During the global outbreak of COVID-19 pandemic, “cytokine storm” conditions are regarded as the fatal step resulting in most mortality. Hemoperfusion is widely used to remove cytokines from the blood of severely ill patients to prevent uncontrolled inflammation induced by a cytokine storm. This article discovers, for the first time, that 2D Ti\textsubscript{3}C\textsubscript{2}Tx MXene sheet demonstrates an ultrahigh removal capability for typical cytokine interleukin-6. In particular, MXene shows a 13.4 times higher removal efficiency over traditional activated carbon absorbents. Molecular-level investigations reveal that MXene exhibits a strong chemisorption mechanism for immobilizing cytokine interleukin-6 molecules, which is different from activated carbon absorbents. MXene sheet also demonstrates excellent blood compatibility without any deleterious side influence on the composition of human blood. This work can open a new avenue to use MXene sheets as an ultraefficient hemoperfusion absorbent to eliminate the cytokine storm syndrome in treatment of severe COVID-19 patients.

1. Introduction

The outbreak of coronavirus disease 2019 (COVID-19) has been evolved into a global health crisis.\textsuperscript{[1]} By the end of December 2020, more than 71.9 million cases have been confirmed and over 1 million of casualties have been reported all over the world.\textsuperscript{[2]} Although the majority of COVID-19 patients show mild respiratory symptoms or even no symptoms, there are still 15–20% patients deteriorating into pneumonia.\textsuperscript{[3]} Serological tests demonstrate that patients with severe pneumonia suffer from cytokine storm syndrome (CSS) caused by the excessive activation of the human immune system, which is one of the major causes for organ failure and death. Therefore, calming the cytokine storm is the key to cure the severely ill COVID-19 patients and reduce the mortality.\textsuperscript{[4]}

As a typical low molecular weight extracellular signal protein, cytokines are emitted by various immune cells, including macrophage, lymphocyte, mastocyte, and many other cells such as endothelial cells. In the human body, there are many kinds of cytokines such as interleukin (IL), interferons (IFN), lymphokine, chemokines, and tumor necrosis factors (TNF). Once the human cells are infected, cytokines can kill pathogens by stimulating the human immune system, clear the damaged cells, and repair the damaged tissues.\textsuperscript{[5]} In most circumstances, cytokines can defect the aggravations of pathogens and protect our health system.\textsuperscript{[6]}

However, when the balance is broken, the fatal cytokine storm will occur. CSS and cytokine release syndrome (CRS) are a kind of common, virus infection-induced systematic inflammation.\textsuperscript{[7]} This kind of uncontrolled inflammatory reaction normally results in septic shock, organ injury, finally leading to multiple organ dysfunction syndromes (MODS). According to the latest research on COVID-19, cytokine storm is the major factor causing mortality.\textsuperscript{[8]}

To date, a range of medicines have been reported for reducing or eliminating the cytokine storm and improving the overall clinical outcomes. However, the potential risks of using these drugs are still ambiguous. For example, tocilizumab, a humanized anti-interleukin-6-receptor that is effective for the treatment of COVID-19, may result in jaw osteonecrosis.\textsuperscript{[9]} Another treatment method using glucocorticoids is also controversial.\textsuperscript{[10]} The detrimental effects using glucocorticoids include prolonged viral presence in the short term and increased risk of osteonecrosis, avascular necrosis, and steroid-induced diabetes.\textsuperscript{[11,12]} On the other hand, hemoperfusion as a conventional continuous renal replacement therapy (CRRT) has been widely used to cure the cytokine storm. Hemoperfusion is normally used for blood purification in continuous renal replacement therapies, in which the toxins can be removed via an adsorption process of absorbents media.\textsuperscript{[13]} Owing to its advantages in terms of cost, feasibility, and reliability, this method is also
applied for decreasing the concentration of cytokines in severely ill patients, thereby alleviating the multiple organ dysfunction syndrome derived from a cytokine storm.[14] Particularly, eliminating interleukin-6 (IL-6) in the blood is critically important as it is recognized as one of the pivotal cytokines that correlate with disease severity.[15]

Currently, commercial absorbents for hemoperfusion are usually made of activated carbon (AC) or resins, which can provide high surface area for the physisorption of toxins. However, the low removal capacity of these conventional absorbents cannot meet the increasing demands for high efficiency, especially in recent months when public health systems have been under high pressure owing to the COVID-19 pandemic.[14]

Recently, MXenes, a new family of 2D materials including transition metal carbides, nitrides, and carbonitrides, have been extensively investigated for many functional applications,[15] owing to their intriguing physical and chemical properties.[16–18] In this work, we first explored Ti$_3$C$_2$T$_x$ MXene nanosheets as a potential hemoperfusion absorbent to remove a typical cytokine IL-6. We discovered that Ti$_3$C$_2$T$_x$ MXene sheets had demonstrated an ultrahigh efficiency to remove IL-6 cytokine, which is 13.4 times higher than that of traditional AC absorbent. More importantly, full blood tests have proven that MXene sheets have an excellent blood compatibility, which is evidence that the common components of blood are not interfered after being purified by the MXene nanosheet absorbent.

2. Results and Discussion

Ti$_3$C$_2$T$_x$ MXene nanosheets were prepared via a wet-etching route using hydrofluoric acid (HF) as an etching agent. The morphology of the as-prepared MXene nanosheets was observed by scanning electron microscopy (SEM) and transmission electron microscopy (TEM). As shown in Figure 1a, MXene nanosheets display an accordion-like layer structure after etching. These multilayer MXene nanosheets were further exfoliated via sonication and then centrifuged to obtain Ti$_3$C$_2$T$_x$ dispersion in deionized water (the insets in Figure 1b and Figure S1, Supporting Information). The TEM image shows that the exfoliated MXene nanosheets are ultrathin with a large lateral size, which endows large surface for adsorption (Figure S2, Supporting Information). The high-resolution TEM (HRTEM) image reveals the atomic structure of the as-synthesized MXene nanosheets, in which three layers of Ti atoms can be clearly identified with an interlayer thickness of 1.8 nm (Figure 1c). The (00l) peak in the X-ray diffraction (XRD) pattern of Ti$_3$C$_2$T$_x$ becomes broader and shifts to lower angle compared with MAX phase, which is consistent with the HRTEM analysis results (Figure S3, Supporting Information). The energy-dispersive X-ray spectroscopy (EDS) mapping shows that MXene nanosheets consist of C, Ti, O, and F elements (Figure S4, Supporting Information). The surface chemistries of Ti$_3$C$_2$T$_x$ MXene nanosheets were unrecognised by the X-ray photoelectron spectroscopy (XPS) analysis, demonstrating that the MXene nanosheets surfaces are mainly terminated with hydrophilic (−F, −O, and =O) functional groups (see details in Figures S5 and S6, Supporting Information). Figure 1d illustrates the designed hemoperfusion process using MXene nanosheet absorbent to remove cytokine IL-6.

To investigate the removal ability of MXene for IL-6 cytokine, we examined the adsorption of IL-6 in the stroke-physiological saline solution (SPSS). According to the previous data, when the cytokine storm breaks out, the concentration of IL-6 in patients’ blood could soar rapidly from 20 to 400–700 pg mL$^{-1}$.[16] Therefore, we used 619 pg mL$^{-1}$ as the experimental concentration of IL-6, and the measurement temperature was set at 37 °C to mimic the situation herein a cytokine storm usually occurs in a human body. As shown in Figure 2a, when the same amount (0.2 mg) of adsorbents were added into 619 pg mL$^{-1}$ IL-6 SPSS, the decrease of IL-6 concentration using the MXene nanosheet absorbent is much quicker than that of using the AC absorbent. In the period from 5 to 30 min, the concentration of IL-6 solution using MXene absorbent decreased rapidly from 619 to 677 pg mL$^{-1}$ and continued to reduce at a slowing rate in the following 90 min. In contrast, the concentration of IL-6 with AC absorbent only slightly decreased to 592 pg mL$^{-1}$ in the first 15 min and almost unchanged in the following time. To achieve a quantitative comparison between the removal abilities of two absorbents, adsorption capacity $q$ was quantified by the formula (1)

$$ q = \frac{(C_0 - C_t)V}{m_{ads}} \quad (1) $$

where $C_0$ and $C_t$ are the solute concentrations in the original solution and after a time $t$, respectively. $V$ is the volume of solution, and $m_{ads}$ stands for the weight of sorbent. As shown in Figure 2b, after 120 min, the adsorption capacity of MXene sheets for IL-6 has reached 8.35 ng mg$^{-1}$, while AC just absorbed 0.62 ng mg$^{-1}$ IL-6. This clearly demonstrates that MXene has achieved 13.4 times adsorption ability than that of AC absorbent under the same condition. The higher adsorption capacity means higher removal efficiency toward cytokine molecules, which can significantly alleviate the harm of cytokine storm. More importantly, the adsorption rate of MXene nanosheets is much faster than that of traditional AC. The improvement of adsorption rate can greatly accelerate the treatment of hemoperfusion. Figure 2c shows the equilibrium IL-6 adsorption isotherms of MXene nanosheets at 37 °C and curve fitting of the experimental data using Langmuir and Freundlich models. The Freundlich isotherm model ($R^2 = 0.94$) presents a better fit than that of Langmuir model ($R^2 = 0.89$). The Langmuir isotherm theory assumes monolayer coverage of adsorption over a homogeneous adsorbent surface. Once the adsorption sites are filled, no further sorption can take place at that site. The Freundlich isotherm theory is used to describe heterogeneous system and assume that as the absorbent concentration increases, its concentration on the adsorbent’s surface increases as well.[20] The fitting result of equilibrium concentration indicates that the adsorption of IL-6 on MXene nanosheets is a kind of multilayer adsorption process, which is quite different from the physical adsorption process of traditional AC. To explore the effect of different adsorbent dosages on IL-6, we tested the relationship between adsorbent mass and IL-6 clearance rate from 0.2 up to 2.4 mg. As shown in Figure 2d, at a mass loading of 2.4 mg, MXene nanosheets demonstrated a high removal efficiency as high as 99.8%. In contrast, AC just removed 22.6% of IL-6 from the SPSS solution. This unambiguously elucidates that MXene
A nanosheet absorbent has a much higher adsorption capacity toward IL-6 than AC absorbent in different dosages. Compared with graphene and carbon nanotubes (CNTs), MXene has a larger adsorption capacity than graphene \[^{[21]}\] and a quicker removal rate than CNTs.\[^{[22]}\]

According to previous reports, powder forms of absorbent materials usually are not directly used owing to the issues of clogging, aggregation blocking, and difficult recycling.\[^{[23]}\] Hence, multilayered MXene beads were prepared to address these issues (Figure S7a, Supporting Information). The SEM image (Figure S7b, Supporting Information) shows that a multilayered MXene bead was composed of many MXene layers, which displays the integrity of accordion-like morphology. This special morphology not only keeps the high surface area and abundant activated sites of MXene but also prevents them from exfoliating into the blood causing severe side effects. Figure S8 (Supporting Information) demonstrated that after adding 0.2 mg MXene beads into IL-6 SSPS solution, the concentration of IL-6 decreased quickly. After 2 h, the removal capacity of MXene beads has increased to 6.23 ng mg\(^{-1}\), which is regarded as a strong removal performance. Compared with exfoliated MXene nanosheets, the slightly decreased adsorption capacity of accordion-like MXene beads originates from the shielding of some active sites on the surface of MXene nanosheets. Furthermore, to obtain more information about the adsorption ability of MXene in the real complex environment of blood, we added 0.2 mg MXene absorbent to 3 mL serum containing 601.8 pg mL\(^{-1}\) IL-6 to monitor the removal efficiency

**Figure 1.** a) SEM image of Ti\(_3\)C\(_2\)T\(_x\) MXene nanosheets after etching by HF. b) TEM image of few-layer Ti\(_3\)C\(_2\)T\(_x\) MXene nanosheets after delamination. The inset is a digital photograph of an aqueous dispersion of few-layer Ti\(_3\)C\(_2\)T\(_x\), which shows the typical Tyndall effect. c) HRTEM image of Ti\(_3\)C\(_2\)T\(_x\) MXene nanosheet and the corresponding atomic model. d) Schematic illustration of the hemoperfusion therapy process and mechanism by using the 2D MXene nanosheet absorbent.
of MXene. As shown in Figure S9 (Supporting Information), compared with pure SPSS environment, the removal efficiency of IL-6 in blood was slightly interfered. However, after 1 h, the concentration of IL-6 still dropped to 232.5 pg mL$^{-1}$ which confirms that MXene has the strong ability to resist the nonspecific interaction with plasma proteins and can achieve a removal efficiency toward IL-6 in the real complex environment of blood.

To further understand the adsorption process of IL-6 on MXene nanosheets, SEM observations were performed to characterize the surface morphology of MXene after absorbing IL-6. As shown in Figure 3a,b, after immersed in 619 pg mL$^{-1}$ IL-6 SPSS solution for 2 h, the morphology of MXene surfaces changed dramatically. Specifically, the original MXene surface is smooth, while the IL-6 immobilized MXene nanosheet surface is quite rough. When magnifying the SEM image (see inset in Figure 3b), we observed massive “coral”-like patterns covering on the MXene surface. According to a previous report, these coral-like patterns are derived from the aggregation of proteins.[24] Figure 3c shows the TEM characterization of the MXene covered with absorbed IL-6, on which a layer of polymeric substance can be observed in marked contrast to pristine MXene (Figure 1b). Figure 3d shows a HRTEM image of MXene covered with IL-6, on which the polymeric IL-6 can be observed around the Ti$_3$C$_2$T$_x$ lattice structure. It should be noted that the crystal structure of MXene has been maintained after adsorption (as shown in the inset of Figure 3d), confirming their stability in the aqueous environment. HRTEM EDS mapping (Figure S10, Supporting Information) indicates that after the adsorption, the signals of N and Cl appear on the surface of MXene nanosheets. N is mainly derived from IL-6 and Cl originates from NaCl in SPSS. To further investigate the immobilization of IL-6 molecules on the MXene, we used a two-photon confocal laser scanning microscopy (TP-CLSM) to characterize the distribution of IL-6 on the MXene absorbent surface. Figure S11 (Supporting Information) shows that the bare MXene absorbents emit fluorescence with an emission wavelength of 405 nm under the ultraviolet (UV) light. To more clearly distinguish the signal of MXene and IL-6, we used 8-anilino-1-naphthalenesulfonic acid (1,8-ANS) as the fluorescent dye to mark the IL-6 as it can be loaded inside the hydrophobic groups of IL-6 (Figure 3e). Under the UV light, we can clearly observe the different fluorescence signals emitted by MXene nanosheet and dyed IL-6, because the fluorescence emission wavelengths from MXene and IL-6 are 405 nm (Figure 3f) and 488 nm (Figure 3g), respectively. The high overlap level of the two fluorescence signals means that IL-6 can be simultaneously immobilized on the MXene nanosheet absorbents, which is in good agreement with the SEM characterization results.

XPS analyses were performed to investigate the chemisorptive details and affinity between the MXene absorbent and IL-6 molecules. Figure 4a shows high-resolution XPS C1s spectrum of MXene nanosheets before and after adsorption of IL-6. After adsorbing IL-6, peaks corresponding to the C=Ti and C=O bonds shifted from 282.4 and 286.7 eV to 282.13
and 286.51 eV, respectively. The slight negative shifts of peaks (−0.27 and −0.19 eV) can be ascribed to the influence of electron donors from IL-6 on the C=Ti bond. Besides this effect, two new peaks were spotted at 287.67 and 287.67 eV, which can be attributed to (C=O)—OH and (C=O)—N from IL-6 peptide bonds. The slight peak shift can also be observed on the Ti 2p spectrum (Figure 4b), where the original peaks at 455.78 and 457.10 eV moved to lower binding energy by −0.36 and −0.48 eV, respectively. The peaks appearing at 458.87 and 464.5 eV can be assigned to TiO₂, which reflects the partial oxidation of MXene nanosheets in SPSS. Compared with Ti and C, which are mostly located inside MXene, the O1s and F1s spectra can clearly elucidate the adsorption mechanism during the immobilization of IL-6 because both of them are on the surface of MXene. As shown in Figure 4c, after absorbing IL-6, the peaks corresponding to Ti—O (530.28 eV), C=O (531.69 eV), and C—O (532.28 eV) slightly shift by −0.34, −0.18, and −0.60 eV, respectively. While the new peak at 533.83 eV originates from the O—C=O groups of IL-6. According to previous reports, this obvious shift toward lower binding energy is because of the formation of hydrogen bonds, which are formed between —O groups and peptides of IL-6 such as Ti—O···H—N—C or C—O···H—N—C. Figure 4d elucidates the shifts corresponding to C—F (−0.28 eV) and Ti—F (−0.93 eV) bonds after IL-6 adsorption, which also verifies the formation of hydrogen bonds between MXene nanosheets and IL-6. The hydrogen bonds usually endow stronger binding energy than that of other intermolecular forces such as van der Waals forces. Therefore, the formation of hydrogen bonds (Ti—X···H—N—C=O (X is —F, —O—, or OH—)) plays an important role in achieving ultrahigh efficiency for Ti₃C₂Tₓ MXene nanosheets toward the removal of IL-6 cytokines.

We used Fourier transform infrared spectrometry (FTIR) to identify more details of IL-6 adsorption mechanism for MXene
absorbents. FTIR spectroscopy is sensitive to protein structure changes as it recognizes up to nine characteristic bands, namely, amide A, B, I, II to VII. Among these bands, the amide I band (between 1700 and 1600 cm\(^{-1}\)) is mainly associated with C=O stretching vibration (70–85%), which is directly related to the backbone conformation. However, the amide II band indicates information about N-H bending vibration (40–60%) and the C-N stretching vibration (18–40%). As shown in Figure 4e, after being absorbed on MXene nanosheets, the peak of amide I at 1726 cm\(^{-1}\) downshifts to 1639 cm\(^{-1}\). This confirmed that the secondary structure of IL-6 has transformed from an \(\alpha\)-helix to a \(\beta\)-sheet dominated structure. Furthermore, the peak at 1583 cm\(^{-1}\) corresponding to the N-H moved downward to 1415 cm\(^{-1}\), which is much larger than the shifts that reported previously. The larger shift of N-H bond also indicates the formation of N-H-X-Ti hydrogen bonds will influence the H donor groups peak (such as N-H) to further transfer to a lower wavenumber. Besides this effect, the sharp peak at 3445 cm\(^{-1}\) is because of the existence of hydroxyl groups on MXene absorbent and the absorbed external H\(_2\)O. Except FTIR, the secondary structure transformation of IL-6 has also been verified by circular dichroism (CD) spectrum. As shown in Figure 4f, the CD spectrum of the pristine IL-6 has two negative peaks at 222 and 209 nm and a positive peak at 193 nm, respectively, which correspond to a typical secondary structure of \(\alpha\)-helix (IL-6 is composed of four helices and a long loop). After immobilized by MXene absorbent, the CD spectrum of IL-6 changed to a negative peak at 225 nm and a...
positive peak at 196 nm, corresponding to the secondary structure of β-sheet.\textsuperscript{[35,36]} This secondary structure transformation is mainly because of the hydrogen bond formed between the hydrophilic groups (–F, –O, and –OH) on MXene nanosheet surface and the peptide bond in IL-6.

The secondary structure change of IL-6 before and after immobilization by MXene is schematically illustrated in Figure 5a. When α-helix IL-6 molecules contact the surface of a MXene nanosheet, the rich hydrophilic groups on the surface of MXene nanosheets can attract those hydrophilic groups to form hydrogen bonds, hence promoting the IL-6 molecules to “stretch” as β-sheet structure.\textsuperscript{[37,38]} More importantly, when the secondary structure of IL-6 is changed, the hydrophobic functional groups which are originally wrapped inside IL-6 molecules are exposed, which greatly reduces their dispersibility in aqueous solutions.\textsuperscript{[39,40]} On the contrary, the surfaces of most traditional commercial absorbents (ACs or resins, etc.) are hydrophobic, and therefore there is no chemical adsorption ability for absorbing IL-6 molecules.\textsuperscript{[41]} Moreover, the large volume of IL-6 molecules (5 × 5 × 12.2 nm) could block

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**Figure 5.** a) Schematic diagram demonstrates transformation of IL-6 secondary structure before and after immobilization by MXene nanosheets. b) Effects of MXene nanosheets immersed in the real blood environment. c) The comparison demonstrates average variation ratios of different typical components in human blood before and after adding MXene (red)/AC (blue) absorbents.
the internal nanochannel of traditional porous adsorbents, which significantly reduces their utilization efficiency. Such drawbacks can be avoided with 2D Ti$_3$C$_2$T$_x$ MXene absorbents. Apart from absorbing capacity, the blood compatibility of absorbents is also critically important for hemoperfusion. Unlike in traditional, a hemodialysis, hemoperfusion adsorbent is in direct contact with the patient’s blood during the treatment, hence requiring a higher standard of blood compatibility. Poor blood compatibility is usually regarded as the main cause of hemoperfusion complications, such as particulate micro emboli formation, internal hemolysis, and blood coagulation. Although previous studies have shown that MXene nanosheets have good biocompatibility, the research on blood compatibility is still obscure yet. In this research, we investigated the compatibility of Ti$_3$C$_2$T$_x$ MXene nanosheets in human blood (Figure 5b). Tables S1 and S2 (Supporting Information) show the details of different blood parameters before and after adding MXene/AC absorbents with the same mass loading in 12 blood samples (6 for MXene while 6 for AC). Average variations ratio of all parameters are listed and compared in Figure 5c. Compared with the AC absorbent, MXene nanosheets have much better blood compatibility as it reflects smaller variations of the key parameters. For platelets and red blood cell, not only the number and concentration of platelets does not decrease significantly but also red blood cell distribution width (RDW) and platelet distribution width (PDW) are also controlled in the normal range. The minor variations in RDW and PDW measurements confirm that the morphology and integrity of red blood cells and platelets can be kept rather than physically and mechanically damaged after contacting with MXene nanosheets. Regarding leukocytes (neutrophil, lymphocyte, monocytes, acidophilic granulocyte, and sbasophil), their concentrations and numbers after the adsorption still remained within their normal range. This also suggests that MXene absorbents have good blood compatibility, which fully meets the requirement of hemoperfusion treatments. To further determine the hemocompatibility of MXene absorbent, we investigated the hemolysis ratio, coagulation time, and platelet activation of Ti$_3$C$_2$T$_x$ MXene. As shown in Figure S12 (Supporting Information), compared with negative control (the plasma distributed in the phosphate-buffered saline (PBS) environment), no visible hemolysis phenomena were spotted for MXenes even at high dosages. When 2 mg mL$^{-1}$ of MXene was used, the hemolysis ratio was only 2.8%, which is far below the standard established by the American Society of Testing Materials (ASTM) (5%). The coagulation time tests include activated partial thromboplastin time (APTT), thrombin time (TT), and prothrombin time (PT), which can reveal the coagulant property of MXene absorbents (Figure S13, Supporting Information). The APTT and TT can assess the antithrombogenicity of the samples in vitro, and PT can indicate the exogenous coagulation performance. Compared with the control group (the control groups were the fresh culture medium without any samples), the values of APTT, TT, and PT for MXene in various dosages (0.1–2 mg mL$^{-1}$) show no significant decreases. The small differences confirm that MXene does not induce any obvious coagulation. In addition, the blood clotting times and platelet activation were further investigated. Compared with the control group, the whole blood clotting time for the sample containing high concentration MXene (2 mg mL$^{-1}$) did not decrease significantly (Figure S14, Supporting Information). This suggests that MXene has negligible blood coagulation effect. We used platelet factor 4 (PF4) concentration level to evaluate the platelet activation for MXene. The PF4 concentration shows almost no increase for MXene at the tested concentrations compared with the control group (Figure S15, Supporting Information). This test result clearly demonstrates that MXene does not induce platelet activation.

3. Conclusion

We have discovered that 2D Ti$_3$C$_2$T$_x$ MXene is an ultrahigh efficient hemoperfusion absorbent to eliminate cytokines. IL-6 has been used as the representative cytokine. Ti$_3$C$_2$T$_x$ MXene has demonstrated 13.4 times higher removal capacity toward IL-6 than that of traditional AC absorbent and much faster removal rate. XPS, FTIR, and CD spectroscopy analyses reveal that the formation of hydrogen bonding between MXene nanosheets and IL-6 is the main mechanism for achieving ultrahigh removal capacity. In addition, the secondary structure transformation of IL-6 from $\alpha$-helix to $\beta$-sheet can further promote the immobilization of IL-6 on the surface of MXene nanosheets. The blood compatibility test verifies that MXene nanosheets absorbent has an excellent compatibility with blood cells without any deleterious side influence on normal blood compositions. This work clearly elucidates that 2D MXene nanosheets can be applied as hemoperfusion absorbents to block cytokine storm for treatment of severe COVID-19 infection.

4. Experimental Section

Preparation of MXene Absorbent: Ti$_3$AlC$_2$ (Jilin 11 Technology Co., Ltd., China) with a particle size of $<$38 $\mu$m was synthesized. 3 g of as-prepared Ti$_3$AlC$_2$ powder was etched in a mixture of 30 mL 9 M HF (Fisher Scientific) at $\sim$35 °C for 24 h to extract the Al atoms and obtain multilayer Ti$_3$C$_2$T$_x$ suspension. The obtained suspension was repeatedly rinsed with distilled water and centrifuged (3500 rpm) until the pH of the supernatant was higher than 6. Then the sediment (etched Ti$_3$C$_2$T$_x$) was delaminated in deaerated water by ultrasonication to obtain few-layer MXene nanosheet colloidal solution.

Adsorption Kinetics Experiment: 3 mL 619 pg mL$^{-1}$ IL-6 (recombinant human interleukin-6 (>95%), Dalian Meilun Biotechnology Co.) SPSS was prepared and 0.2 mg MXene/AC (coconut shell activated carbon, Zhengzhou Furun Chemical Products Co., Ltd.) was added under the stirring. The adsorption process was kept in a water bath tank at 37 °C, and the adsorption time was controlled at 30 s, 60 s, 180 s, 10 min, 15 min, 30 min, 60 min, and 120 min. The change of concentration of IL-6 was conducted by an automatic biochemical immune analyzer (Cobas 8000, Roche Diagnostics GmbH, Germany) in Northern Jiangsu Hospital, Yangzhou, China.

SEM Characterization: After adsorption kinetics experiment (1 mg MXene was added into 619 pg mL$^{-1}$ IL-6 SPSS), the solution was dropped onto the platform of SEM and dried in vacuum chamber for 12 h before the SEM characterization (Zeiss Supra 55VP, Germany).

HRTEM Characterization: 1 mg MXene was added into 619 pg mL$^{-1}$ IL-6 SPSS, shaken for 2 min, and kept at 37 °C for 2 h. The solution was dropped on the copper mesh and dried in a vacuum chamber. HRTEM was performed at 300 kV electron microscope (Tecna G2 F30 S-TWIN, FEI).
Two-Photon Confocal Laser Scanning Microscopy: 1 mg MXene was added into 619 pg mL⁻¹ IL-6 ultrapure water, after shaken for 2 min and kept at 37 °C for 2 h, the sample was freeze-dried before characterization and encapsulated in 1 g of KBr (Nicolet 6700 Spectrometer).

X-Ray Photoelectron Spectroscopy: 1 mg MXene was added into 619 pg mL⁻¹ IL-6 SPSS, shaken for 2 min and kept at 37 °C for 2 h. The solution was dropped on the glass sample slice and covered by cover slice. Before the characterization, the sample was dyed by 1,8-ANS dye (Aladdin A106735, China), and the excessive solution was absorbed by the tissue (LSM 880NLO, Germany).

The solution was dropped on the glass sample slice and covered by 1,8-ANS dye (Aladdin A106735, China), and the excessive solution was absorbed by the tissue (LSM 880NLO, Germany).

CD Spectra: CD spectra of IL-6 were collected on a Jasco CD Spectra 5000 instrument.

Spectroscopy, and XPS measurements. Volunteers took part in these experiments following informed consent, under approval from the Ethics Committee of Clinical Medical School, Yangzhou University.

Supporting Information
Supporting Information is available from the Wiley Online Library or from the author.

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Conflict of Interest
The authors declare no conflict of interest.

Keywords
blood purification, COVID-19, cytokine storm, hemoperfusion, interleukin-6, MXene nanosheet

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