Synergistic Integration of MXene and Graphene Pioneering 2D Nanomaterials for Wearable Electronics and Cancer Therapy

Parthasarathy P

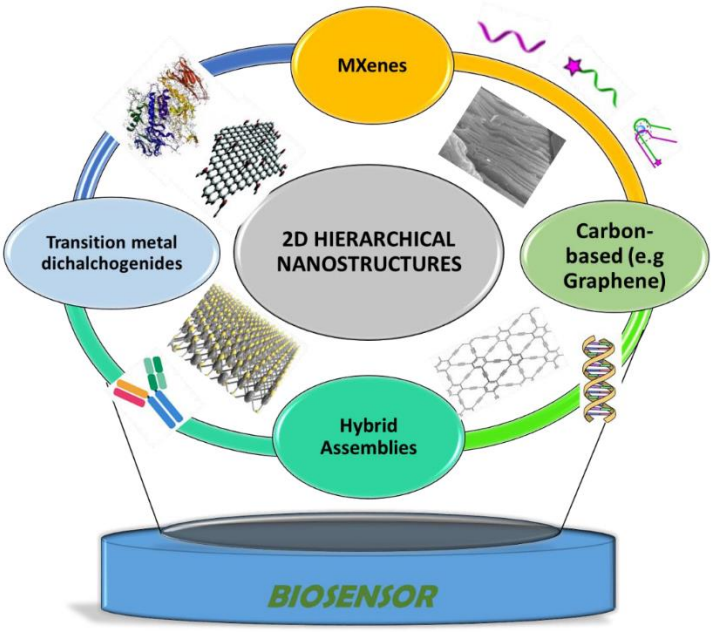
Assistant Professor, Department of ECE, CMR Institute of Technology, Bengaluru – 560037, Karnataka, India

Author Mail Id: arjunsarathii@gmail.com

Highlights

Explores the combined potential of MXene and Graphene, two advanced 2D nanomaterials. Highlights the complementary properties of MXene and Graphene in enhancing the performance of wearable electronics and cancer therapy applications. Discusses the application of MXene-based hydrogels in flexible and wearable electronic devices. Emphasizes MXene's superior electrical conductivity, large surface area, and biocompatibility. Reviews the manufacturing processes and design considerations for integrating MXene in wearable sensors. Highlights the multifunctional nature of Graphene in drug delivery, tumor imaging, and therapy. Focuses on the mechanisms by which Graphene-based materials can induce reactive oxygen species and enhance cancer treatment efficacy. Addresses the critical aspects of biocompatibility and the immune response for both MXene and Graphene in biomedical applications. Reviews the current understanding and challenges related to the safe use of these nanomaterials in clinical settings.

Graphical abstract



Abstract

Stretchability, self-adhesion, transparency, and biocompatibility make hydrogels popular. They excel in flexible electronics, human-machine interfaces, sensors, and actuators. MXene, a newly found two-dimensional nanomaterial with a negative charge, hydrophilicity, biocompatibility, wide surface area, changeable characteristics, and high electrical conductivity, could be a wearable sensor. MXene hydrogels are promising materials for wearable and flexible electronics due to their increased endurance. Despite substantial MXene-based composite research, MXene hydrogels in wearable electronics are currently being studied. This paper outlines MXene hydrogel applications, manufacturing procedures, and design considerations to promote sensor development. Additionally, graphene-based materials offer great potential in sensing, imaging, gene and drug delivery, tumor therapy, diagnostics, cell engineering, and regenerative medicine. Graphene oxides and nanostructures based on MXene induce reactive oxygen species and are drug-loadable, making them appealing cancer treatments. Graphene-based materials can be made by liquid-phase exfoliation, chemical vapor deposition, Hummer's process, and others. Biocompatibility, compatibility, and inflammatory reactions must be assessed for clinical and biomedical device use. These compounds' anticancer activity depends on concentration, detecting methods, cell types, and surface properties. This article discusses graphene and its oxides' cancer treatment advances, problems, and future prospects. This article examines the synergistic potential of MXene and graphene for wearable electronics and multifunctional cancer therapy by combining their unique properties.

Keywords: Hydrogel, MXene, Wearable Electronics, Cancer Therapy, Graphene, Biomedical Application

1. Introduction

Computer vision and intelligent sensing have become prominent disciplines due to the rapid progress in society and technology. Because of changes in people's lifestyles and the aging population, chronic diseases like obesity, diabetes, asthma, and coronary artery disease are becoming more common. This underscores the crucial requirement for wearable sensors capable of monitoring physiological data in real time and assisting in the timely identification of diseases. No matter what kind of input—biological, chemical, mechanical, electrical, optical, or thermal—a sensor can take it in from the outside world and turn it into a measurable signal. In addition to being extremely mechanically flexible, they need to be very sensitive, have a large detection range, and be able to sense consistently and responsively. Hydrogels have been extensively studied and are used in flexible electronic devices and automation for biomedical purposes. This is because they possess remarkable mechanical and electrical properties and are compatible with human tissues. Two-dimensional materials called MXenes were found for the first time in 2011. They are a subset of MAX phases ($M_{n+1}AX_n$). Here, M stands for a transition metal like Ti, Zr, etc., A denotes an elemental group from 13 to 16; and X can be carbon or nitrogen. Three possible values for n are displayed in Figure 1. The selective removal of the A layer from the MAX phase allows for the generation of MXenes, thanks to the stronger M-X bond compared to the M-A bond.

MXenes are a type of material with functional groups like F, Cl, or O on its surface. They have the molecular formula Mn+1XnTx [1-4]. As a result of its plentiful chemical composition, metallic conductivity, and flexibility to be handled in solution, MXene displays extensive applications in various fields, including biomedicine, flexible electronics, energy storage, and catalysis. Because of hydrogen bonding and van der Waals attraction, MXene tends to self-aggregate in water, severely limiting its usefulness. In comparison to other two-dimensional materials, such as black phosphorus (BP), MXenes are more hydrophilic, electrically conductive, and mechanically strong. Consequently, research into MXene-based flexible materials that may be tailored to different uses can be expanded by the incorporation of MXenes into hydrogel systems [5]. During the process of manufacturing hydrogels, MXene Nanosheets (NSs) tend to form clusters, which poses a challenge in achieving uniform MXene-based hydrogels. Although there are numerous evaluations available on MXene-based 3D composites, there is a notable lack of information regarding MXene hydrogels. There is currently a dearth of a thorough compendium of methods for preparing MXene hydrogels and their uses. Hence, we present a concise summary of the techniques employed in the past for producing composite hydrogels based on MXene, with a specific emphasis on their functional characteristics and potential uses [6].

Since its discovery half a century ago, the two-dimensional, hexagonally-bonded, sp2 hybridized carbon structure known as graphene (G) has attracted extensive interdisciplinary interest due to its exceptional properties. G's singular, multi-layered (fewer than ten), flattened honeycomb structure is what gives it its special properties, such as its infinite surface area, great hardness, resistance, thermal and electrical conductivity, and optical transparency [7]. Graphite (G) is the unoxidized form; the oxidized form, graphene oxide (GO), is formed by subjecting G to extreme oxidation conditions. GO is more hydrophilic than G because its carbon surface is functionalized with oxygen groups like hydroxyl, carboxyl, and epoxide. Nanocomposites can have their thermal conductivity, mechanical/electrical properties, and surface area enhanced by including G layers. G-based nanocomposites that offer intriguing options for the targeted distribution of chemotherapeutic drugs/genes and diagnostic substances due to their significant surface dimension, ease of functionalization, significant loading capacity, and reactive oxygen species, also known as ROS, induction potential [8]. Optical and electrical characteristics, as well as absorption in solution form, can be improved through the use of several derivatives of G and GO. These nano systems have gained a lot of attention because of their superior drug bio-distribution, fewer side special effects on strong cells, increased selectivity/sensitivity, and enhanced healing concentration. However, they have significant drawbacks, such as the requirement for extensive in vivo investigations/protein folding studies and the complexity of their synthesis techniques, which could cause inflammation, growth in annoyance, immunogenicity, cell disruption at higher concentrations, and so on. Nanocomposites containing G and GO have shown promise in a variety of fields, including biosensing and bio-imaging, Nano detection and labelling, gene and medication delivery, tissue engineering and regenerative medicine, and many more. A high capacity for drug loading and a high degree of selectivity G or GO nanocarriers have been used for the delivery of anti-cancer medicines.

Large surface areas, simplicity of functionalization/modification, and photothermic properties make advanced functional structures based on G appealing for cancer nano therapy [9]. Reduced-GO structures created from Euphorbia heterophylla have been demonstrated to possess good biocompatibility as well as been employed within cytotoxicity evaluations; nevertheless, more research is required to fully investigate their other biomedical potentials, such as their high cytotoxic effects in vitro towards A550 and HepG1 human cancerous cells. Using Bacillus Marisela as a stabilizing and reducing agent, we have developed further reduced-GO compounds with dose-dependent effects on cytotoxicity against MCF-7 cells. These 60 g ml-1 of GO resources, which have been decreased by bacteria, may increase ROS production and initiate lactate dehydrogenase release. Han et al. looked at how GO-cantered nanomaterials could be functionalized and optimized for drug and gene delivery. There has been a lot of research towards functionalizing G and GO, and many methods have been tried. Covalent techniques (including addition, water retention, and nucleophilic/electrophilic substitution) and non-covalent techniques are included. Some of the most notable advantages of these functionalized materials are higher electrical conductivity, better dispersibility, more functionality, and biocompatibility. However, some of these functionalization methods, like addition, may be hard to control, thus researchers should look into control label selection alternatives. Flexible, biocompatible, biodegradable, poisonous, surface-functionalized, and fluorescence-quenching potentials are just some of the concerns that must be taken into account while developing improved G-based nano systems for cancer diagnosis and treatment. Various polymeric materials can be used to modify and functionalize the surface of G-based materials. Surface functionalization with bioactive substances (such as L-ascorbic acid, cellulose, and gelatine) can increase the biocompatibility and targeting abilities of these G-based polymers. It has been observed that functional groups introduced to the surfaces of important substances including galactose, hyaluronic acid (HA), and folic acid improve the targeted and selectivity of chemotherapeutic delivery systems. Here, we address the key difficulties and future potential of G- and GO-based substances while discussing the current developments in the area of cancer therapy [10-12].

2. Synthesis and Fabrication Strategies

2.1 Synthesis Strategies

Since MXene has been successfully scaled up for numerous applications. Research into the MXene synthesis technology has picked up steam as a result of the material's successful scaling up for numerous uses. Etching can be classified into two major types: etching from MAX and non-etching means such as vapor deposition. The MAX phase is often etched using hydrogen fluoride, HCl-LiF, sodium hydroxide, and tetrabutylammonium hydroxide [13]. MXene can also be synthesized via other innovative non-etching methods, such as intercalation and hydrothermal processes. The performance of electronics based on MXene is greatly influenced by several factors such as temperature, etching time, and agitation during the synthesis of MXene. These factors have a considerable effect on the mechanical and chemical properties of the final product [14].

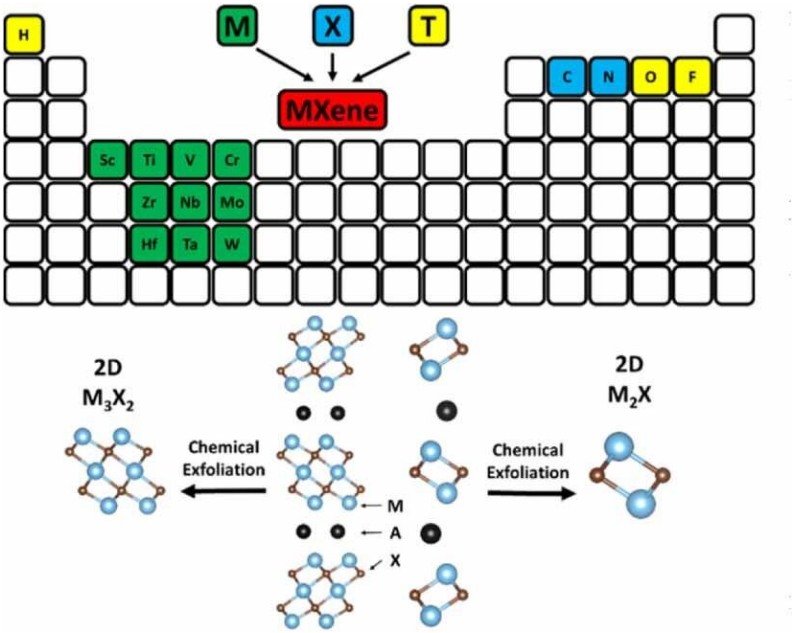


Fig.1. Periodic table with MAX phase (MXenes are surface functional groups) [10]

Future research on devices based on MXene will benefit from a solid understanding of the synthesis process. This paper provides a concise overview of the various methods for manufacturing MXene. Since the initial finding in 2011 that concentrated hydrofluoric acid (HF) could dissolve Al layers in MAX phase precursors (Ti3C2), selective etching has been extensively employed in MXene synthesis. It is common practice to selectively etch the a-element layer in the MAX precursor using HF for MXenes produced from synthetic carbides. The length of the synthesis process and the concentration of the HF solution are the primary factors that determine the size, shape, and surface properties of the MXene. Using a present concentration, the MAX phase precursor powder is mixed with an HF aqueous solution, as shown in Figure 2. To isolate the solids from the liquid, filtration is employed in the mixture [14-15].

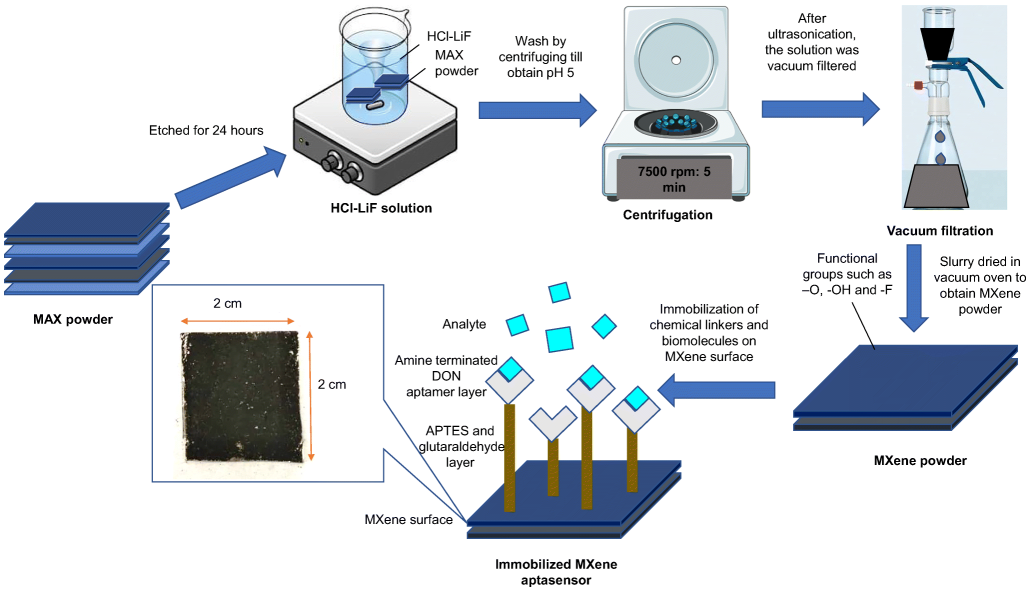


Fig.2. MAX phase precursor powder preparation method [12]

The gold standard for MXene synthesis involves etching with an HF solution. Nevertheless, the conventional synthesis method employs HF etchant, known for its high toxicity and corrosiveness, and requires lengthy etching periods. These factors greatly restrict the range of study possibilities for MXene. Scientists have been searching for secure substitutes to HF as a substance used for etching. Ghidiu et al. devised and described a safer etchant consisting of a mixture of the acid hydrochloric (HCl) and fluoride of lithium (LiF). By incorporating Li+ ions and its accompanying hydrated capsule into the multimodal interstitial area, the solvent not only improves safety but also guarantees the elimination of multiple layers. [15-16].

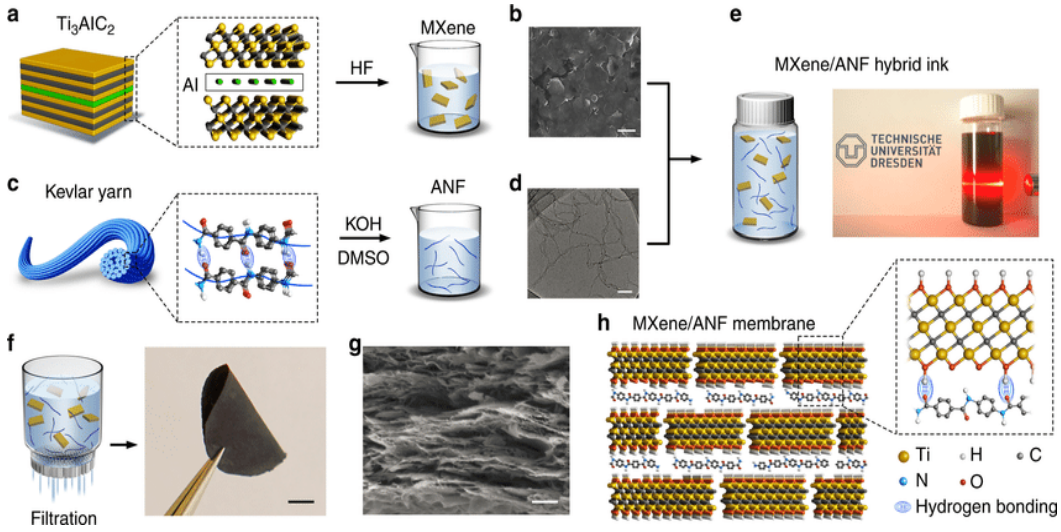


Fig.3. Fluoride-free approach for fabricating Mo2C MXenes [15]

The simultaneous etching and intercalation operations also allowed for the creation of a wide variety of MXenes with tailorable architectures and characteristics. The changes were made by adjusting the content and characteristics of the fluoride salt that was utilized for intercalation. Figure 3 (a-h) displays the outcomes of a method for creating Mo2C MXenes without the use of fluoride, as proven by Song's research team. The as-obtained MO2C material displayed a platelet-like structure, which was distinct from the platelet structures observed in HCl-etched MXenes such as Ti3C2Tx and V2CTx. The HCl etching procedure forms surface functional groups on as-produced MO2C electrodes, which contribute to their exceptional electrochemical capabilities in batteries and supercapacitors. In MXene synthesis, most MAX phases are ternary MAX phases, with A representing the ingredient Aluminum (Al) and making up around 20% of the total. It is crucial to find new ways to etch MAX phase family members onto MXene materials because so far only 20% of them have been recognized. Many more MXene compounds are now possible thanks to the Lewis acid melt salt synthetic synthesis process. Using a redox-controlled A-site, Huang et al. were the first to fabricate Ti3C2 by etching off MAX (Ti3SiC2) phases in CuCl2 Lewis acidic melts at 750°C. A wide variety of MAX precursors, including A-site elements like Ga, Zn, and Al, were readily available, which added credence to the method's practicability. Talapin et al. (2017) used a variety of molten inorganic salts to suggest a series of Zn-based MAX phases and Cl-terminated MXene. Two primary procedures make up the synthetic approach [17-19].

Initially, by employing substitution procedures, novel MAX phases were synthesized, including Ti3ZnC2, Ti2ZnC, Ti2ZnN, and V2ZnC. MXene materials, specifically Ti3C2Cl2 and Ti2CCl2, were effectively synthesized by exfoliating them in an excess molten ZnCl2 reaction environment. The cessation of the material with Cl- was facilitated by the strong Lewis acidic of molten ZnCl2. It is often important to include bulk-stacked nanostructures into a structure with two dimensions in order to take use of its numerous distinct properties. Wet etching MXenes results in multi-layered materials, however, monolayer and few-layered versions possess unique chemical and physical properties and offer more promise for many applications. Therefore, it is crucial to produce MXene with excellent quality and stability, whether in multilayer or monolayer form. To produce MXenes consisting of only a few or single layers, it is necessary to carry out intercalation and delamination either sequentially or simultaneously as part of the etching process. Currently, most intercalating agents are composed of molecular, anionic, and organic bases. Injecting certain compounds between each layer of MXene can disrupt or weaken the van der Waals bonds. Gotosi et al. initially reported that the c-lattice parameters were increased from 19.5 to 26.8 by intercalating multilayers of Ti3C2 with the compound hydra and co-intercalating with N, H-dimethylformamide (DMF) as the molecule-mediated intercalator. The creation of monolayers was achieved by a painstaking delamination procedure that involved the multilayer MXenes. Incorporating intercalating chemicals like urea and hydrazine hydrate (HM) in varying concentrations with dimethyl sulfoxide (DMSO) was the key to success [20].

Currently, cation-mediated intercalation is a commonly employed method for producing few-layer or monolayer MXene. This can be accomplished using a diverse range of cations, including NH4+, H+, Li+, Na+, K+, Ca2+, Mg2+, and Al3+. Using an electrochemical process, researchers employed a non-aqueous Na+ electrolyte to investigate the mechanism of reversible Na+ intercalation/DE intercalation into the interlayer region of MXene Ti3C2Tx [21]. At the beginning of iodization, there was a dissolution intercalation process where Na+ ions and solvent molecules were inserted between the layers of Ti3C2Tx. Because of this, the Ti3C2Tx interlayer distance increased from 0.97 to 1.2 nm. While not all MXenes are suitable for use as ionic chemical or molecular intercalants, organic macromolecules are one possibility. One study found that when exposed to DMSO, Ti3C2Tx experienced intercalation and delamination, but Ti3CNTx did not. One example of an organic chemical that can be utilized as an intercalant is urea, along with propylene carbonate (PC), isopropylamine (i-PrA), cetyltrimethylammonium bromide (CTAB), tetrabutylammonium hydroxide (TBAOH), and tetramethylammonium hydroxide (TMAOH). While i-PrA successfully inserted and separated layers of Ti3C2Tx, Nb2CTx, and Nb4C3Tx, TBAOH successfully inserted and separated layers of Ti2CTx, Ti3CNTx, V2CTx, Mo2CTx, Mo1.33CTx, TiVCTx, Ti3CNTx, and Ti4N3Tx. It is still challenging to achieve big-area, stable, thin-layer MXenes with outstanding performance, even though the liquid-phase intercalation technique has the ability to create MXenes with enormous lateral dimensions. Therefore, in order to progress MXene research, additional examination is necessary [22].

2.2 Fabrication Strategies

MXene has challenges in independently producing hydrogels due to the tendency of its nanosheets to undergo polymerization and re-stack as a result of the high interlayer attraction caused by van der Waals forces. MXene's numerous surface terminations, strong hydrophilicity, and significant flexibility allow it to easily combine with other compounds through hybridization [8]. To create MXene-based hydrogels, it is commonly required to introduce an additional element, known as a cross-linker, into the hydrogel structure. This is done to balance out the hydrophilic nature of MXenes and maintain the three-dimensional arrangement of two-dimensional nanosheets (2D NSs). Furthermore, MXenes are inherently prone to reacting with ambient oxygen, which ultimately restricts their potential applications. MXenes can potentially be protected from oxidation by employing physical and chemical surface engineering techniques. Organic ligands can deprotonate and bind to the surface of the creation of MXene hydrogels is facilitated by the atoms on the surface of MXene, which exhibit a low work function and strong electronegativity. This prevents oxidation of MXene. There are essentially three types of hydrogels based on MXene: There are various varieties of MXene nanocomposite hydrogels. One group includes inorganic materials, another group includes polymers, and a third group includes a combination of metal and MXene [23-25].

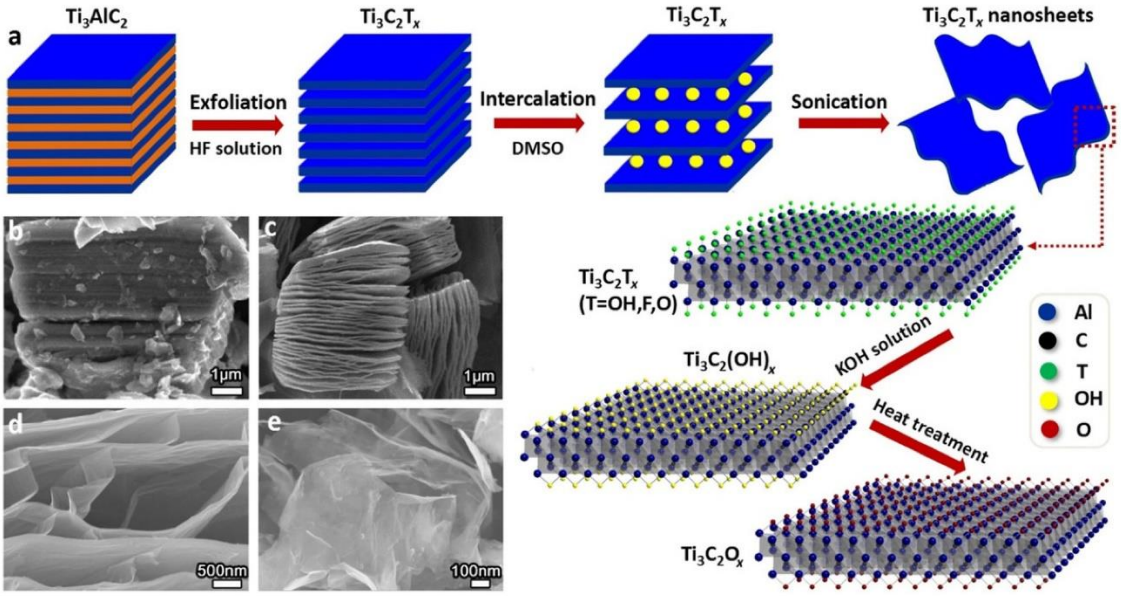


Fig.4. Schematic of MO2CT MXene synthesis and fabrication process [25]

As a gelling agent, graphene oxide (GO) interacts with the MXene NS surface thanks to its two-dimensional carbon structure, high specific surface area, and outstanding conductivity. This is because there are only a limited number of crosslinking sites on the surface of MXene. Because of this, MXene NSs are less likely to stack, which opens up more possibilities for using MXene in hydrogel materials [25]. A 3D macroscopic hydrogel composed of rGO/MXene was initially detailed by Xu et al. utilizing a self-convergence method that eliminates the requirement for organic components. By using Ti3C2Tx as a reducing agent in mild conditions, the oxygen-containing groups that make graphene oxide hydrophilic were removed, and the hydrophobic and conjugated structure of reduced graphene oxide (rGO) was enhanced.

Thanks to this procedure, the rGO/MXene 3D structure came into being. To create 3D hydrogels using MXene, GO, and ethylenediamine (EDA), Shang's group suggested using a self-assembly technique. During the reduction of GO caused by Ti3C2Tx, EDA hinders the epoxy rings on the GO flakes, which leads to the formation of oxygen suspension bonds. The formation of hydrogels occurred through the application of van der Waals forces between layers of heterogeneous nanosheets (NSs), resulting in the transformation of the MXene-rGO heterostructure [26-28].

The MXene family, consisting of Nb2CTx, Ti3C2Tx, and Mo2Ti2C2Tx, has been enhanced by Nicolosi et al.'s straightforward 4D printing technique. This method incorporates MXene, PEDOT: PSS, and additives such as DMSO, H2SO4, and sodium L-ascorbate. Figure 3e demonstrates that the composite inks were initially 3D-printed into different patterns. Then, a second printing step was performed, during which the inks self-assembled from MXene sols into MXene hydrogels. The 4D-MXene hydrogels exhibited remarkable particular capacitance and the capability to function at sub-zero temperatures (-20 ℃). Wang et al. created a triboelectric nanogenerator (TENG) that is both flexible and elastic. They achieved this by using nanosheets made of MXene (NSs) and PVA hydrogel shells as electrodes. This TENG is specifically intended for wearable sensors that operate themselves that monitor body movements [29]. While the MXene-based hydrogels were gelating, oxidation inevitably degraded a small portion of them. To successfully avoid the reaggregation of MXene nanosheets, enhance the mitigation of oxidation effects, and accelerate the separation of MXenes from water, it is required to speed the gelation process. Using a metal-assisted electro-gelation technique, Ye et al. suggested a way to directly produce porous, tunable MXene hydrogels. This adaptable technology offers a more in-depth and effective way to create patterns than 3D printing or laser patterning, which require specialist equipment or entail multiple processes. Electrolysis starts the electro-gelation process by interacting electrostatically with the MXene NSs, releasing metal cations. The identification of bivalent metal ions (Fe2+) as the primary factor responsible for the rapid gel formation of the MXene in dispersions made from water was initially reported by Yang et al. The crucial function was mostly carried out as a result of the robust interactions among metal ions and -OH groups that exist on the outermost portion of the MXene.

3. MXENE – For Wearable Electronics

Hydrogels, which are pliable and adaptable materials, are extensively used in the domain of wearable electronics because they may react to different chemical and physical triggers, resulting in noticeable alterations in their shape, light-related characteristics, and electrical attributes. However, the majority of conventional hydrogel sensors exhibit limited sensitivity to mechanical stimuli such as strain or pressure, and their viscoelastic properties frequently lead to signal hysteresis and fluctuations. MXene materials play a vital role in the fabrication of conductive hydrogels because they have great mechanical deformability, high electrical conductivity, and a wide range of surface functional groups. By interacting with the polymer network, MXene improves its mechanical and electrical properties, hence boosting the sensing capacities and biological compatibility of the polymer. Wearable electronics, including electronic skin, smart sensors, and individualized healthcare monitoring systems, are thus

anticipated to make use of hydrogels based on MXene. One of the biggest challenges in developing wearable human-computer interfaces and improving wound healing for aftercare is getting conductive hydrogel flexible sensors to detect electrophysiological signals with high sensitivity, even though these sensors are used extensively in e-skin and personalized medicine. Wan et al. developed a healable, degradable, antibacterial epidermal sensor to identify weak physiological signals and design effective wound infection treatments. Figure 5 shows the MXene-based hydrogel that was formed by integrating Ag NPs/MXene into the polymer network. The network is composed of guar gum (GG) and sodium alginate grafted with phenylboronic acid (Alg-PBA). This hydrogel, derived from MXene, possesses the potential to monitor a broad spectrum of energy activities as well as tiny electrophysiological signals. This feature makes it valuable for therapeutic applications in rehabilitative training and problems related to the cardiovascular system [28-29].

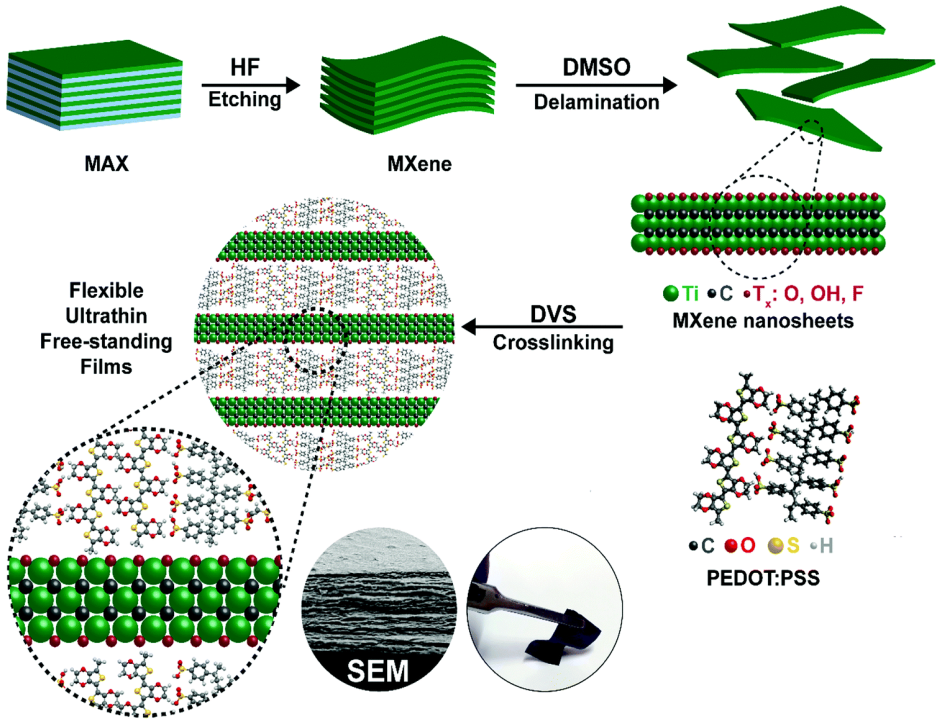


Fig.5. MXene interlayered cross-linked conducting polymer film [26]

The integration of MXene into hydrogel strain sensors is expected to yield significant advantages, since it combines the favorable electrical properties of MXene with the scalable mechanical flexibility of hydrogel. The hydrogel created by Alshareef et al., which is based on MXene, exhibits remarkable sensitivity to tensile strain, with a gauge factor (GF) of 25. This GF is 10 times greater than that of the original hydrogel. Furthermore, the hydrogel exhibits potential in touch sensing and bio-signal monitoring applications owing to its robust tensile properties, self-repairing capabilities, and excellent compatibility and adhesion to various surfaces. Yu's team developed a hydrogel called MNH by substituting water with ethylene glycol (EG) as the dispersion medium. The hydrogel is strain-sensitive and is based on MXene. The MNH exhibits enhanced freeze resistance (up to 40°C) and long-term stability in retaining fluids, surpassing that of conventional hydrogels. The MNH possesses a substantial measurement factor and an extensive strain range, reaching up to 400% strain.

Consequently, it has the potential to function as a flexible sensor for monitoring human biological motion in extremely cold temperatures. Many contemporary stretchable electronics that utilize MXenes as conductive Nano-fillers often employ MXenes for this purpose. However, Alshareef et al. took a different approach by using Ti3C2Tx MXene as a multifunctional cross-binding agent. This agent was able to activate hydrogels and facilitate rapid gelation from a diverse array of monomer or polymer precursors [29].

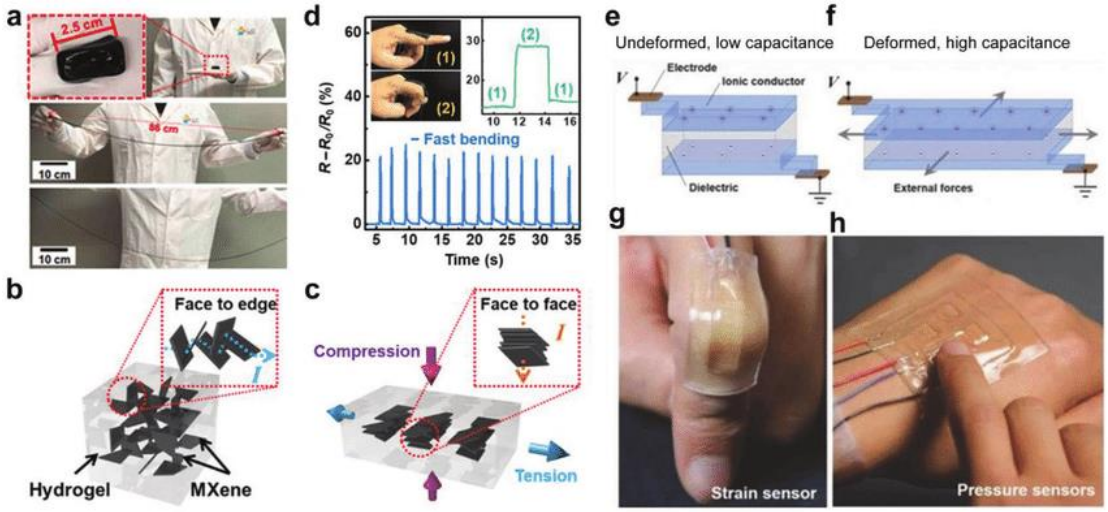


Fig.6. Schematic of the MXene hydrogel and its applications in the field of sensors [27]

The demand for new diagnostic methods in human health is always growing, and scientists are particularly interested in user-friendly biosensors. Utilizing personal diagnostic sensing devices to monitor both sick and healthy individuals have the potential to facilitate early detection and prevention of illnesses. Various hydrogel-based biosensors have been created to concurrently detect multiple biomarkers or physiological signals, such as glucose, triglycerides (TG), and heartbeat (pulse), by employing electrical and optical transducing methods. MXene materials are highly suitable for the advancement of novel electrochemical detection and biosensing devices due to their distinctive surface chemistry, exceptional electrical conductivity, and compatibility with living beings. This is an encouraging indication of the progress in developing future small and wearable instruments for monitoring and diagnosing health conditions. Crucial factors that impact human existence are temperature, humidity, and air pollution. Sulphur dioxide (SO2) is a prevalent form of gaseous pollution that poses a significant risk to both human well-being and the natural surroundings [28-30]. It has been associated with severe respiratory and cardiovascular issues in individuals. Furthermore, Wang's team provided a description of a sensor consisting of MXene/TiO2/SnSe, which is driven by triboelectric Nanogenerators (TENG). An ionic hydrogel electrode and an ECTFE film make up this sensor. With a detection sensitivity for SO2 gas that is fourteen times higher (U/Ua = 170% at 30 ppm), the newly developed sensor outperforms the resistive sensor. By combining Ti3C2 with sodium alginate (SA), Lin and co-workers were able to achieve high-performance biochemical detection at tissue interfaces [29]. With a limit of detection (LOD) of 12 nM, this detection technique showed sensitivity to hydrogen peroxide.

Problems with device fabrication, integration complexity, and cost prevent flexible sensing systems for hydrogels from being widely used in many settings. MXene-bonded hydrogel sensors with outstanding strain and temperature sensing capabilities might be made using a viable and inexpensive 3D-printed direct-ink-writing technology suggested by Huang's group. Figure 6 shows how MXene-based hydrogel is used in sensing applications [30].

4. Graphene: A Multifunctional Material for Cancer Therapy

Water purification, air filtration, antibacterial characteristics, cell examination, healthcare and biological applications, delivery of drugs, tissue engineering, energy studies, and many other fields are actively studying G and GO because of their remarkable inherent properties. G and GO have had their promising potential established, but they are also relatively complex and expensive to prepare, which may limit their use on big industrial scales [28]. While many researchers have established different ways for oxidizing the G to create GO, and modifications thereof have made them more efficient, cheaper, and ecologically friendly, the main obstacles still exist. Chemical exfoliation and chemical vapor deposition have also been developed for the synthesis of G and GO, although they are both time-consuming, labor-intensive, and costly. Another environmental concern is that these processes can produce harmful gases including nitrogen oxide (NO2), nitrogen dioxide (N2O4), chlorine monoxide (ClO2), and explosive gases like hydrogen peroxide (H2O). Because scaling up the fabrication of G-based structures takes costly resources and specialized tools, and can be ecologically unfriendly, there is an urgent need for easy and environmentally beneficial techniques for synthesizing these materials. One of them is the environmentally friendly production of these G-based products from agricultural wastes like walnut shells and husks. Future research is needed to address potential environmental issues caused by the product's high-temperature demand and the creation of some harmful syngas [29-31].

4.1 Photothermal Therapy

Cancer is a leading cause of death around the world, thus early diagnosis and efficient treatment are crucial for increasing the overall survival rate for cancer patients. The special physicochemical features of G-based materials make them useful for cancer diagnosis and therapy [32]. For instance, in vitro and in vivo studies using a combination of GO and polyethene glycol (PEG) have shown Photothermal treatment effects against malignancies and tumors. After near-infrared (NIR) light irradiation, the polarization status of macrophage cell lines was examined using flow cytometry and an mRNA expression investigation. GO-PEG demonstrated excellent Photothermal effect, enhanced biocompatibility, and great thermal stability. These Photothermal structures significantly reduced the M2 polarization of macrophages generated by interleukin-4 and modulated their anticancer activities. As a result, human osteosarcoma lost its ability to metastasize and invade, leading to the expected antitumor effects. In addition, folic acid was coupled to chitosan-functionalized GO Nano platforms for use in guiding Photothermal cancer therapy, with the end result being the full destruction of malignant cells under laser irradiation in vitro. In addition, investigations conducted in vivo demonstrated that 20 days after the setting up of these tailored nano systems during laser irradiation, the tumors remained fully suppressed with no recurrence [31-32].

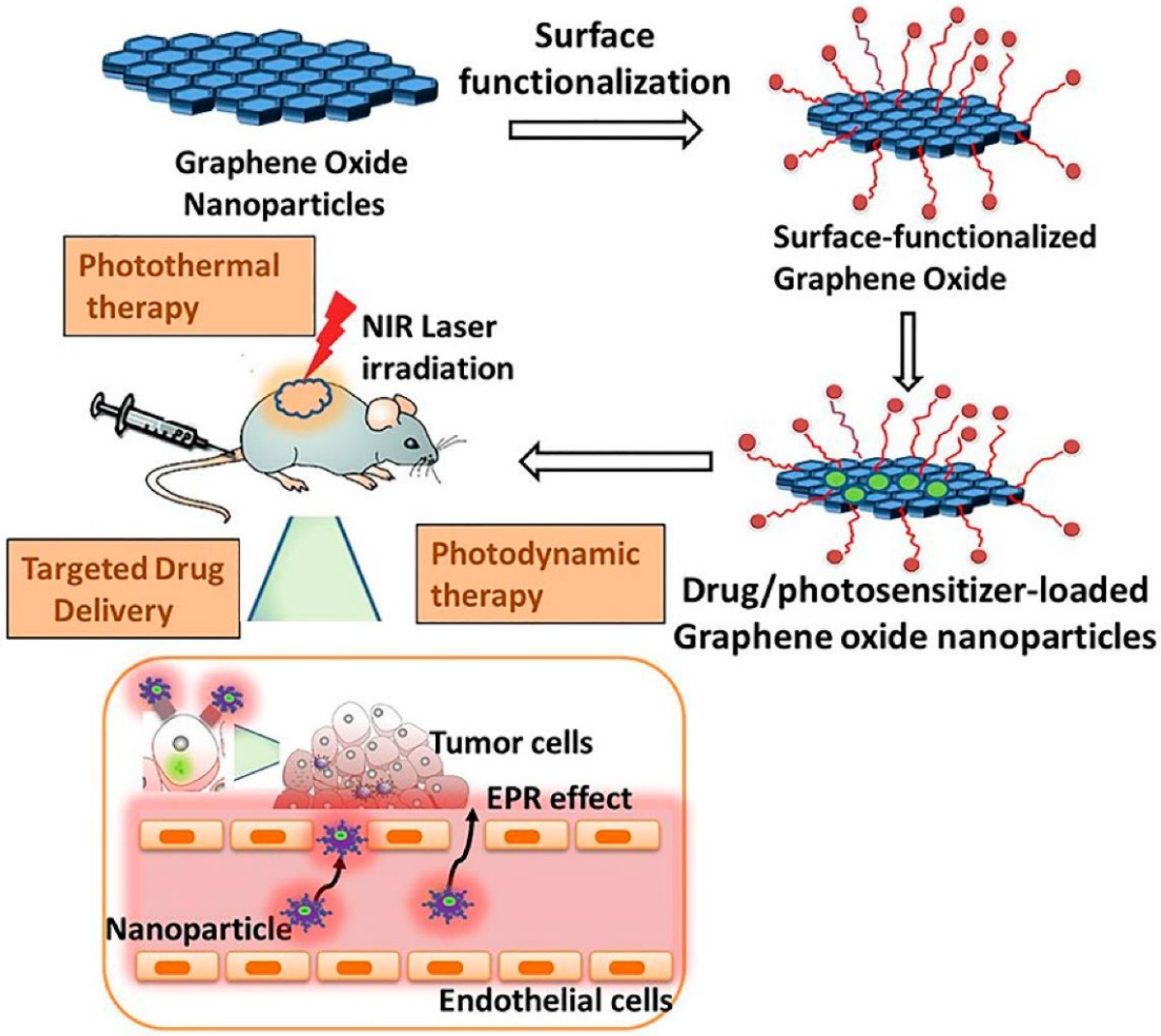


Fig.7. Nanosheets of graphene oxide (GO) functionalized with chitosan (CS) for cancer therapy [30]

Using GO, G quantum dots (GQDs), and curcumin, researchers were able to build G-based nanostructures that are very stable and efficiently transport curcumin inside malignant cells. The human breast carcinoma cell lines MDAMB-468 and MCF-7 were evaluated with varying amounts of GO-curcumin & GQDs-curcumin complexes. Cell viability was greater than 85% after 45 hours of culture with the respective cell lines, however, it was only 30% when curcumin alone (about 90 g/ml-1) was used. Following 48 hours of the therapy, 50, eighty, and 95% elimination of cells were seen at a dosage of 90 g ml-1. Furthermore, silver-GO nanocomposites (30-90 g/ml-1) have been studied for their potential to kill cancer cells; these nanocomposites demonstrated the expected cytotoxic effects, but their efficacy was inferior compared to that of free silver (Ag) nanoparticles because of the latter's smaller size and enhanced absorption. For effective and specific cancer nanotherapy, Cu2O nanoparticles (5 nm) were coated on GO.

These Cu2O-GO nanocomposites were tested in vitro under visible light irradiation for their anticancer effects on HK-2, 220 and A549 cells [31-32]. Additionally, both an acidic (pH = 5.0) and physiological (pH = 7.4) environment were used to test the manufactured GO-PEGylated folate nanocarrier. After 48 hours of treatment, the loaded anticancer medication camptothecin was able to be released at a rate of 21.5% under physiological settings and at a rate of 71.0% under acidic conditions.Confocal microscopy images taken from HeLa cells treated (for 8 hours) with the GO-PEGylated folate nanosystems showed that camptothecin was delivered specifically to the nucleus and cytoplasm of the cells. For the purpose of delivering cisplatin and photosensitizer (Ce6), Zhou et al. created smart multifunctional MnO2-doped GO nanosystems. This resulted in a decrease in glutathione levels in the tumors that were being targeted, a catalyzed breakdown of hydrogen peroxide into oxygen, and enhanced antitumor effects due to the progression of a Fenton-like reaction. Increased cellular toxicity and tumor growth inhibition were seen after hyaluronic acid was added to the surface of the produced nanosystems to boost its targeting characteristics [31-33].

The PEG-functionalized GO-based nanocomposite has been decorated with folic acid for paclitaxel delivery. These nanosystems were found to have minimal cytotoxicity and high biocompatibility, with cell viability being 60% after treatment with free paclitaxel medication and 30% following treatment with the developed nanosystems. Evaluations with fluorescence microscopy showed that the nanosystems successfully delivered paclitaxel to the tumor cells of interest. As the drug content was raised, a drop in blue luminescence confirmed the declining cell number and an effective entry of the drug a nanocarrier into the cells. Nanosystems for the targeted delivery of the chemotherapy drug were developed by taking advantage of the potent combination of alkaline functional categories of cancers and the hydroxyl group of G's by adding PEG to improve the physiological compatibility of hydrogenated G produced by the solid-state ball milling process. After 48 hours of exposure to the nanosystems (10 g ml-1), the viability for both tumor cells (OCM-1) & healthy cells (ARPE-19) was less than 10%. Confocal microscopy demonstrated that hydroxylated GO was present within the cells after 12 hours, outside the cells after 48 hours, and completely gone after 60 hours [18-20]. This study's findings showed that the nanocomposite showed low toxicity to normal cells while having effective anticancer effects against OCM-1 tumors. Poly lactic-co-glycolic acid was used to coat magnetic GO nanostructures so that 5-iodo-2-deoxyuridine may be delivered to patients with glioblastoma, thereby increasing their sensitivity to radiation [31]. Studies demonstrated that better blood-brain barrier penetration and magnetic targeting were possible. The usage of these nanocarriers was also found to have a synergistic impact, increasing the dosage augmentation factor and radio-sensitizing effects, prolonging the half-life in the bloodstream by more than 140 hours, and effectively suppressing and apoptosis the C6 glioma tumor [32]. In order to get the doxorubicin into the cancer cells, polydopamine was used to load gold nanorods onto the GO nanocomposites.

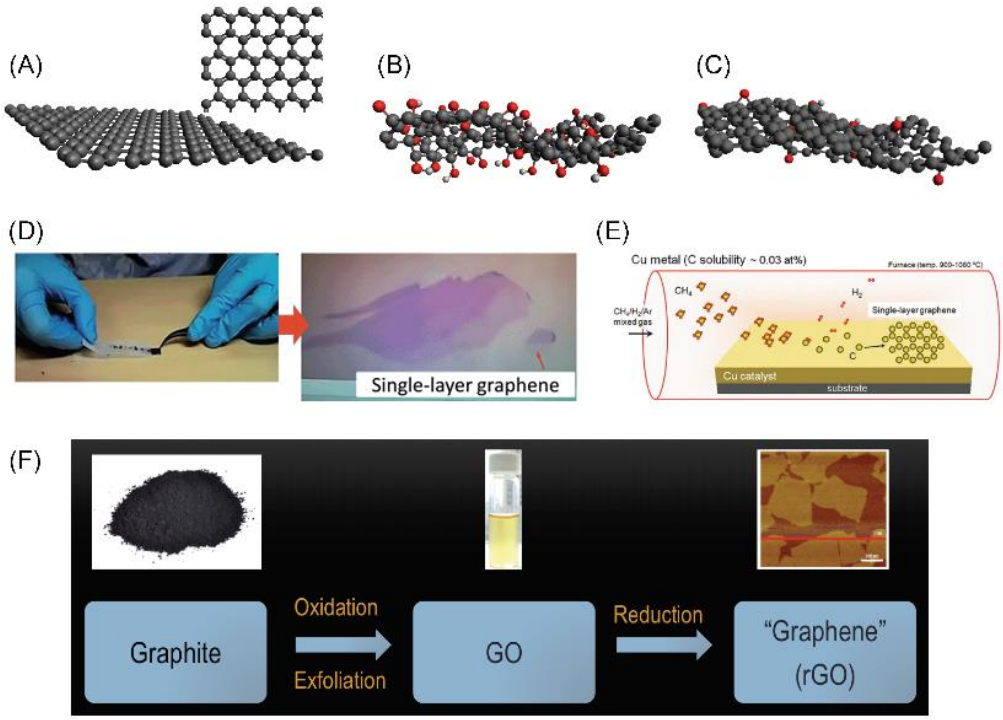


Fig.8. Schematic of Graphene and Graphene Oxide Synthesis by CVD method [33]

These Nanosheets showed great biocompatibility and low cytotoxicity after forty-eight hours of therapy, even at an amount of 250 g ml-1. Multi-functionality has been found to be a significant consideration for the regulation and treatment of malignancies, as the multi-functionalized GO-based systems demonstrated efficient chemotherapeutic delivery of medicines and inhibiting activity against hepatocarcinoma malignant cells [32]. The surface was functionalized with PEG-linked lacto carboxylic acid and fluorescein isothiocyanate, and any remaining amine groups in the PEI were acetylated. Increased target specificity and sensitivity to pH release behaviour were also seen in the nanosystem, which had significant growth-inhibiting impacts on the cancer cells (Figure 2, a-f) [34]. The examined strength spectrum has shown that this nanocarrier is excellent for cell feasibility, making it one of its primary qualities. Using reduced GO, pH-sensitive doxorubicin nanocarriers were fabricated. The developed nanosystem was determined to be satisfactory due to its substantial drug loading capacity or capacity, pH-sensitive, endured, controlled and controlled release behaviour. Through a process of nonspecific endocytosis (Figure 9), this Nano hybrid system was shown to be cytotoxic to MCF-7 and A549 cells. It was discovered that zoledronic acid may be conjugated with GO-based Nano platforms to create nanosystems with enhanced performance against breast cancer, resulting in synergistic effects for the treatment of osteoporosis and metastasis [23-25]. For the purpose of administering anticancer drugs, nanocomposites based on modified GO have been developed. For instance, gelatine and reduced GO Nanosheets modified with folic acid were used to create a nanocarrier for transporting the anticancer medication chlorambucil. This nanocarrier was both biocompatible and biodegradable. This nanosystem had a significant loading capacity and regulated release behaviour. As a result, acidic surroundings resulted in a greater drug release rate than neutral ones.

In addition, Pluronic F127 molecules, which have been functionalized noncovalently with GO, have been presented for tumor-targeting therapy [35].

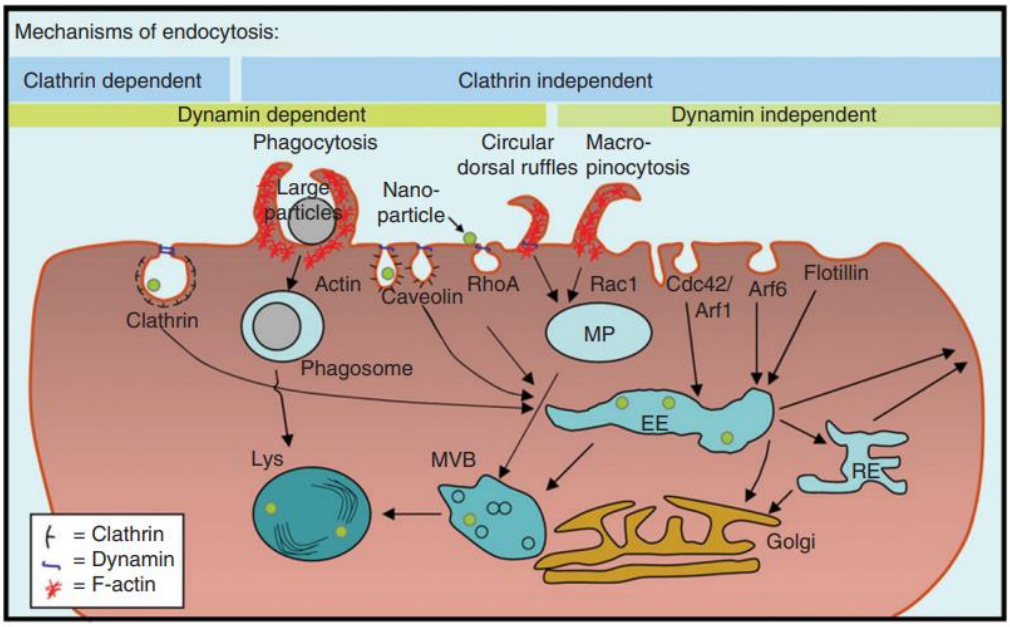


Fig.9. Schematic of Nonspecific endocytosis [24]

4.2 Combinational Therapy

One area of research focus in the field of cancer treatment is the use of functionalized nanostructures to create combination therapies with reduced toxicity and enhanced targeted benefits. Hydrothermal reaction suggested that Fe3O4@Au/reduced GO nanoparticles might be created for radiotherapy and Photothermal therapy combination. In this case, the effectiveness of Photothermal conversion was close to 61%. These nanosystems were found to be biocompatible and cytotoxic enough for use against KB cell lines derived from oral squamous cancer. To create a nano platform with outstanding biocompatibility, good dispersion in water, and Photothermal heat via high NIR, Fe3O4 was covalently bonded to glycerol oligomer (GO) polymers produced from -cyclodextrin hyaluronic acid. The packing strength of doxorubicin can be increased to greater than 485.43 mg/g-1 by mixing hyaluronic acid with -cyclodextrin. In low-acid liquids, the created nanosystem facilitated a quick photothermal reaction that triggered the release of anticancer medicines [31-33]. The doxorubicin-loaded nanocomposites demonstrated chemo-photothermal synergistic anticancer effects and CD44 receptor facilitation of active-directing identification. Liu et al. presented a drug delivery nanosystem based on GO Nanosheets for combinatorial chemo-photothermal therapy of malignancies; the tumor internal microenvironment and photothermal stimulation had stimulating effects on the release of anticancer medicines from nanocarriers. However, photodynamic therapy, which is used to cure cancer without causing any harm to healthy tissue, can generate large amounts of ROS that are hazardous to cells. Preventing the function of the homologous 1 enzyme (DNA damage and repair protease) can increase cell responsiveness to positively charged oxygen species (ROS), hence enhancing the efficacy of photodynamic treatment.

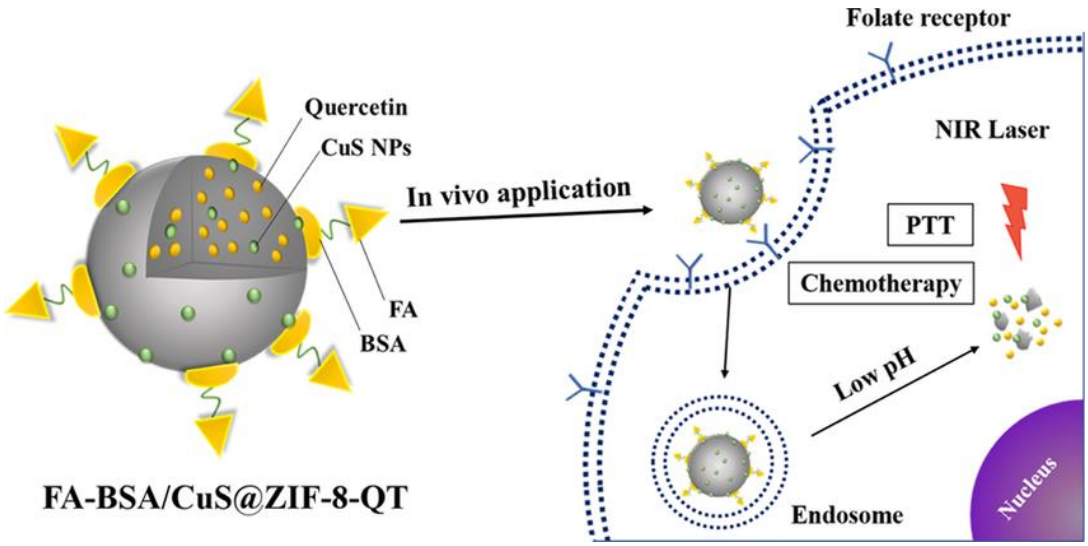


Fig.10. Schematic of basic combinational therapy [35]

In order to transport the MTH1 inhibitor and doxorubicin, one study employed PEG, folic acid, and a photosensitizer called indocyanine green to create functionalized GO-based nanosystems. As a chemo-photodynamic therapy, this nanotechnology showed promise in halting the metastasis of osteosarcoma cells. The increased chemo-photodynamic therapy triggered apoptosis and autophagy by suppressing homolog 1 polypeptide and increasing ROS production. In another experiment, researchers used magnetic nanoparticles in conjunction with the chemo-photodynamic agent camptothecin to treat cancer [35]. An allylamine linker was used to join 4-hydroxy coumarin to reduce GO. After 24 hours of treatment, 75% of cells were still alive in a concentration of 100 g/ml-1 of nanocarriers designed to kill human breast cancer. These nanocarriers were biocompatible and had no discernible toxic impact on cells that were normal (WS-1 cells). As much as 38% of cancer cells can be eradicated with photodynamic treatment employing UV-visible irradiation (> 365 nm). Laser irradiation was found to generate more ROS for efficiently suppressing malignant cells, and this work demonstrated its synergistic anti-tumor activity and significant apoptosis of targeted cells.

5. Important Perspectives

In conclusion, there are potential advantages and special qualities of using G- and GO-based nanomaterials with enhanced electrical conductivity, endurance, and rigidity in the design and production of anticancer nanosystems. Long-term cytotoxicity/histopathology, immunity, bio-persistency, multi-drug resistance, authorization mechanism, inside-cell absorption, bioaccumulation, and the impact of particle size on cellular viability are just a few of the significant barriers that still need to be rigorously evaluated by researchers. Long-term respiratory contact with G and carbon black has been linked to metastasis and advancement of lung cancer, as stated by Bi et al. Therefore, cell necrosis and the subsequent release of molecular patterns associated with damage (such as mitochondria DNA) are likely to have occurred, with the former having the capacity to potently stimulate the secretion of agonists in alveolar macrophages. Barriers that limit the diffusion of substances are another important topic, which is why biological membranes are so important.

The effect of GO Nanosheets transporting Teague medication on the permeability of cell membranes demonstrates the necessity for novel drug delivery nanosystems with enhanced membrane permeability characteristics. Cancer photothermal therapy employing G-based materials can be hampered by an insufficiently stable bio-medium. Functionalized GO enhanced by an amphiphilic polymer exhibited enhanced colloidal stability, sufficient compatibility, a suitable size distribution, and a neutral surface charge; these findings highlight the need to investigate an extensive variety of polymers for the functioning of these materials. To improve biocompatibility and cellular absorption, scientists have also investigated hybrid functional G-based nanocomposites. Potentially promising cancer treatments include hybrid G-based nanocomposites [30-35]. The complex of GO and GQDs, for instance, demonstrated enhanced photothermal impacts, increased biocompatibility, and excellent cytotoxic performances against malignancies, making it a promising candidate for use in Theragnostic and cell imaging applications. Additional analytical analyses targeted at improving selectivity and reducing the risk of toxicity, as well as more research into such synergy and optimized hybrid nanostructures, are necessary. Researchers have begun extensive investigations into novel nanostructures, resulting to the production of an array of potential nanosystems for the therapy of tumors as a response to the devastating side effects and non-targeting limits of chemotherapy techniques [35].

Customized anticancer systems encounter significant obstacles in terms of both efficacy and biosafety, including particle size/morphology, composition of chemicals, reaction/physiological conditions, and surface chemical properties. It is also crucial that no compounds that could be hazardous to human health (such as those that cause skin irritation, autoimmune reactions, or even poisoning) be used in the construction of these anticancer systems. Green and sustainability synthetic techniques, as well as green functionalization technologies, can be employed to build G-based nanosystems; these have advantages in terms of repeatability and scalability. Researchers should place more emphasis on methods based on green chemistry to decrease and remove environmental and health concerns and to promote biocompatibility and sustainability [35]. Using a straightforward and eco-friendly building method, cancer cells were exposed to curcumin at concentrations between 80 and 400 g/ml-1 (the harmful effects varied with the intensity of the sample). When using G-based materials in cancer treatment, immunogenicity, inflammatory reactions, and hemocompatibility are all crucial factors to consider. Studies have indicated that G-based nanocomposites are hazardous in a dose-dependent manner, with potential effects including DNA damage to mitochondria, inflammation, autophagy, necrosis, and apoptosis. One study found that the hemolytic effects of GO can be prevented by functionalizing or modifying the surface of the material to make it more compatible, as the electrostatic attraction between GO structures and the red blood cell membrane is the root cause of these effects. A considerable uptick in TNF-, IL-6, and IL-1 showed that GO is highly immunogenic; however, the functionalized GO structures demonstrated improved immunological compatibility. Interleukin-6, interleukin-12, tumor necrotic factor-, interferon, and monocyte chemotactic protein were all shown to have significant inflammatory effects when GO structures were applied.

GO activated the NF-kappa pathway by binding toll-like receptors, whereas functionalized G-based nanomaterials, which disrupt the opsonin-protein connection, may protect macrophages from this inflammatory response.

G-based chemicals are widely used in biomedicine, making it all the more important to weigh the risks associated with them. Numerous studies show that G-based materials are toxic to animal and human cells at a range of doses, causing adverse consequences like cell death, diminished viability, and apoptosis in the lungs and the liver and kidneys, respectively. The toxicological profile of these materials is affected by a number of factors, including their alteration, surface architecture, groups, lateral size, plasma effect, charge, and pollutants. The toxicity of G- and GO-cantered entities may be associated with events and mechanisms such as apoptosis, DNA damage, oxidative damage, mitochondria necrosis, physical injury, inflammatory responses, and autophagy; however, each of these must be explored separately.

6. Conclusion and Future Outlooks

Nanomaterials based on G and GO have been studied extensively throughout the past few years due to their potential application in cancer therapy. Due to their impressive physicochemical properties, including as their two-dimensional planar structures, enormous surface areas, high chemical/mechanical stability, and significant conductivity, these structures have been studied for prospective use in a variety of pharmaceutical and biological appliances. Functionalization techniques, both covalent and non-covalent, have been used to enhance the chemical composition and biological compatibility of G and GO, both of which may be deficient in their unmodified forms. There has not been nearly enough research into G-based Nanosystems and their potential to provide molecular insights into the sustained release of anticancer drugs and the discharge of anticancer chemicals. Future G-based nanosystems in the battle against cancer will need to be able to effectively produce antitumor medications in tumor targets/tissues, have controlled cellular uptake capabilities, exhibit tumor-targeted drug absorption behaviour, and selectively injure cells. Functionalized G-based tiny systems have gained attention because they improve drug bio-distribution, have less adverse effects on healthy cells, are more selective and sensitive, and increase local therapeutic absorption. Before G-based products may be employed in biological or clinical settings, researchers need to take into account concerns about their toxicity and biosafety.

Hydrogels made of MXene have recently shown a lot of promise for usage in sensors that people can wear. Despite the potential, further research into the production method and longevity of MXene hydrogels is necessary. This review delves deeply into the methodologies utilized for the synthesis of 2D MXene and the fabrication of hydrogels based on MXene. The results suggest that the dispersion of MXene can be enhanced through surface modification of MXene nanosheets. Additionally, 2D MXene can function as an interaction platform for generating self-assembled hydrogels. Hydrogels that have been changed by MXene demonstrate enhanced sensing capabilities because to their enhanced mechanical and electrical properties, which are comparable to those of traditional hydrogels.

Furthermore, hydrogels based on MXene have favorable biocompatibility, allowing their utilization in healthcare environments. MXene-based hydrogels have recently been developed for the purpose of creating wearable sensors. These sensors exhibit significant promise in the domains of smart skin, surveillance of health, and sensitive devices. MXene-based hydrogels provide numerous benefits in comparison to hydrogels fabricated using other 2D nanomaterials like graphene: Due to their strong affinity for water, (1) photodynamic and photothermal agents derived from MXene exhibit excellent dispersion and stability in biological fluids. MXene-based hydrogels have the ability to autonomously organize and break down due to the relatively lesser strength of their covalent and noncovalent crosslinking. MXene-based hydrogels may be synthesized using various methods, and they possess environmentally friendly and biocompatible characteristics. Additionally, their surface properties can be adjusted to meet diverse application requirements. Despite the promising characteristics of MXene-based hydrogels, further progress is needed before they can be widely utilized in practical applications.

Acknowledgements

Not Applicable

References

[1]. Y. Ang, Y. Song, X. Bo, J. Min, O.S. Pak, L. Zhu, M. Wang, J. Tu, A. Kogan, H. Zhang, et al., "A laser-engraved wearable sensor for sensitive detection of uric acid and tyrosine in sweat," Nat. Biotechnol., vol. 38, pp. 217-224, 2020.

[2]. H.C. Ates, A.K. Yetisen, F. Güder, and C. Dincer, "Wearable devices for the detection of COVID-19," Nat. Electron., vol. 4, pp. 13-14, 2021.

[3]. J. Kim, A.S. Campbell, B.E. de Avila, and J. Wang, "Wearable biosensors for healthcare monitoring," Nat. Biotechnol., vol. 37, pp. 389-406, 2019

[4]. J.R. Sempionatto, J.A. Lasalde-Ramirez, K. Mahato, J. Wang, and W. Gao, "Wearable chemical sensors for biomarker discovery in the omics era," Nat. Rev. Chem., vol. 6, pp. 899-915, 2022.

[5]. P. Parthasarathy, "Synthesis and UV detection characteristics of TiO2 thin film prepared through sol-gel route," in IOP Conference Series: Materials Science and Engineering, vol. 360, no. 1, p. 012056, IOP Publishing, September 2018

[6]. M. Naguib, M. Kurtoglu, V. Presser, J. Lu, J. Niu, M. Heon, L. Hultman, Y. Gogotsi, and M.W. Barsoum, "Two-dimensional nanocrystals produced by exfoliation of Ti3AlC2," Adv. Mater., vol. 23, pp. 4248-4253, 2011

[7]. X. Li, Z. Huang, C.E. Shuck, G. Liang, Y. Gogotsi, and C. Zhi, "MXene chemistry, electrochemistry and energy storage applications," Nat. Rev. Chem., vol. 6, pp. 389-404, 2022.

[8]. C. Zhang, Y. Ma, X. Zhang, S. Abdolhosseinzadeh, H. Sheng, W. Lan, A. Pakdel, J. Heier, and F. Nüesch, "Two-Dimensional Transition Metal Carbides and Nitrides (MXenes): Synthesis, Properties, and Electrochemical Energy Storage Applications," Energy Environ. Mater. vol. 3, pp. 29-55, 2020.

[9]. P. Parthasarathy and S. Vivekanandan, "Biocompatible TiO2-CeO2 nano-composite synthesis, characterization and analysis on electrochemical performance for uric acid determination," Ain Shams Engineering Journal, vol. 11, no. 3, pp. 777-785, 2020.

[10]. B. Anasori, M.R. Lukatskaya, and Y. Gogotsi, "2D metal carbides and nitrides (MXenes) for energy storage," Nat. Rev. Mater., vol. 2, p. 16098, 2017

[11]. M. K. Kumawat, M. Thakur, R. Bahadur, et al., "Preparation of graphene oxide-graphene quantum dots hybrid and its application in cancer Theranostic," Mater. Sci. Eng. C, vol. 103, p. 109774.

[12]. M. Rasoulzadeh and H. Namazi, "Carboxymethyl cellulose/graphene oxide bio-nanocomposite hydrogel beads as anticancer drug carrier agent," Carbohydr. Polym. vol. 168, pp. 320-326, 2017.

[13]. P. Parthasarathy, "Synthesis and UV detection characteristics of TiO2 thin film prepared through sol-gel route," in IOP Conference Series: Materials Science and Engineering, vol. 360, no. 1, p. 012056, IOP Publishing, September 2018.

[14]. F. Barahuie, B. Saifullah, D. Dorniani, et al., "Graphene oxide as a nanocarrier for controlled release and targeted delivery of an anticancer active agent, chlorogenic acid," Mater. Sci. Eng. C, vol. 74, pp. 177-185, 2017.

[15]. Y. Guo, H. Xu, Y. Li, et al., "Hyaluronic acid and Arg-Gly-Asp peptide modified graphene oxide with dual receptor-targeting function for cancer therapy," J. Biomater. Appl., vol. 32, no. 1, pp. 54-65, 2017.

[16]. Y.-S. Huang, Y.-J. Lu, and J.-P. Chen, "Magnetic graphene oxide as a carrier for targeted delivery of chemotherapy drugs in cancer therapy," J. Magn. Magn. Mater. vol. 427, pp. 34-40, 2017.

[17]. T. V. Padmavathy, M. N. Vimalkumar, S. Nagarajan, G. C. Babu, and P. Parthasarathy, "Performance analysis of pre-cancerous mammographic image enhancement feature using non-subsampled shearlet transform," Multimedia Tools and Applications, vol. 80, pp. 26997-27012, 2021.

[18]. N. Karki, H. Tiwari, M. Pal, et al., "Functionalized graphene oxides for drug loading, release and delivery of poorly water-soluble anticancer drug: a comparative study," Colloids Surf. B, vol. 169, pp. 265-272, 2018.

[19]. K. Ma, D. Fu, Y. Liu, et al., "Cancer cell targeting, controlled drug release and intracellular fate of biomimetic membrane encapsulated drug-loaded nano-graphene oxide nanohybrids," J. Mater. Chem. B, vol. 6, no. 31, pp. 5080-5090, 2018.

[20]. P. Parthasarathy and S. Vivekanandan, "Detection of suspicious human activity based on CNN-DBNN algorithm for video surveillance applications," in 2019 Innovations in Power and Advanced Computing Technologies (i-PACT), vol. 1, pp. 1-7, IEEE, March 2019.

[21]. M. Abbasian, M. M. Roudi, F. Mahmoodzadeh, M. Eskandani, and M. Jaymand, "Chitosan-grafted-poly (methacrylic acid)/graphene oxide nanocomposite as a pH-responsive de novo cancer chemotherapy nanosystem," Int. J. Biol. Macromol., vol. 118, pp. 1871-1879, 2018.

[22]. P. Parthasarathy, "Synthesis and UV detection characteristics of TiO2 thin film prepared through sol-gel route," in IOP Conference Series: Materials Science and Engineering, vol. 360, no. 1, p. 012056, IOP Publishing, September 2018.

[23]. B. Liu, C. Che, J. Liu, et al., "Fabrication and antitumor mechanism of a nanoparticle drug delivery system: graphene oxide/chitosan oligosaccharide/γ-polyglutamic acid composites for anticancer drug delivery," Chemistry Select, vol. 4, no. 43, pp. 12491-12502, 2019.

[24]. Y. Luo, Y. Tang, T. Liu, et al., "Engineering graphene oxide with ultrasmall SPIONs and smart drug release for cancer Theranostic," ChemComm, vol. 55, no. 13, pp. 1963-1966, 2019.

[25]. S. M. Vincent Paul, S. Balasubramaniam, P. Panchatcharam, P. Malarvizhi Kumar, and A. Mubarakali, "Intelligent framework for prediction of heart disease using deep learning," Arabian Journal for Science and Engineering, pp. 1-11, 2022.

[26]. S. Alqahtani, S. B. Changalasetty, P. Parthasarathy, L. S. Thota, and A. Mubarakali, "Effective spectrum sensing using cognitive radios in 5G and wireless body area networks," Computers and Electrical Engineering, vol. 105, p. 108493, 2023.

[27]. P. Parthasarathy and S. Vivekanandan, "Biocompatible TiO2-CeO2 nano-composite synthesis, characterization and analysis on electrochemical performance for uric acid determination," Ain Shams Engineering Journal, vol. 11, no. 3, pp. 777-785, 2020.

[28]. J. A. Jaleel, S. M. Ashraf, K. Rathinasamy, and K. Pramod, "Carbon dot festooned and surface passivated graphene-reinforced chitosan construct for tumour-targeted delivery of TNF-α gene," Int. J. Biol. Macromol., vol. 127, pp. 628-636, 2019.

[29]. Y. Yin, T. L. Nguyen, B. Wang, et al., "Simultaneous delivery of DNA vaccine and hydrophobic adjuvant using reducible polyethyleneimine-functionalized graphene oxide for activation of dendritic cells," J. Ind. Eng. Chem., vol. 80, pp. 870-876, 2019.

[30]. Basha, S. Vivekanandan, and P. Parthasarathy, "Evolution of blood pressure control identification in lieu of post-surgery diabetic patients: a review," Health Information Science and Systems, vol. 6, pp. 1-10, 2018.

[31]. N. Ma, A. Song, Z. Li, and Y. Luan, "Redox-sensitive prodrug molecules meet graphene oxide: an efficient graphene oxide based nano vehicle toward cancer therapy," ACS Biomater. Sci. Eng., vol. 5, no. 3, pp. 1384-1391, 2019.

[32]. R. Sang, M. Chen, Y. Yang, et al., "HAp@GO drug delivery vehicle with dual-stimuli-triggered drug release property and efficient synergistic therapy function against cancer," J. Biomed. Mater. Res. A, vol. 107, no. 10, pp. 2296-2309, 2019.

[33]. Basha, S. Vivekanandan, and P. Parthasarathy, "Blood glucose regulation for post-operative patients with diabetes and hypertension continuum: a cascade control-based approach," Journal of Medical Systems, vol. 43, pp. 1-8, 2019.

[34]. Mubarakali, S. Gopinath, P. Parthasarathy, U. A. Kumar, and A. A. Basha, "Highly efficient and sensitive non-enzymatic glucose biosensor based on flower-shaped CuO-colloid nanoparticles decorated with graphene-modified nanocomposite electrode," Measurement, p. 113145, 2023.

[35]. N. Navashree and P. Parthasarathy, "A comparative study on the electrochemical behaviour of various electrolytes by cyclic voltammetry: GCE as electrode material," Materials Today: Proceedings, 2023.

Names of the referees

1. Michael Jay, Associate Professor, Middlesex University, London, michaeljay.inoventive@gmail.com

2. Ramya Mohan, Associate Professor, King Khalid University, Saudi Arabia, ramyamohan95@outlook.com

3. Manjunath Gudur, Assistant Professor, University of Bisha, manjuvgudur@gmail.com