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2D Nanomaterials: A Potent Antiviral Agent

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Abstract: ***In this study, we have thoroughly studied the potentiality of 2D nanomaterials against different viruses. The extremely high surface-volume ratio is beneficial for surface-related reactions like catalysis, this provides flexibility and other intrinsic properties. The antimicrobial activity of nanomaterials is well established. Here we go through different 2D nanomaterials, showing a variety of antiviral actions through the generation of ROS and oxidative stress. The antiviral action of nanosheets has been attributed to their negative surface charge and the presence of a layered nanoscale morphology with sharp edges and corners. Due to their strong electrostatic activity with envelope and non-envelop viruses the sharp edge causes physical damage, and protein disruption causes virus damage. 2D nanomaterials have a wide opening in the field of research and development.***
Keywords: Nanomaterials, Antiviral agent, 2D nanoparticles, Nanosheets, Graphene

I. INTRODUCTION

The development of 2-D nanomaterials began with the exfoliation of graphene in 2004 by Dr. Andre Geim and Dr. Konstantin Novosolev.[1] The 2-D nanostructures are composed of nanosheets that have a thickness of at least a few atomic layers leading to weak Van der Waals forces and in-plane bonding. The thin layer of the nanosheets helps provide electron transport without interlayer interactions; the extremely high surface-volume ratio is beneficial for surface-related reactions like catalysis. The surface area available helps in changing the intrinsic properties of the materials at points and provides flexibility in modulating the structure-property relationship. The 2-D nanomaterials can be broadly subclassified based on the chemical composition into organic, inorganic, and hybrid 2-D nanomaterials or more commonly based on the number of layers as layered (less than 5 nm) or non-layered (few atoms thick). The layered nanomaterials are fabricated through various exfoliation strategies while the bottom-up approaches such as chemical vapor deposition (CVD) and wet-chemical synthesis have been primarily used for the synthesis of non-layered 2-D nanomaterials[2]. Additional methods of synthesis such as solution-based synthesis[3], a hydrothermal method, an epitaxial growth[5] are also being explored. Apart from graphene, the transition metal dichalcogenides[6], phosphorene[7], borophene[8], transition metal oxides, carbides and nitrides9,10], metal oxides[11], hexagonal boron nitride[12], graphitic carbon nitride[13], perovskites[14], niobates[15], MXenes[16], silicates[17], and polymers[18] are being explored for the synthesis of ultra-thin 2-D nanomaterials[19]. The fascinating properties of graphene such as high mechanical strength, high specific surface area, flexibility, electronic properties, excellent conductivity, astonishing thermal stability, and easy modifications have made it into a wonder material [15-16]. These features play a key role in antimicrobial and antiviral activity. The antimicrobe, as well as antiviral activity of GO. GO is well demonstrated and established thee ed in literature. Many of these 2D nanosheets have shown excellent antimicrobial and antiviral activity. [11-21]. Like graphene, MoS_2 is another nanosheet having specialized physiochemical properties. Similar to graphene, the presence of 2D planar structure with a high surface to volume ratio makes this nanosheet highly effective as antibacterial agent[11]. Production of ROS, superoxide anions, oxidative stress and membrane damage are the major ways exerted by MoS_2 to destroy the microbial cells**.** MXene has also emerged as a new class of 2D nanosheets having outstanding antimicrobial properties. Its special ultrathin lamellar structure, size and shape have great impact on its antimicrobial activities[11-14]. Also, black phosphorus is another 2D material that have shown potential as an antimicrobial agent [15].

Table 1: Summary of antiviral activity of 2D nanomaterials

Dimension of Nanostructure	Type of Nanostructure	Viral species tested	Antiviral efficiency	Reference
2D nanomaterials	GO	Porcine epidemic diarrhea virus (PEDV, RNA virus) Pseudorabies virus (PRV, DNA virus)	1.5-6 µg/mL.	[12]
	GO	Herpes Simplex Virus Type-1	5 µg/mL	[25]
	GO	EV71 H9N2 H7N9	3.24 log10 PFU/mL.	[26]
	GO	Ebola virus	-	[27]
	GO	Respiratory syncytial virus (RSV)	5.00 µg/mL.	[28]

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II. MECHANISM OF ANTIVIRAL ACTION OF NANOSHEETS

The antiviral action of nanosheets has been attributed to their negative surface charge and presence of a layered nanoscale morphology with sharp edges and corners[12]. The primary mechanism of antiviral action observed in studies involving GO and rGO nanosheets against both enveloped and non-enveloped viruses is the direct interaction of the nanosheets with the virus surface through strong electrostatic interactions, which ultimately results in inducing physical damage to the viral structure via sharp edge-mediated effect, as also observed in case of bacteria[12]. Table-1 shows the potentiality of antiviral agents against different viruses.

The importance of monolayer structure of nanosheets in determining their antiviral activity was evaluated by comparing the antiviral properties of graphite, graphite oxide, graphene oxide and reduced graphene oxide[12], and it was observed that only GO and rGO with a monolayer structure and nanoscale size could demonstrate significant antiviral activity, whereas graphite and graphite oxide which act as precursors to these nanostructures showed very weak or complete absence of antiviral activity due to their multi-layered morphology and larger lateral size [12].

In addition to morphology and size, surface charge is another key factor influencing the antiviral action of nanosheets. Studies have shown that it is the charge density and not charge identity that actually determines the antiviral activity of these nanosheets[23]. GO and rGO both possess similar net negative charge but differs in the type of functional groups present on their surfaces. The antiviral activity of GO and rGO was found to be similar demonstrating that the presence of different functional groups did not affect the antiviral action[12]. This has been further supported by comparing the antiviral properties of GO and sulfonated rGO nanosheets[23]. It was observed that introduction of additional negatively charged sulphonate groups in the GO structure did not improve its antiviral activity, as both GO and sulphonated rGO had the same negative charge density.

This disruption of viral structure and viral proteins by nanosheets can also arise from the chemical properties of nanosheets, where the nanosheets can meditate their antiviral action through disruption of key protein-protein interactions that play crucial role in maintaining virus structural integrity and infectivity. MD simulation studies have shown that graphene nanosheets can interact very strongly with Ebola virus VP40 oligomers through hydrophobic interactions and break apart these oligomers by penetrating through them. VP40 proteins are very crucial in forming the Ebola virus matrix[25]. VP40 hexamers undergo oligomerization through their C-terminal domains with adjacent hexamers forming VP40 filaments which make up the entire Ebola virus matrix. Thus, disrupting the formation of these filaments can directly inactivate the virus and act as a mode of antiviral action. Graphene sheets owing to their strong hydrophobic nature insert themselves through the hydrophobic CTD-CTD interactions of the hexamers and separates the hexameric domains from each other. Similar observation have also been reported for HIV-1 integrase proteins, where the dimeric conformation of the integrase protein is destroyed by graphene nanosheet [26].

Thus, nanosheets with a net negative surface charge and a monolayer morphology exert their antiviral activity by strongly attaching itself to the surface of positively charged virus particles through electrostatic interactions, thereby capturing them on its surface, which in turn inhibits the attachment of these viruses to the cell surface and thus prevents the viral entry into the cells. This is coupled with nanosheet edge-mediated physical destruction of the viruses, which finally leads to their inactivation.

III. CONCLUSION

The mode of antiviral action for nanosheets are found to be quite different. Nanosheets are found to act upon the viruses by directly destroying their structure and membrane/envelope proteins. Nanotubes, on the other hand are not found to exert any antiviral activity. This opens a wide area to do research on different 2D nanometerials as potent antiviral agent. The mechanism of antiviral agent is know well established thus this provides young researchers a hope to study more about the unknown side of 2D nanosheets.

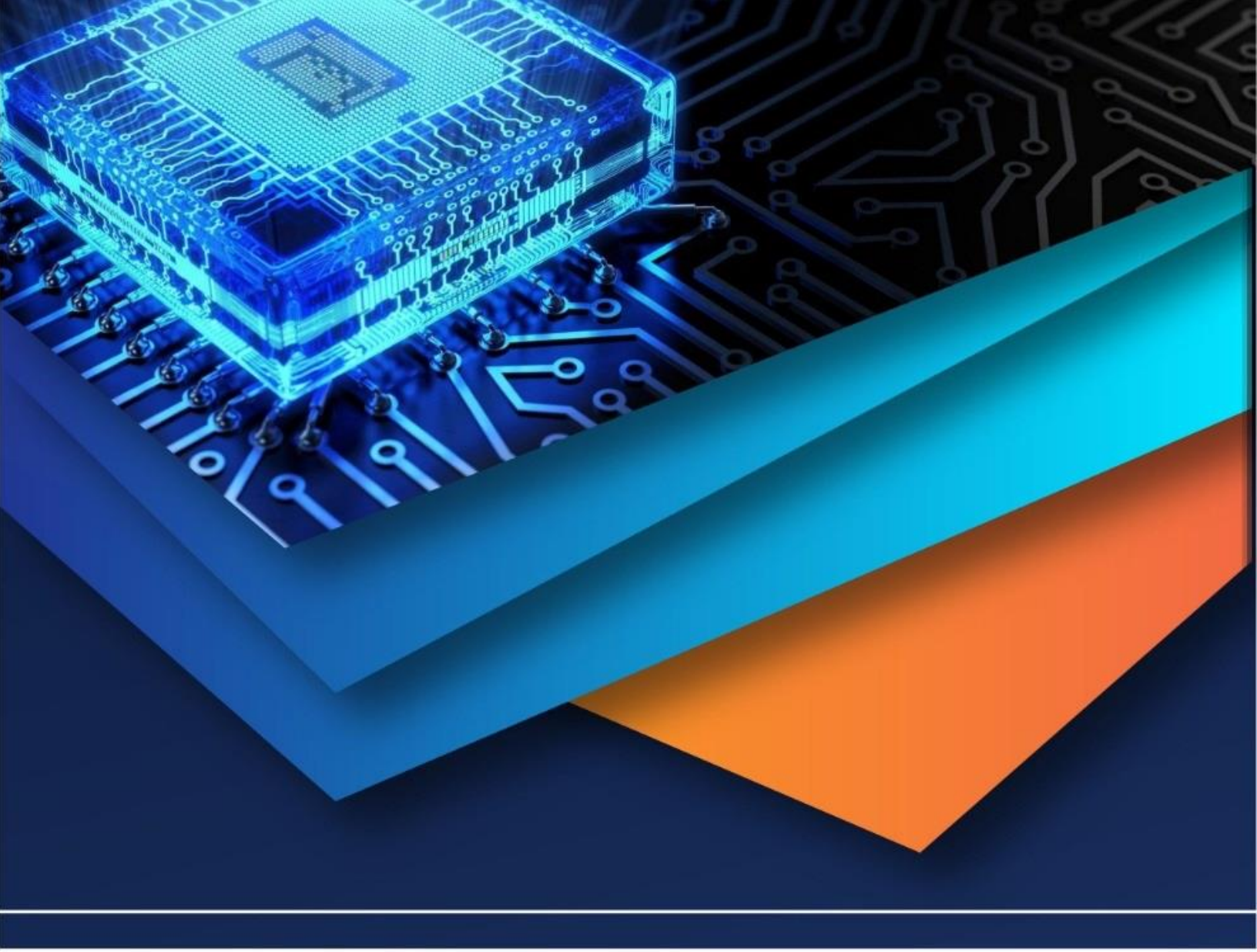
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