MXene and thermoplastic polyurethane.</p> <p>-The incorporation of MXene resulted in strain-sensing capabilities and effective electromagnetic interference shielding performance.</p> <p>-The strain sensor design exhibited remarkable sensing functionality, demonstrating an exceptional recognition threshold.</p>	
$Ti_3C_2T_x/PCL$	Neurite regeneration and angiogenesis	<p>-The PCL layer was covered with MXene, and figured out the excellent cell adhesion and biocompatibility during cell culturing.</p> <p>-MXene-PCL composite for nerve guidance conduits showed similar results with the autograft in angiogenesis, electrophysiological examination, and nerve regeneration morphology in both in vivo and in vitro studies.</p>	Nan et al. [129]
$Ti_3C_2T_x/PLA$	Nerve guidance conduits	<p>-The functionalized layer exhibited biocompatibility and non-toxicity through the Cell culturing test and gram-positive bacterial adhesion assay.</p> <p>-MXene directly influences cellular membranes and damages the cell morphology.</p> <p>-Fabulous electroconductivity properties were confirmed with an electrical conductivity assay due to the MXene involved in PLA membranes.</p>	Kyrylenko et al. [130]
$Ti_3C_2T_x/PCL$	Tissue engineering	<p>-The effect of MXene layer thickness was evaluated, showing the most appropriate results of cell attachment, adhesion, and proliferation, as well as antibacterial behavior through repeating the immersing process 2 and 3 times.</p> <p>-These samples exhibited samples illustrated the least bacteria adhesion due to the inhibitory effect of the MXene thin layers on the membrane surface through physical damaging of the cell walls.</p>	Diedkova et al. [131]
$Ti_3C_2T_x/PLGA$	Nerve tissue regeneration	<p>-The formation of a more brittle structure via exceeding the MXene ratio from 0.1 g.</p> <p>- Antibacterial property of the produced scaffolds against <i>E. coli</i>, <i>S. aureus</i>, and <i>C. albicans</i>, due to high hydrophilicity and the bacteria absorption by surface anions of MXene nanosheets.</p> <p>- The results of the biocompatibility test were performed with the cultivation of Schwann cells on the scaffolds, illustrating the cell survival on the scaffolds containing 0.3 and 0.6 MXene, which is due to the increased hydrophilicity and conductivity.</p>	Zhang et al. [132]



788 Overall, flexible nanofibrous networks with tunable morphological features, as well as  
789 mechanical strength, could be feasibly synthesized through the electrospinning method. The highly  
790 porous structure of the electrospun fibers with interconnected pores could offer favorable features  
791 for biomedical targets and mimic the native extracellular matrix, integrating cell adhesion, growth,  
792 and proliferation in various organs. Although electrospun nanofibers embedded with MXene  
793 nanostructures have showcased promising configurations for biomedical targets, a lack of long-  
794 term evaluation is sensed in the performed analysis. As an example, mechanical properties are  
795 considered as one of the main features, requiring to be optimized considering each application. For  
796 example, in the context of tissue engineering, the designed structure must possess mechanical  
797 properties that are appropriate for the desired vein. Failure to do so may result in the degradation  
798 of the original tissue or the collapse of the new structure when subjected to load [2]. The analysis  
799 of the mechanical stability in bodily fluids or under cyclic loadings mimicking bodily movements  
800 could provide valuable insights into their long-term durability in biomedical applications. To  
801 assess the mechanical properties of the designed structures, it is recommended that they be tested  
802 under conditions that are similar to those found in vivo. For instance, the samples should be  
803 immersed in a buffer solution or subjected to cell culture. Furthermore, it is advisable to test the  
804 samples under both unidirectional and multidirectional conditions, depending on the intended  
805 application. Consequently, the mechanical properties of the designed structures must be carefully  
806 evaluated to ensure that they are fit for purpose [133].

807 Moreover, long-term cytotoxicity analysis is assumed to be a critical issue in biomedical  
808 applications. Therefore, verifying the long-term compatibility and non-toxicity of materials is of  
809 utmost importance. While various case studies have investigated the acute toxicological effects of  
810 MXene-based compositions in vitro and in vivo, few studies have been dedicated to highlighting  
811 its long-term toxicology behavior [134]. To address this, in vitro studies utilizing long-term cell  
812 cultures and monthly observations are recommended. Additionally, the degradation of samples  
813 under physiological conditions should be investigated over an extended period to ascertain if any  
814 toxic substances are released or if the pH and other environmental factors are altered over time [2,  
815 133].

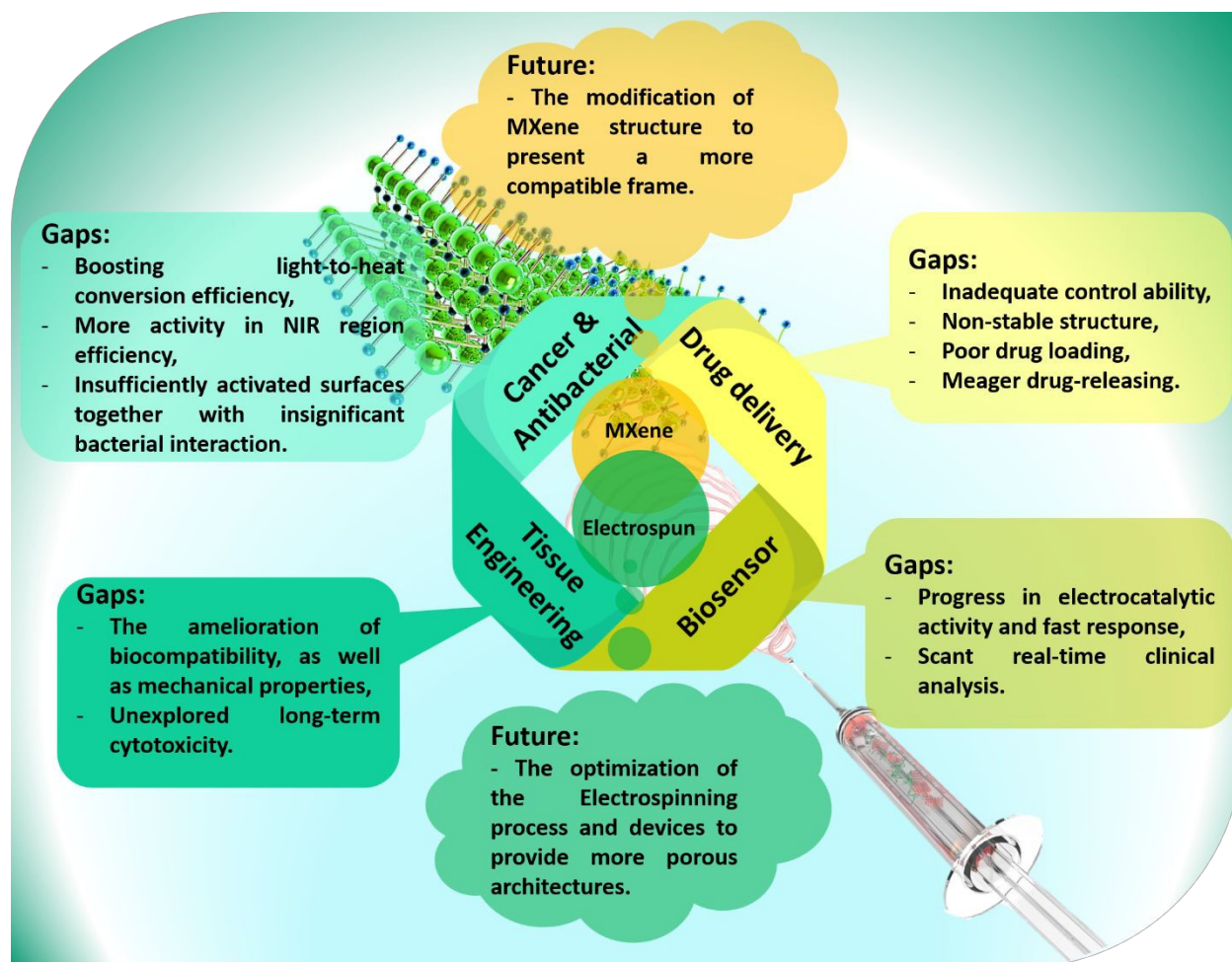
## 816 **Conclusion and perspectives**

817 As a very promising emerging material, the MXene family has shown outstanding features for a  
818 wide range of applications. Several inherent MXene characteristics, including frequent functional  
819 groups on the surface, biocompatibility, large surface-to-volume ratio, physiochemical properties,  
820 and many more, have caused a plethora of benefits for biomedical usages and tissue engineering  
821 targets. Among various MXene-loaded compositions, the electrospun fibrous architectures have  
822 represented promising features resulting from the large surface area, highly porous networks, tiny  
823 and interconnected pores, etc. The integration of electrospun fibers with MXene nanosheets could  
824 boost hydrophilicity and enhance dimensional and mechanical stability. Additionally,  
825 biocompatibility, antibacterial activity, as well as cell adhesion, growth, and proliferation could be  
826 integrated into these platforms, leading to approaching ideal bone, nerve, skin, and heart tissues.



827 Accordingly, the electrospun tissues embedded with MXene nanosheets could alleviate the  
828 challenges faced by individual components, benefiting from their synergetic effects.

829



830

831 **Figure 8.** Prospects for the future and gaps in biomedical applications; the developed path of  
832 MXene and electrospun frameworks.

833

834 Despite the great consequences observed for the MXene-loaded nanocomposites, few researches  
835 have been conducted in this era, leading to several remaining challenges (**Fig. 8**). First, in  
836 competition with the present strategies, synthesis modification, surface functionalizing, and  
837 morphology altering are proposed to be investigated more, since they could be influential on the  
838 cytotoxicity and biocompatibility. Also, MXene is nonstable in the atmosphere and physiological  
839 environments. The employed synthesis method should be progressed to achieve an eco-friendly,  
840 long-term stable, adjustable, and cost-effective technique with least-hazard byproducts. In addition,  
841 the biological behavior of the MXene-loaded materials should be focused more to further evaluate  
842 long-term toxicity, the reaction of MXene with cells, drugs, blood, and organs, biodegradability,  
843 biosafety, and histopathological properties. It is important to consider that the use of toxic and



844 corrosive liquids in the synthesis of MXene could result in negative effects. Also, most of the  
845 research in this era is focused on the use and development of titanium carbide-based additives,  
846 while the MXene family is very broad, and the lack of suitable explorations is deeply felt. This  
847 route could also be continued through the design and analysis of the MXene combination or  
848 coating with other organic and inorganic compounds in the electrospun configurations. It is  
849 worthwhile to manipulate the electrospinning fabrication procedure to obtain more monotonous  
850 fibrous networks comprising tunable pore sizes and porosity rates.

851 In the biomedical path, the physiological, biological, and mechanical features of nanofibrous  
852 membranes play a critical role in the final success of designed architectures. In this regard, it is  
853 proposed to amend the surface of nanofibrous layers through direct electrospinning of polymers  
854 with organic-based components, as well as applying surface modification techniques, such as  
855 plasma treatment, surface polishing, and others. The electrospun membranes could be integrated  
856 with other MXene-loaded arrays, such as hydrogel, 3D-printed, or electro-written layers. Moreover,  
857 in vitro and in vivo analyses are suggested to be carried out on various tissues generated with the  
858 MXene and MXene derivatives-loaded materials. Furthermore, comprehensive studies along with  
859 the simulation and modeling are offered for the prediction of MXene-loaded nanofibrous tissues'  
860 behavior without the need for animal studies. However, it is also understandable that most studies  
861 are currently limited to lab scale, which can create skepticism towards MXene-embedded  
862 electrospun structures. Accordingly, a need is recognized for more comprehensive studies in order  
863 to alleviate these concerns and ensure a safer and more sustainable approach. MXene-embedded  
864 electrospun structures have the potential to revolutionize various fields by offering unique  
865 combinations of properties and functionalities. Ongoing research and development efforts will  
866 further advance this material system and unlock its full potential for next-generation technologies.

867

## 868 **Funding.**

869 The authors acknowledge the Foundation of China (Grant No.51702204), the Natural Science  
870 Foundation of Shaanxi Province (Grant No. 2017JQ2043), Xianyang Science and Technology  
871 Research Project of China (Grant No. 2021ZDYF-GY-0040), and Xianyang City Qinchuangyuan  
872 Science and Technology Innovation Special Project (Grant No. L2022-QCYZX-GY-006).

## 873 **Contributions.**

874 X. Li: Collecting data, Writing the paper, and Validating data.

875 S. Wang: Collecting data, Writing the paper, and Designing the figures.

876 M. Zheng: Writing the paper and Approved data

877 Z. Ma: Writing the paper and Designing the figures

878 Y. Chen: Collecting Data and Writing the paper

879 L. Deng: Designing the project and Collecting data

880 W. Xu: Writing the paper, Approving data, and Designing figures

881 G. Fan: Administrating the paper and Revising the paper



882 S. Khademolqorani: Writing and revising the paper and Designing the figures

883 SN. Banitaba: Writing and revising the paper and Designing the figures

884 Al. Osman: Administrating the paper and Revising the paper

885

## 886 **References.**

- 887 [1] K. Ghosal, C. Agatemor, Z. Špitálský, S. Thomas, and E. Kny, "Electrospinning tissue engineering  
888 and wound dressing scaffolds from polymer-titanium dioxide nanocomposites," *Chemical*  
889 *Engineering Journal*, vol. 358, pp. 1262-1278, 2019.
- 890 [2] S. Khademolqorani, H. Tavanai, I. S. Chronakis, A. Boisen, and F. Ajalloueiian, "The determinant  
891 role of fabrication technique in final characteristics of scaffolds for tissue engineering  
892 applications: A focus on silk fibroin-based scaffolds," *Materials Science and Engineering: C*, vol.  
893 122, p. 111867, 2021.
- 894 [3] M. Nasari, N. Poursharifi, A. Fakhrali, S. N. Banitaba, S. Mohammadi, and D. Semnani,  
895 "Fabrication of novel PCL/PGS fibrous scaffold containing HA and GO through simultaneous  
896 electrospinning-electrospray technique," *International Journal of Polymeric Materials and*  
897 *Polymeric Biomaterials*, pp. 1-17, 2022.
- 898 [4] S. Khademolqorani and S. N. Banitaba, "Application of electrosprayed nanoparticles as targeted  
899 drug delivery systems: A mini review," *Journal of Applied Sciences and Nanotechnology*, vol. 2,  
900 no. 2, pp. 1-7, 2022.
- 901 [5] M. Rahmati *et al.*, "Electrospinning for tissue engineering applications," *Progress in Materials*  
902 *Science*, vol. 117, p. 100721, 2021.
- 903 [6] X. Xie *et al.*, "Electrospinning nanofiber scaffolds for soft and hard tissue regeneration," *Journal*  
904 *of Materials Science & Technology*, vol. 59, pp. 243-261, 2020.
- 905 [7] A. P. Rickel, X. Deng, D. Engebretson, and Z. Hong, "Electrospun nanofiber scaffold for vascular  
906 tissue engineering," *Materials Science and Engineering: C*, vol. 129, p. 112373, 2021.
- 907 [8] E. R. Ghomi *et al.*, "Advances in electrospinning of aligned nanofiber scaffolds used for wound  
908 dressings," *Current Opinion in Biomedical Engineering*, p. 100393, 2022.
- 909 [9] S. N. Banitaba *et al.*, "Biopolymer-based electrospun fibers in electrochemical devices: versatile  
910 platform for energy, environment, and health monitoring," *Materials Horizons*, vol. 9, no. 12, pp.  
911 2914-2948, 2022.
- 912 [10] S. Khademolqorani, S. N. Banitaba, S. Azizi, and M. Kouhi, "Chapter 9 - Gellan gum-based  
913 nanocomposite hydrogels," in *Application of Gellan Gum as a Biomedical Polymer*, A. K. Nayak  
914 and M. S. Hasnain Eds.: Academic Press, 2024, pp. 171-197.
- 915 [11] S. Nagam Hanumantharao and S. Rao, "Multi-functional electrospun nanofibers from polymer  
916 blends for scaffold tissue engineering," *Fibers*, vol. 7, no. 7, p. 66, 2019.
- 917 [12] R. A. Surmenev *et al.*, "Electrospun composites of poly-3-hydroxybutyrate reinforced with  
918 conductive fillers for in vivo bone regeneration," *Open Ceramics*, vol. 9, p. 100237, 2022.
- 919 [13] S. Khademolqorani, A. Zeinal Hamadani, and H. Tavanai, "Response Surface Modelling of  
920 Electrospayed Polyacrylonitrile Nanoparticle Size," *Journal of Nanoparticles*, vol. 2014, p.  
921 146218, 2014/08/10 2014, doi: 10.1155/2014/146218.
- 922 [14] L. Yang *et al.*, "Wearable pressure sensors based on MXene/tissue papers for wireless human  
923 health monitoring," *ACS Applied Materials & Interfaces*, vol. 13, no. 50, pp. 60531-60543, 2021.





- 924 [15] R. Ding *et al.*, "Skin inspired multifunctional crumpled Ti<sub>3</sub>C<sub>2</sub>T<sub>x</sub> MXene/Tissue composite film,"  
925 *Composites Part A: Applied Science and Manufacturing*, vol. 158, p. 106967, 2022/07/01/ 2022,  
926 doi: <https://doi.org/10.1016/j.compositesa.2022.106967>.
- 927 [16] S. Iravani and R. S. Varma, "MXenes and MXene-based materials for tissue engineering and  
928 regenerative medicine: Recent advances," *Materials Advances*, vol. 2, no. 9, pp. 2906-2917,  
929 2021.
- 930 [17] S. Pan *et al.*, "2D MXene-integrated 3D-printing scaffolds for augmented osteosarcoma  
931 phototherapy and accelerated tissue reconstruction," *Advanced Science*, vol. 7, no. 2, p.  
932 1901511, 2020.
- 933 [18] C. Yang, Y. Luo, H. Lin, M. Ge, J. Shi, and X. Zhang, "Niobium carbide MXene augmented medical  
934 implant elicits bacterial infection elimination and tissue regeneration," *ACS nano*, vol. 15, no. 1,  
935 pp. 1086-1099, 2020.
- 936 [19] J. Zhang, Y. Fu, and A. Mo, "Multilayered titanium carbide MXene film for guided bone  
937 regeneration," *International journal of nanomedicine*, pp. 10091-10103, 2019.
- 938 [20] J. Yin *et al.*, "MXene-based hydrogels endow polyetheretherketone with effective osteogenicity  
939 and combined treatment of osteosarcoma and bacterial infection," *ACS applied materials &*  
940 *interfaces*, vol. 12, no. 41, pp. 45891-45903, 2020.
- 941 [21] Q. Yang *et al.*, "Engineering 2D mesoporous Silica@ MXene-integrated 3D-printing scaffolds for  
942 combinatory osteosarcoma therapy and NO-augmented bone regeneration," *Small*, vol. 16, no.  
943 14, p. 1906814, 2020.
- 944 [22] G. Ye *et al.*, "Mussel-inspired conductive Ti<sub>2</sub>C-cryogel promotes functional maturation of  
945 cardiomyocytes and enhances repair of myocardial infarction," *Theranostics*, vol. 10, no. 5, p.  
946 2047, 2020.
- 947 [23] R. Huang *et al.*, "MXene composite nanofibers for cell culture and tissue engineering," *ACS*  
948 *Applied Bio Materials*, vol. 3, no. 4, pp. 2125-2131, 2020.
- 949 [24] M. Naguib *et al.*, "Two-dimensional nanocrystals produced by exfoliation of Ti<sub>3</sub>AlC<sub>2</sub>," *Advanced*  
950 *materials*, vol. 23, no. 37, pp. 4248-4253, 2011.
- 951 [25] Y. Fu *et al.*, "MXene-Functionalized Ferroelectric Nanocomposite Membranes with Modulating  
952 Surface Potential Enhance Bone Regeneration," *ACS Biomaterials Science & Engineering*, 2023.
- 953 [26] M. Rafiq *et al.*, "Recent progress in MXenes incorporated into electrospun nanofibers for  
954 biomedical application: Study focusing from 2017 to 2022," *Chinese Chemical Letters*, vol. 34,  
955 no. 7, p. 108463, 2023/07/01/ 2023, doi: <https://doi.org/10.1016/j.ccllet.2023.108463>.
- 956 [27] B. Pant, M. Park, and A. A. Kim, "MXene-Embedded Electrospun Polymeric Nanofibers for  
957 Biomedical Applications: Recent Advances," *Micromachines*, vol. 14, no. 7, p. 1477, 2023.
- 958 [28] Y. Feng *et al.*, "The collagen-based scaffolds for bone regeneration: A journey through  
959 electrospun composites integrated with organic and inorganic additives," *Processes*, vol. 11, no.  
960 7, p. 2105, 2023.
- 961 [29] S. N. Banitaba, A. A. Gharehaghaji, and A. A. A. Jeddi, "Fabrication and characterization of hollow  
962 electrospun PLA structure through a modified electrospinning method applicable as vascular  
963 graft," *Bulletin of Materials Science*, vol. 44, pp. 1-7, 2021.
- 964 [30] J. Xue, T. Wu, Y. Dai, and Y. Xia, "Electrospinning and electrospun nanofibers: Methods,  
965 materials, and applications," *Chemical reviews*, vol. 119, no. 8, pp. 5298-5415, 2019.
- 966 [31] M. Z. A. Zulkifli, D. Nordin, N. Shaari, and S. K. Kamarudin, "Overview of Electrospinning for  
967 Tissue Engineering Applications," *Polymers*, vol. 15, no. 11, p. 2418, 2023.
- 968 [32] D. Ji *et al.*, "Electrospinning of nanofibres," *Nature Reviews Methods Primers*, vol. 4, no. 1, p. 1,  
969 2024.
- 970 [33] R. Jalili, S. A. A. HOSSEINI, and M. Morshed, "The effects of operating parameters on the  
971 morphology of electrospun polyacrylonitrile nanofibres," 2005.



- 972 [34] K. Matabola and R. Moutloali, "The influence of electrospinning parameters on the morphology  
973 and diameter of poly (vinylidene fluoride) nanofibers-effect of sodium chloride," *Journal of*  
974 *Materials Science*, vol. 48, pp. 5475-5482, 2013.
- 975 [35] H. Liu, S. Vijayavenkataraman, D. Wang, L. Jing, J. Sun, and K. He, "Influence of  
976 electrohydrodynamic jetting parameters on the morphology of PCL scaffolds," *International*  
977 *Journal of Bioprinting*, vol. 3, no. 1, 2017.
- 978 [36] A. Jabur, L. Abbas, and S. Muhi Aldain, "Effects of ambient temperature and needle to collector  
979 distance on PVA nanofibers diameter obtained from electrospinning technique," *Engineering*  
980 *and Technology Journal*, vol. 35, no. 4A, pp. 340-347, 2017.
- 981 [37] S. Shen, Y. Wu, Y. Liu, and D. Wu, "High drug-loading nanomedicines: progress, current status,  
982 and prospects," *International journal of nanomedicine*, pp. 4085-4109, 2017.
- 983 [38] H. Laroui *et al.*, "Nanomedicine in GI," *American Journal of Physiology-Gastrointestinal and Liver*  
984 *Physiology*, vol. 300, no. 3, pp. G371-G383, 2011.
- 985 [39] Z. Chen, M. Guan, Y. Bian, and X. Yin, "Multifunctional Electrospun Nanofibers for Biosensing  
986 and Biomedical Engineering Applications," *Biosensors*, vol. 14, no. 1, p. 13, 2023.
- 987 [40] S. Gungordu Er, A. Kelly, S. B. W. Jayasuriya, and M. Edirisinghe, "Nanofiber based on electrically  
988 conductive materials for biosensor applications," *Biomedical Materials & Devices*, vol. 1, no. 2,  
989 pp. 664-679, 2023.
- 990 [41] S. N. Banitaba *et al.*, "Recent progress of bio-based smart wearable sensors for healthcare  
991 applications," *Materials Today Electronics*, vol. 5, p. 100055, 2023.
- 992 [42] S. N. Banitaba, A. A. Q. Ahmed, M.-R. Norouzi, and S. Khademolqorani, "Biomedical applications  
993 of non-layered 2DMs," 2023.
- 994 [43] J. T. McCann, M. Marquez, and Y. Xia, "Highly Porous Fibers by Electrospinning into a Cryogenic  
995 Liquid," *Journal of the American Chemical Society*, vol. 128, no. 5, pp. 1436-1437, 2006/02/01  
996 2006, doi: 10.1021/ja056810y.
- 997 [44] C. Huang and N. L. Thomas, "Fabricating porous poly(lactic acid) fibres via electrospinning,"  
998 *European Polymer Journal*, vol. 99, pp. 464-476, 2018/02/01/ 2018, doi:  
999 <https://doi.org/10.1016/j.eurpolymj.2017.12.025>.
- 1000 [45] N. E. Zander, J. A. Orlicki, A. M. Rawlett, and T. P. Beebe Jr, "Electrospun polycaprolactone  
1001 scaffolds with tailored porosity using two approaches for enhanced cellular infiltration," *Journal*  
1002 *of Materials Science: Materials in Medicine*, vol. 24, no. 1, pp. 179-187, 2013.
- 1003 [46] P. Fomby *et al.*, "A review of key challenges of electrospun scaffolds for tissue-engineering  
1004 applications," *Ann. Am. Thorac. Soc*, vol. 12, pp. 181-204, 2010.
- 1005 [47] L. Yang *et al.*, "Electrospun silk fibroin/fibrin vascular scaffold with superior mechanical  
1006 properties and biocompatibility for applications in tissue engineering," *Scientific Reports*, vol. 14,  
1007 no. 1, p. 3942, 2024/02/16 2024, doi: 10.1038/s41598-024-54638-0.
- 1008 [48] H. Lee *et al.*, "Enhancement of mechanical properties of polymeric nanofibers by controlling  
1009 crystallization behavior using a simple freezing/thawing process," *RSC Advances*,  
1010 10.1039/C7RA06545K vol. 7, no. 69, pp. 43994-44000, 2017, doi: 10.1039/C7RA06545K.
- 1011 [49] D. Xu, Z. Li, Z. Deng, X. Nie, Y. Pan, and G. Cheng, "Degradation profiles of the poly ( $\epsilon$ -  
1012 caprolactone)/silk fibroin electrospinning membranes and their potential applications in tissue  
1013 engineering," *International Journal of Biological Macromolecules*, p. 131124, 2024.
- 1014 [50] H. Budharaju *et al.*, "Carboxymethyl cellulose-agarose hydrogel in poly (3-hydroxybutyrate-co-3-  
1015 hydroxyvalerate) nanofibers: A novel tissue engineered skin graft," *International Journal of*  
1016 *Biological Macromolecules*, p. 130565, 2024.
- 1017 [51] Y. H. Jeong, M. Kwon, S. Shin, J. Lee, and K. S. Kim, "Biomedical Applications of CNT-Based  
1018 Fibers," *Biosensors*, vol. 14, no. 3, p. 137, 2024. [Online]. Available:  
1019 <https://www.mdpi.com/2079-6374/14/3/137>.



- 1020 [52] N. Nazeri, M. A. Derakhshan, R. Faridi-Majidi, and H. Ghanbari, "Novel electro-conductive  
1021 nanocomposites based on electrospun PLGA/CNT for biomedical applications," *Journal of*  
1022 *Materials Science: Materials in Medicine*, vol. 29, pp. 1-9, 2018.
- 1023 [53] M. C. Barbosa *et al.*, "Production of rGO-Based Electrospinning Nanocomposites Incorporated in  
1024 Recycled PET as an Alternative Dry Electrode," *Polymers*, vol. 14, no. 20, p. 4288, 2022. [Online].  
1025 Available: <https://www.mdpi.com/2073-4360/14/20/4288>.
- 1026 [54] Z. Liu *et al.*, "Graphene-based materials prepared by supercritical fluid technology and its  
1027 application in energy storage," *The Journal of Supercritical Fluids*, vol. 188, p. 105672, 2022.
- 1028 [55] A. Ivanoska-Dacicj *et al.*, "Electrospun PEO/rGO Scaffolds: The Influence of the Concentration of  
1029 rGO on Overall Properties and Cytotoxicity," *International Journal of Molecular Sciences*, vol. 23,  
1030 no. 2, p. 988, 2022. [Online]. Available: <https://www.mdpi.com/1422-0067/23/2/988>.
- 1031 [56] M. Gozutok, V. Sadhu, and H. T. Sasmazel, "Development of poly (vinyl alcohol)(PVA)/reduced  
1032 graphene oxide (rGO) electrospun mats," *Journal of Nanoscience and Nanotechnology*, vol. 19,  
1033 no. 7, pp. 4292-4298, 2019.
- 1034 [57] Y. Zhong, X. Xia, F. Shi, J. Zhan, J. Tu, and H. J. Fan, "Transition metal carbides and nitrides in  
1035 energy storage and conversion," *Advanced science*, vol. 3, no. 5, p. 1500286, 2016.
- 1036 [58] M. Naguib, M. W. Barsoum, and Y. Gogotsi, "Ten years of progress in the synthesis and  
1037 development of MXenes," *Advanced Materials*, vol. 33, no. 39, p. 2103393, 2021.
- 1038 [59] I. A. Vasyukova, O. V. Zakharova, D. V. Kuznetsov, and A. A. Gusev, "Synthesis, toxicity  
1039 assessment, environmental and biomedical applications of MXenes: A review," *Nanomaterials*,  
1040 vol. 12, no. 11, p. 1797, 2022.
- 1041 [60] A. Feng, T. Hou, Z. Jia, Y. Zhang, F. Zhang, and G. Wu, "Preparation and characterization of epoxy  
1042 resin filled with Ti3C2Tx MXene nanosheets with excellent electric conductivity," *Nanomaterials*,  
1043 vol. 10, no. 1, p. 162, 2020.
- 1044 [61] L. Liu *et al.*, "Exfoliation and delamination of Ti3C2Tx MXene prepared via molten salt etching  
1045 route," *ACS nano*, vol. 16, no. 1, pp. 111-118, 2021.
- 1046 [62] Y. Guan *et al.*, "A hydrofluoric acid-free synthesis of 2D vanadium carbide (V2C) MXene for  
1047 supercapacitor electrodes," *2D Materials*, vol. 7, no. 2, p. 025010, 2020.
- 1048 [63] N. Driscoll *et al.*, "Two-dimensional Ti3C2 MXene for high-resolution neural interfaces," *Acs*  
1049 *Nano*, vol. 12, no. 10, pp. 10419-10429, 2018.
- 1050 [64] F. Ming, H. Liang, G. Huang, Z. Bayhan, and H. N. Alshareef, "MXenes for rechargeable batteries  
1051 beyond the lithium-ion," *Advanced Materials*, vol. 33, no. 1, p. 2004039, 2021.
- 1052 [65] P. Urbankowski *et al.*, "Synthesis of two-dimensional titanium nitride Ti4N3 (MXene),"  
1053 *Nanoscale*, vol. 8, no. 22, pp. 11385-11391, 2016.
- 1054 [66] M. Li *et al.*, "Element replacement approach by reaction with Lewis acidic molten salts to  
1055 synthesize nanolaminated MAX phases and MXenes," *Journal of the American Chemical Society*,  
1056 vol. 141, no. 11, pp. 4730-4737, 2019.
- 1057 [67] W. Sun *et al.*, "Electrochemical etching of Ti2AlC to Ti2CTx (MXene) in low-concentration  
1058 hydrochloric acid solution," *Journal of Materials Chemistry A*, vol. 5, no. 41, pp. 21663-21668,  
1059 2017.
- 1060 [68] S. Yang *et al.*, "Fluoride-free synthesis of two-dimensional titanium carbide (MXene) using a  
1061 binary aqueous system," *Angewandte Chemie*, vol. 130, no. 47, pp. 15717-15721, 2018.
- 1062 [69] J.-C. Lei, X. Zhang, and Z. Zhou, "Recent advances in MXene: Preparation, properties, and  
1063 applications," *Frontiers of Physics*, vol. 10, pp. 276-286, 2015.
- 1064 [70] X. Zhan, C. Si, J. Zhou, and Z. Sun, "MXene and MXene-based composites: synthesis, properties  
1065 and environment-related applications," *Nanoscale Horizons*, vol. 5, no. 2, pp. 235-258, 2020.
- 1066 [71] S. Jung, U. Zafar, L. S. K. Achary, and C. M. Koo, "Ligand chemistry for surface functionalization in  
1067 MXenes: A review," *EcoMat*, vol. 5, no. 10, p. e12395, 2023.



- 1068 [72] R. Ibragimova, P. Erhart, P. Rinke, and H.-P. Komsa, "Surface Functionalization of 2D MXenes:  
1069 Trends in Distribution, Composition, and Electronic Properties," *The Journal of Physical*  
1070 *Chemistry Letters*, vol. 12, no. 9, pp. 2377-2384, 2021/03/11 2021, doi:  
1071 10.1021/acs.jpcclett.0c03710.
- 1072 [73] H. Lin, Y. Chen, and J. Shi, "Insights into 2D MXenes for versatile biomedical applications: current  
1073 advances and challenges ahead," *Advanced Science*, vol. 5, no. 10, p. 1800518, 2018.
- 1074 [74] R. Li, L. Zhang, L. Shi, and P. Wang, "MXene Ti3C2: An Effective 2D Light-to-Heat Conversion  
1075 Material," *ACS Nano*, vol. 11, no. 4, pp. 3752-3759, 2017/04/25 2017, doi:  
1076 10.1021/acsnano.6b08415.
- 1077 [75] W. Gao *et al.*, "3D CNT/MXene microspheres for combined photothermal/photodynamic/chemo  
1078 for cancer treatment," *Frontiers in Bioengineering and Biotechnology*, vol. 10, 2022.
- 1079 [76] J. Chen *et al.*, "Advances in nanomaterials for photodynamic therapy applications: Status and  
1080 challenges," *Biomaterials*, vol. 237, p. 119827, 2020.
- 1081 [77] G. Liu *et al.*, "Surface modified Ti3C2 MXene nanosheets for tumor targeting  
1082 photothermal/photodynamic/chemo synergistic therapy," *ACS applied materials & interfaces*,  
1083 vol. 9, no. 46, pp. 40077-40086, 2017.
- 1084 [78] X. Yu, X. Cai, H. Cui, S.-W. Lee, X.-F. Yu, and B. Liu, "Fluorine-free preparation of titanium carbide  
1085 MXene quantum dots with high near-infrared photothermal performances for cancer therapy,"  
1086 *Nanoscale*, 10.1039/C7NR05997C vol. 9, no. 45, pp. 17859-17864, 2017, doi:  
1087 10.1039/C7NR05997C.
- 1088 [79] A. Szuplewska *et al.*, "2D Ti2C (MXene) as a novel highly efficient and selective agent for  
1089 photothermal therapy," *Materials Science and Engineering: C*, vol. 98, pp. 874-886, 2019.
- 1090 [80] Y. Liu *et al.*, "Two-dimensional MXene/cobalt nanowire heterojunction for controlled drug  
1091 delivery and chemo-photothermal therapy," *Materials Science and Engineering: C*, vol. 116, p.  
1092 111212, 2020/11/01/ 2020, doi: <https://doi.org/10.1016/j.msec.2020.111212>.
- 1093 [81] Y. Xu *et al.*, "2D-ultrathin MXene/DOXjade platform for iron chelation chemo-photothermal  
1094 therapy," *Bioactive Materials*, vol. 14, pp. 76-85, 2022.
- 1095 [82] E. A. Hussein *et al.*, "Plasmonic MXene-based nanocomposites exhibiting photothermal  
1096 therapeutic effects with lower acute toxicity than pure MXene," *International Journal of*  
1097 *Nanomedicine*, vol. 14, pp. 4529-4539, 2019/12/31 2019, doi: 10.2147/IJN.S202208.
- 1098 [83] Y. Li *et al.*, "Muscle-inspired MXene/PVA hydrogel with high toughness and photothermal  
1099 therapy for promoting bacteria-infected wound healing," *Biomaterials Science*,  
1100 10.1039/D1BM01604K vol. 10, no. 4, pp. 1068-1082, 2022, doi: 10.1039/D1BM01604K.
- 1101 [84] F. Li *et al.*, "A bifunctional MXene-modified scaffold for photothermal therapy and maxillofacial  
1102 tissue regeneration," *Regenerative Biomaterials*, vol. 8, no. 6, p. rbab057, 2021, doi:  
1103 10.1093/rb/rbab057.
- 1104 [85] L. Yang *et al.*, "Low-Temperature Photothermal Therapy Based on Borneol-Containing Polymer-  
1105 Modified MXene Nanosheets," *ACS Applied Materials & Interfaces*, vol. 14, no. 40, pp. 45178-  
1106 45188, 2022/10/12 2022, doi: 10.1021/acsnano.2c12839.
- 1107 [86] Y. Ding *et al.*, "Mxene composite fibers with advanced thermal management for inhibiting tumor  
1108 recurrence and accelerating wound healing," *Chemical Engineering Journal*, vol. 459, p. 141529,  
1109 2023.
- 1110 [87] A. Arabi Shamsabadi, M. Sharifian Gh, B. Anasori, and M. Soroush, "Antimicrobial mode-of-  
1111 action of colloidal Ti3C2Tx MXene nanosheets," *ACS sustainable chemistry & engineering*, vol. 6,  
1112 no. 12, pp. 16586-16596, 2018.
- 1113 [88] X. Zhu *et al.*, "A near-infrared light-mediated antimicrobial based on Ag/Ti3C2Tx for effective  
1114 synergetic antibacterial applications," *Nanoscale*, vol. 12, no. 37, pp. 19129-19141, 2020.



- 1115 [89] P. Zhang, X.-J. Yang, P. Li, Y. Zhao, and Q. J. Niu, "Fabrication of novel MXene (Ti<sub>3</sub>C  
1116 2)/polyacrylamide nanocomposite hydrogels with enhanced mechanical and drug release  
1117 properties," *Soft Matter*, vol. 16, no. 1, pp. 162-169, 2020.
- 1118 [90] X. Yang, C. Zhang, D. Deng, Y. Gu, H. Wang, and Q. Zhong, "Multiple stimuli-responsive MXene-  
1119 based hydrogel as intelligent drug delivery carriers for deep chronic wound healing," *Small*, vol.  
1120 18, no. 5, p. 2104368, 2022.
- 1121 [91] R. Maleki and A. Alamdari, "Tuning the surface chemistry of 2D MXenes for optimizing the  
1122 micellization of bio-targeted carriers," *Physica E: Low-dimensional Systems and Nanostructures*,  
1123 vol. 144, p. 115461, 2022/10/01/ 2022, doi: <https://doi.org/10.1016/j.physe.2022.115461>.
- 1124 [92] H. Lin, X. Wang, L. Yu, Y. Chen, and J. Shi, "Two-dimensional ultrathin MXene ceramic  
1125 nanosheets for photothermal conversion," *Nano letters*, vol. 17, no. 1, pp. 384-391, 2017.
- 1126 [93] H. Wen, P. Liu, Z. Jiang, H. Peng, and H. Liu, "Redox-responsive MXene-SS-PEG nanomaterials for  
1127 delivery of doxorubicin," *Inorganic Chemistry Communications*, vol. 147, p. 110227, 2023/01/01/  
1128 2023, doi: <https://doi.org/10.1016/j.inoche.2022.110227>.
- 1129 [94] Z. Wu, J. Shi, P. Song, J. Li, and S. Cao, "Chitosan/hyaluronic acid based hollow microcapsules  
1130 equipped with MXene/gold nanorods for synergistically enhanced near infrared responsive drug  
1131 delivery," *International Journal of Biological Macromolecules*, vol. 183, pp. 870-879,  
1132 2021/07/31/ 2021, doi: <https://doi.org/10.1016/j.ijbiomac.2021.04.164>.
- 1133 [95] Y. Dong, S. Li, X. Li, and X. Wang, "Smart MXene/agarose hydrogel with photothermal property  
1134 for controlled drug release," *International Journal of Biological Macromolecules*, vol. 190, pp.  
1135 693-699, 2021/11/01/ 2021, doi: <https://doi.org/10.1016/j.ijbiomac.2021.09.037>.
- 1136 [96] B. Zhu, J. Shi, C. Liu, J. Li, and S. Cao, "In-situ self-assembly of sandwich-like Ti<sub>3</sub>C<sub>2</sub> MXene/gold  
1137 nanorods nanosheets for synergistically enhanced near-infrared responsive drug delivery,"  
1138 *Ceramics International*, vol. 47, no. 17, pp. 24252-24261, 2021/09/01/ 2021, doi:  
1139 <https://doi.org/10.1016/j.ceramint.2021.05.136>.
- 1140 [97] A. Liu *et al.*, "Engineering of surface modified Ti<sub>3</sub>C<sub>2</sub>Tx MXene based dually controlled drug  
1141 release system for synergistic multitherapies of cancer," *Chemical Engineering Journal*, vol. 448,  
1142 p. 137691, 2022/11/15/ 2022, doi: <https://doi.org/10.1016/j.cej.2022.137691>.
- 1143 [98] L. Jin *et al.*, "NIR-responsive MXene nanobelts for wound healing," *NPG Asia Materials*, vol. 13,  
1144 no. 1, p. 24, 2021/03/08 2021, doi: 10.1038/s41427-021-00289-w.
- 1145 [99] L. Jin *et al.*, "Nanofibers and hydrogel hybrid system with synergistic effect of anti-inflammatory  
1146 and vascularization for wound healing," *Materials Today Advances*, vol. 14, p. 100224, 2022.
- 1147 [100] K. Salimiyan rizi, "MXene nanosheets as a novel nanomaterial with antimicrobial applications: A  
1148 literature review," *Journal of Molecular Structure*, vol. 1262, p. 132958, 2022/08/15/ 2022, doi:  
1149 <https://doi.org/10.1016/j.molstruc.2022.132958>.
- 1150 [101] K. Rasool, M. Helal, A. Ali, C. E. Ren, Y. Gogotsi, and K. A. Mahmoud, "Antibacterial Activity of  
1151 Ti<sub>3</sub>C<sub>2</sub>Tx MXene," *ACS Nano*, vol. 10, no. 3, pp. 3674-3684, 2016/03/22 2016, doi:  
1152 10.1021/acsnano.6b00181.
- 1153 [102] A. Arabi Shamsabadi, M. Sharifian Gh, B. Anasori, and M. Soroush, "Antimicrobial Mode-of-  
1154 Action of Colloidal Ti<sub>3</sub>C<sub>2</sub>Tx MXene Nanosheets," *ACS Sustainable Chemistry & Engineering*, vol.  
1155 6, no. 12, pp. 16586-16596, 2018/12/03 2018, doi: 10.1021/acssuschemeng.8b03823.
- 1156 [103] X. Zhu *et al.*, "A near-infrared light-mediated antimicrobial based on Ag/Ti<sub>3</sub>C<sub>2</sub>Tx for effective  
1157 synergetic antibacterial applications," *Nanoscale*, 10.1039/D0NR04925E vol. 12, no. 37, pp.  
1158 19129-19141, 2020, doi: 10.1039/D0NR04925E.
- 1159 [104] S. Xu *et al.*, "Electroactive and antibacterial wound dressings based on Ti<sub>3</sub>C<sub>2</sub>Tx MXene/poly( $\epsilon$ -  
1160 caprolactone)/gelatin coaxial electrospun nanofibrous membranes," *Nano Research*, vol. 16, no.  
1161 7, pp. 9672-9687, 2023/07/01 2023, doi: 10.1007/s12274-023-5527-z.



- 1162 [105] S. Khademolqorani *et al.*, "Application Scopes of Miniaturized MXene-Functionalized  
1163 Electrospun Nanofibers-Based Electrochemical Energy Devices," *Small*, p. 2309572, 2023.
- 1164 [106] Q. Song *et al.*, "Graphene and MXene nanomaterials: toward high-performance electromagnetic  
1165 wave absorption in gigahertz band range," *Advanced Functional Materials*, vol. 30, no. 31, p.  
1166 2000475, 2020.
- 1167 [107] Y. Zhang, W. Xia, Y. Wu, and P. Zhang, "Prediction of MXene based 2D tunable band gap  
1168 semiconductors: GW quasiparticle calculations," *Nanoscale*, vol. 11, no. 9, pp. 3993-4000, 2019.
- 1169 [108] Z. Ling *et al.*, "Flexible and conductive MXene films and nanocomposites with high capacitance,"  
1170 *Proceedings of the National Academy of Sciences*, vol. 111, no. 47, pp. 16676-16681, 2014.
- 1171 [109] Y. Li *et al.*, "Toward Smart Sensing by MXene," *Small*, p. 2206126, 2022.
- 1172 [110] C. Jin and Z. Bai, "MXene-based textile sensors for wearable applications," *ACS sensors*, vol. 7,  
1173 no. 4, pp. 929-950, 2022.
- 1174 [111] D. Lei *et al.*, "Roles of MXene in pressure sensing: Preparation, composite structure design, and  
1175 mechanism," *Advanced Materials*, vol. 34, no. 52, p. 2110608, 2022.
- 1176 [112] R. B. Rakhi, P. Nayak, C. Xia, and H. N. Alshareef, "Novel amperometric glucose biosensor based  
1177 on MXene nanocomposite," *Scientific Reports*, vol. 6, no. 1, p. 36422, 2016/11/10 2016, doi:  
1178 10.1038/srep36422.
- 1179 [113] Y. Gao *et al.*, "Microchannel-confined MXene based flexible piezoresistive multifunctional micro-  
1180 force sensor," *Advanced Functional Materials*, vol. 30, no. 11, p. 1909603, 2020.
- 1181 [114] S. M. S. Rana, M. T. Rahman, M. Salauddin, H. Cho, and J. Y. Park, "An Electrospun PVDF-  
1182 TRFE/Mxene Nanofibrous Mat-Based Self-Powered Motion Sensor," in *2021 IEEE 34th*  
1183 *International Conference on Micro Electro Mechanical Systems (MEMS)*, 25-29 Jan. 2021 2021,  
1184 pp. 30-33, doi: 10.1109/MEMS51782.2021.9375277.
- 1185 [115] H. Kang *et al.*, "Research Progress on Two-Dimensional Layered MXene/Elastomer  
1186 Nanocomposites," (in eng), *Polymers (Basel)*, vol. 14, no. 19, Sep 29 2022, doi:  
1187 10.3390/polym14194094.
- 1188 [116] G. Basara *et al.*, "Electrically conductive 3D printed Ti(3)C(2)T(x) MXene-PEG composite  
1189 constructs for cardiac tissue engineering," (in eng), *Acta Biomater*, vol. 139, pp. 179-189, Feb  
1190 2022, doi: 10.1016/j.actbio.2020.12.033.
- 1191 [117] G. Ye *et al.*, "Mussel-inspired conductive Ti(2)C-cryogel promotes functional maturation of  
1192 cardiomyocytes and enhances repair of myocardial infarction," (in eng), *Theranostics*, vol. 10,  
1193 no. 5, pp. 2047-2066, 2020, doi: 10.7150/thno.38876.
- 1194 [118] G. P. Awasthi *et al.*, "Synthesis, characterizations, and biocompatibility evaluation of  
1195 polycaprolactone-MXene electrospun fibers," *Colloids and Surfaces A: Physicochemical and*  
1196 *Engineering Aspects*, vol. 586, p. 124282, 2020.
- 1197 [119] S. H. Lee *et al.*, "Ternary MXene-loaded PLCL/collagen nanofibrous scaffolds that promote  
1198 spontaneous osteogenic differentiation," *Nano Convergence*, vol. 9, no. 1, pp. 1-15, 2022.
- 1199 [120] J. Yan *et al.*, "Bionic MXene based hybrid film design for an ultrasensitive piezoresistive pressure  
1200 sensor," *Chemical Engineering Journal*, vol. 431, p. 133458, 2022/03/01/ 2022, doi:  
1201 <https://doi.org/10.1016/j.cej.2021.133458>.
- 1202 [121] J. Fan, M. Yuan, L. Wang, Q. Xia, H. Zheng, and A. Zhou, "MXene supported by cotton fabric as  
1203 electrode layer of triboelectric nanogenerators for flexible sensors," *Nano Energy*, vol. 105, p.  
1204 107973, 2023/01/01/ 2023, doi: <https://doi.org/10.1016/j.nanoen.2022.107973>.
- 1205 [122] X. Xu, S. Wang, H. Wu, Y. Liu, F. Xu, and J. Zhao, "A multimodal antimicrobial platform based on  
1206 MXene for treatment of wound infection," *Colloids and Surfaces B: Biointerfaces*, vol. 207, p.  
1207 111979, 2021.



- 1208 [123] S. Zhang *et al.*, "Titanium carbide/zeolite imidazole framework-8/polylactic acid electrospun  
1209 membrane for near-infrared regulated photothermal/photodynamic therapy of drug-resistant  
1210 bacterial infections," *Journal of Colloid and Interface Science*, vol. 599, pp. 390-403, 2021.
- 1211 [124] E. A. Mayerberger, R. M. Street, R. M. McDaniel, M. W. Barsoum, and C. L. Schauer,  
1212 "Antibacterial properties of electrospun Ti<sub>3</sub>C<sub>2</sub>T<sub>z</sub> (MXene)/chitosan nanofibers," *RSC Advances*,  
1213 10.1039/C8RA06274A vol. 8, no. 62, pp. 35386-35394, 2018, doi: 10.1039/C8RA06274A.
- 1214 [125] T. Krasian *et al.*, "Low cytotoxicity, antibacterial property, and curcumin delivery performance of  
1215 toughness-enhanced electrospun composite membranes based on poly(lactic acid) and MAX  
1216 phase (Ti<sub>3</sub>AlC<sub>2</sub>)," *International Journal of Biological Macromolecules*, vol. 262, p. 129967,  
1217 2024/03/01/ 2024, doi: <https://doi.org/10.1016/j.ijbiomac.2024.129967>.
- 1218 [126] D. Wang, D. Zhang, P. Li, Z. Yang, Q. Mi, and L. Yu, "Electrospinning of Flexible Poly(vinyl  
1219 alcohol)/MXene Nanofiber-Based Humidity Sensor Self-Powered by Monolayer Molybdenum  
1220 Diselenide Piezoelectric Nanogenerator," *Nano-Micro Letters*, vol. 13, no. 1, p. 57, 2021/01/16  
1221 2021, doi: 10.1007/s40820-020-00580-5.
- 1222 [127] A. M. Al-Dhahebi, R. Jose, M. Mustapha, and M. S. M. Saheed, "Ultrasensitive aptasensor using  
1223 electrospun MXene/polyvinylidene fluoride nanofiber composite for Ochratoxin A detection,"  
1224 *Food Chemistry*, vol. 390, p. 133105, 2022.
- 1225 [128] C. Zhang *et al.*, "Stretchable, flexible, and breathable MXene/dopamine/thermoplastic  
1226 polyurethane nanofiber membrane with outstanding strain sensing and electromagnetic  
1227 interference shielding performances," *Materials Today Communications*, vol. 38, p. 107968,  
1228 2024.
- 1229 [129] L.-P. Nan *et al.*, "Ti<sub>3</sub>C<sub>2</sub>T<sub>x</sub> MXene-Coated Electrospun PCL Conduits for Enhancing Neurite  
1230 Regeneration and Angiogenesis," *Frontiers in Bioengineering and Biotechnology*, vol. 10, 2022.
- 1231 [130] S. Kyrlyenko *et al.*, "Bio-functionalization of electrospun polymeric nanofibers by Ti<sub>3</sub>C<sub>2</sub>T<sub>x</sub>  
1232 MXene," in *2020 IEEE 10th international conference nanomaterials: applications & properties*  
1233 *(NAP)*, 2020: IEEE, pp. 02BA10-1-02BA10-5.
- 1234 [131] K. Diedkova *et al.*, "Polycaprolactone–MXene Nanofibrous Scaffolds for Tissue Engineering," *ACS*  
1235 *Applied Materials & Interfaces*, vol. 15, no. 11, pp. 14033-14047, 2023.
- 1236 [132] H. q. Zhang, D. w. Lan, X. Li, Z. Li, and F. Y. Dai, "Conductive and antibacterial scaffold with rapid  
1237 crimping property for application prospect in repair of peripheral nerve injury," *Journal of*  
1238 *Applied Polymer Science*, vol. 140, no. 5, p. e53426, 2023.
- 1239 [133] S. Khademolqorani, H. Tavanai, and F. Ajalloueiian, "Mechanical properties of silk plain-weft  
1240 knitted scaffolds for bladder tissue engineering applications," *Polymers for Advanced*  
1241 *Technologies*, vol. 32, no. 6, pp. 2367-2377, 2021.
- 1242 [134] J. Wu, Y. Yu, and G. Su, "Safety assessment of 2D MXenes: in vitro and in vivo," *Nanomaterials*,  
1243 vol. 12, no. 5, p. 828, 2022.

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