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A REVIEW ON HEXAGONAL BORON NITRIDES NANOSHEETS IN CANCER DRUG DELIVERY

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ABSTRACT
Developments in low-dimensional nanomaterials drug carriers have quickly found application in medicine. Curiously, compared to the increasingly well-known 2D graphene oxide (GO), the two-dimensional (2D) nanomaterials of hexagonal boron nitride (h-BN), also known as "white graphite," are comparatively less studied. On the other hand, h-BN nanoparticles' special qualities make them ideal for the administration of chemotherapy drugs during cancer treatment. According to recent research, the h-BN is a promising option for nanocarriers and nano-transducers in the biological sciences. We go over the many physicochemical characteristics and key ideas related to h-BN nanosheets as anticancer drug carriers in this paper.

KEYWORDS: Boron Nitride (BN), Transition metals, piezoelectricity and Spectroscopy.

I. INTRODUCTION

A crystalline substance known as boron nitride (BN) is made up of atoms of boron (B) and nitrogen (N) in an equal ratio. Different polymorphisms of the BN material are available through the following forms: cubic BN (c-BN), hexagonal BN (h-BN), wurtzite BN (w-BN), and rhombohedral BN (r-BN). With sp^2 hybridised B-N bonds, the h-BN and r-BN exhibit dense structure, whereas the w-BN and c-BN exhibit loose structure with sp^3 hybridised bonds. The two most researched among them are the h-BN (hexagonal) and c-BN (cubic) structures. While (hexagonal) h-BN has a two-dimensional (2D) layered structure, c-BN is well known as the second strongest material, akin to the crystal lattice form of diamond. Since it resembles conventional graphene more, the h-BN is also known as white graphene.[1]

Our goal is to present a critical review of the fast developing graphene two-dimensional materials (2DMs), such as emerging 2D organic polymers, graphitic nitride materials, black phosphorus, and 2D transition metal nanomaterials. It contains a variety of 2D nanomaterials, some of which are mentioned below.[2]

1) 2D transition metal nanomaterials
a) Transition metal chalcogenides(TMCs)
b) Transition metal oxides(TMOs)

2) 2D graphitic nitride materials
a) Graphitic carbon nitride
b) Hexagonal boron nitride

3) 2D black phosphorus
a) Electrochemical sensing and Biosensing
b) Optical Biosensing and Bioimaging

4) 2D organic polymers
a) 2D covalent organic frameworks and metal organic frameworks
b) 2D Polypeptoid

Atoms B and N make up the building blocks of h-BN, which are put together to create a cage structure resembling a honeycomb. In specifics, the cage in the shape of a hexagon is kept together by a strong covalent connection. Furthermore, the hexagonal interlayers in Figure 1 are held in place by weak Vander Waals attraction forces. In this hexagonal interlayer, the B atom is usually positioned exactly up or down relative to the N atoms of the adjacent hexagonal layer. Graphene's carbon-carbon (C-C) network structure differs from BN's electron dispersion in that regard.[3]

The main distinction between graphene and hBNs is that the latter are non-centrosymmetric and strongly polarized due to the presence of electronegative nitrogen atoms. High surface area, biocompatibility, atomically flat surface, and high stability in aqueous solutions are

characteristics of hexagonal bilayer nanostructures (hBNs) that make them a viable tool for biomedical applications including biological sensors (5) and molecular imaging (4). Because of their thin 2D structure and high surface area to volume ratio, hBNs can carry cargo (6) for photodynamic treatment and cancer medication delivery (7). Structure of hBN is shown in fig 1:

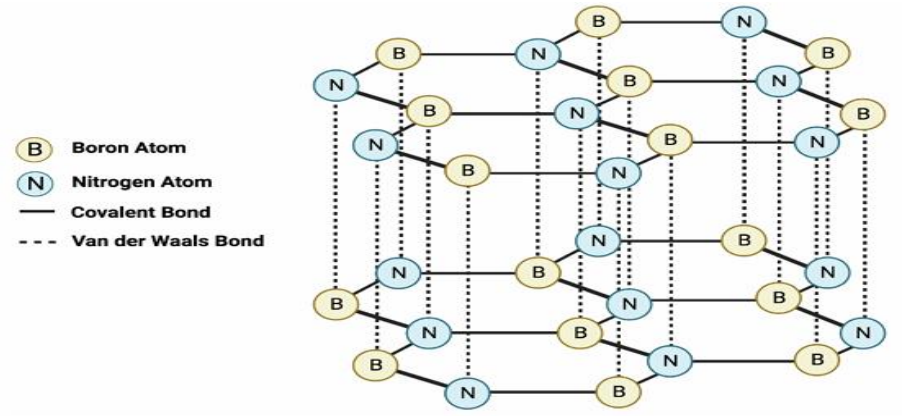

Figure 1: Structure of Hexagonal Boron Nitride.

II. Synthesis of Hexagonal Boron Nitride (hBN): There are two main strategies in the synthesis of hBNs including top-down[8] and bottom-up methods.[9] Descript in fig 2:

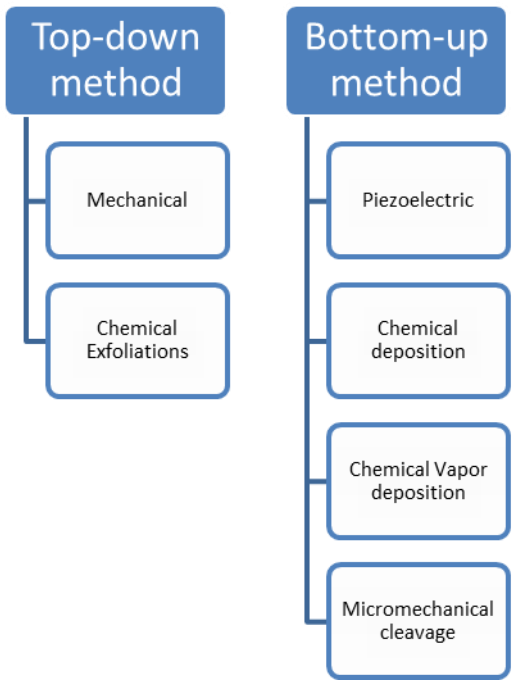

Fig. 2: Synthesis of hBN by Top-down and bottom-up methods.[3]

III. Properties of hBN

High Surface Area and Functionalization: Because of their large surface area, h-BNNS enable effective drug loading. Several compounds can be used to functionalize them in order to increase their targeting and interaction with cancer cells.[10]

Biocompatibility and Low Toxicity: Because of their exceptional biocompatibility and minimal toxicity, h-BNNS are well-suited for use in biomedical applications. This is essential to reducing adverse effects while receiving cancer treatment.[11]

Stimuli-Responsive Drug Release: It is possible to programme h-BNNS to react to particular stimuli like light, pH, or temperature. This makes it possible to release drugs in a regulated and targeted manner, ensuring that they reach the tumour location and causing the least amount of harm to healthy tissues.[10]

Photothermal and Photodynamic Therapy: It is possible to combine h-BNNS with either photothermal or photodynamic therapy. In order to kill cancer cells, these treatments use light to activate the nanosheets, which subsequently produce heat or reactive oxygen species.[1]

Enhanced Drug Delivery Efficiency: The efficacy of h-BNNS as drug carriers is facilitated by their special qualities, which include their great mechanical strength and chemical stability. They can guarantee that the medication reaches the intended location and prevent it from degrading.[11]

IV. Characterization of hBNs[12]

High Resolution transmission electron microscopy (HRTEM): NMs' size, distribution, and morphology were examined using HRTEM at an accelerated voltage of 80 keV. On a copper grid covered in carbon, NMs were examined.

Fourier Transform Infrared spectroscopy (FTIR): By using FTIR, the chemical makeup of hBNs was identified. Each and every NMs analysis was done in powder form, and the 600–4000 cm–1 region was scanned 20 times at a resolution of 4 cm–1.

X-ray diffraction (XRD): XRD was used to evaluate the crystal structure of hBNs using CuKα radiation. Step scanning mode with tube current of 10 mA and voltage

of 30 kV. The scan speed in that mode was one second per step, with a step size of 0.02°. The measurement was taken between 2θ = 5 and 90°.

Thermogravimetric Analysis (TGA): TGA was used to examine the thermal stability of hBNs. The analysis was done in an argon environment and heated to 800 °C at a rate of 10 °C per minute.

Dynamic light scattering (DLS): The hydrodynamic size and surface charge of hBNs and hBN-Dox were determined using DLS. One milligramme each of hBNs and hBN-Dox, individually distributed in deionized water (diH2O)/cell culture medium, was utilised for the DLS measurements.

Raman Spectroscopy: hBNs' Raman spectra was acquired using a 532 nm laser. Materials in the powder form within the range of 100–3200 cm-1 were used for the analysis. The settings for exposure duration and laser power were 10s and 1, respectively.

UV-Visible spectroscopy: Every material underwent uv-vis examination between 200 and 800 nm. Materials were dissolved in the appropriate solvent using an ultrasonic bath prior to analysis.

Atomic force & Piezoresponse force microscopy: To assess the piezoelectricity of hBNs and hBN-Drug, AFM's capability to measure local piezoelectric response parallel to topography data was employed. Piezoresponse Force Microscopy (PRFM) is the term used to describe this type of AFM operation. A thin, conductive probe that makes contact with a piezoelectric material's surface and scans it is used to achieve visualisation.

V. Evaluation of hBNs[13]

1. Drug adhesion onto boron nitrides nanomaterials (BNNs, BNTs and BNC)
2. DOS analysis
3. MEP Surface analysis
4. Quantum theory of atoms in molecules(QTAIM) analysis

VI. Biocompatibility Challenges of BNNs

Researchers employ several strategies to address the biocompatibility challenges of boron nitride nanosheets (BNNS) in drug delivery systems:

1. Surface Modification: By functionalizing the surface of BNNS with biocompatible polymers, proteins, or other molecules, researchers can improve their interaction with biological systems and reduce potential toxicity.[14]
2. Encapsulation: Encapsulating BNNS within biocompatible materials such as liposomes or polymeric nanoparticles can enhance their stability and reduce direct exposure to biological tissues, thereby minimizing adverse reactions.[15]
3. In Vitro and In Vivo Testing: Extensive in vitro (cell culture) and in vivo (animal) studies are conducted to evaluate the biocompatibility and toxicity of BNNS. These studies help in understanding how BNNS interact with cells and tissues and in identifying any potential side effects.[14]
4. Optimizing Dosage and Administration: Researchers work on optimizing the dosage and administration routes of BNNS to ensure they are delivered in a safe and effective manner. This includes determining the appropriate concentration and frequency of administration to minimize toxicity.[14]
5. Long-Term Studies: Long-term studies are essential to assess the chronic effects of BNNS. These studies help in understanding the long-term biocompatibility and potential accumulation of BNNS in the body.[14]
6. Regulatory Compliance: Ensuring that BNNS-based drug delivery systems comply with regulatory standards is crucial. Researchers work closely with regulatory bodies to meet safety and efficacy requirements.[14]

These strategies collectively help in overcoming the biocompatibility challenges associated with BNNS, paving the way for their safe and effective use in drug delivery systems.

VII. Challenges in hBN for cancer drug delivery

The clinical translation of hexagonal boron nitride nanosheets (h-BNNS) for cancer drug delivery faces several significant challenges:

Reproducibility and Consistency: Ensuring batch-to-batch consistency in the production of h-BNNS is crucial. Variations in size, shape, and surface properties can affect their performance and safety.[16]

i. Agglomeration in Polymer Composites

a. When incorporating BNNS into polymer composites, one common challenge is agglomeration. BNNSs tend to cluster together, affecting the dispersion and overall performance of the composite material.

b. Strategies to address this issue include surface functionalization of BNNSs to improve their compatibility with the polymer matrix and prevent agglomeration.[17]

ii. Chemical Inertness and Functionalization

a. BNNSs are considered chemically inert, which makes them challenging to functionalize. Many applications require new surface functionalities, but achieving this with BNNSs is not straightforward.[18]

b. Researchers are actively exploring methods to modify the surface of BNNSs to enhance their reactivity and tailor their properties for specific applications.

iii. Alignment in Macroscopic Forms

a. While BNNSs exhibit remarkable thermal and dielectric properties, their self-assembly and alignment in macroscopic forms remain challenging.

The chemical inertness of boron nitride contributes to this difficulty.[19]

b. Achieving controlled alignment of BNNSs in bulk materials is crucial for maximizing their performance in applications such as thermal management.

iv. Bonding at Heterojunction Interfaces

a. BNNSs are often combined with other 2D materials (e.g., graphene, carbonitride, semiconductors) to form heterostructures. Designing the bonding at the interfaces is essential for optimizing device performance.[20]

b. Understanding the nature and function of defects in BNNSs is critical for developing advanced applications based on these heterostructures.

c. Physiological Stability: Maintaining the stability of h-BNNS in physiological conditions is challenging. They need to remain stable in the bloodstream and within the body to effectively deliver drugs to the target site.[21]

d. Toxicity and Biocompatibility: While h-BNNS are generally considered biocompatible, their long-term effects and potential toxicity need thorough investigation. Ensuring they do not induce adverse reactions in the body is essential.[22]

e. Regulatory Hurdles: The innovative nature of h-BNNS demands the reevaluation and evolution of existing regulatory frameworks. Navigating the regulatory approval process can be time-consuming and complex.[21]

f. Scalability and Manufacturing: Producing h-BNNS at a large scale with consistent quality is challenging. The manufacturing process needs to be optimized to ensure reproducibility and cost-effectiveness.[16]

g. Preclinical and Clinical Testing: Adequate preclinical models that accurately predict human responses are essential. Additionally, designing and conducting clinical trials to demonstrate the safety and efficacy of h-BNNS-based drug delivery systems can be complex and costly.[22]

VIII. Surface modification of BNNs

Surface modification of boron nitride nanosheets (BNNS) is a crucial step to enhance their properties and make them suitable for various applications, including drug delivery. Here are some common methods and their benefits:

v. Non-Covalent Functionalization: This involves coating BNNS with molecules that adhere to their surface without forming strong chemical bonds. For example, polydopamine (PDA) can be used to coat BNNS, preserving their crystal structure while improving their dispersion in various media.[23]

vi. Covalent Functionalization: This method involves forming strong chemical bonds between BNNS and functional groups. For instance, hydroxylation (adding -OH groups) can be done via nitric acid oxidation or ball-milling. Edge-hydroxylation, where -OH groups are added at the edges of BNNS, helps maintain the basal crystal structure and enhances properties like dielectric strength.[23]

vii. Amphiphilic Modifiers: Stearic acid (SA) is an example of an amphiphilic molecule used to modify BNNS. It has both hydrophilic (water-attracting) and hydrophobic (water-repelling) parts, which improve the compatibility of BNNS with various solvents and enhance their dispersion stability.[24]

viii. Magnetic Functionalization: Introducing magnetic nanoparticles like Fe3O4 onto BNNS surfaces can impart magnetic properties, allowing for magnetic alignment and targeted delivery in biomedical applications.[25]

These modifications help improve the dispersion, stability, and functionality of BNNS, making them more effective for applications like drug delivery, heat transfer, and electronic devices.

IX. Advancement in BNNs[26]

Recent advancements in boron nitride nanosheets (BNNS)-based drug delivery research have focused on enhancing their functionality and effectiveness. Here are some notable developments:

1. **Surface Functionalization**: Researchers have made significant progress in functionalizing BNNS to improve their drug loading capacity and targeting abilities. This includes attaching various functional groups or molecules to the surface of BNNS to enhance their interaction with drugs and target cells.
2. **Stimuli-Responsive Systems**: Advances have been made in developing BNNS that respond to specific stimuli such as pH, temperature, or light. These systems allow for controlled and targeted drug release, improving the precision and effectiveness of treatments.
3. **Combination Therapies**: BNNS are being explored for use in combination therapies, where they can deliver multiple drugs or therapeutic agents simultaneously. This approach aims to enhance the overall therapeutic effect and reduce the likelihood of drug resistance.
4. **Enhanced Biocompatibility**: Efforts have been made to improve the biocompatibility of BNNS, ensuring they are safe for use in the human body. This includes modifying the surface properties of BNNS to reduce potential toxicity and improve their interaction with biological systems.
5. **Photothermal and Photodynamic Therapy**: BNNS are being investigated for their potential in photothermal and photodynamic therapy. These therapies use light to activate BNNS, which can then generate heat or reactive oxygen species to kill cancer cells or other targeted cells.
6. **Nanocarrier Systems**: BNNS are being integrated into various nanocarrier systems, such as liposomes and polymeric nanoparticles, to improve their stability, drug loading capacity, and targeting abilities.

These advancements are paving the way for more effective and targeted drug delivery systems using BNNS.

X. Previous work of Boron Nitrides on Cancer Drug Delivery Systems

The nanocarrier encapsulated anticancer drug has the potential to maximized therapeutic effect and minimized unwanted side effects. However, it is still challenging to design such capable nanocarrier that are simultaneously biocompatible, soluble, and stable in physiologic environments, and could deliver required anticancer drugs. In this case, 2D h-BN like nanomaterials has great potential as anticancer nano-carriers.

Table 1: Recent studies of BN on anticancer drugs.

Sl.No	Form of Boron Nitride(BN)	Loading	Application	Reference
1	h-BN	Doxarubicin	Anticancer therapy	[27]
		Carboplatin		[28]
		Cisplatin		[29]
2	$B_{22}N_{24}$	5-Fluoro uracil	Anticancer therapy	[30]
3	$B_{12}N_{12}$	Cisplatin		[31]

XII. APPLICATIONS

i. **Anticancer Drug Delivery:**[32] The hexagonal boron nitrides (h-BN) and boron nitride nanotubes (BNNT) are promising nanomaterials since they possess large surface area, excellent mechanical strength, and required biocompatibility.

ii. **Gene Delivery:**[33] In gene delivery, the therapeutic efficacy is mostly limited due to nuclease degradation and reduced cellular internalization. For example, the CpG oligodeoxynucleotides (CpG ODNs) hold a promising immunostimulatory activity in cancer immunotherapy.

iii. **h-BN Based Therapeutic Agent Delivery:**[34] The in situ deposition of Pd nanoparticles on the surface of the h-BN Nanosheets (Pd@OH-BNNS) has endowed the photothermal property.

iv. **BN Carrier for the Targeted Nano-Radio Therapeutic Agent:**[35] The fabricated BN nanostructures materials have unique physical, chemical, optical, and mechanical features, which are potential features for complex biological systems. Currently, the boron neutron captures therapy (BNCT), a kind of radiotherapy draw attention for use against cancer cells. In this therapy, a thermal neutron beam focused on boron-10 isotope that generates a lithium atom, a gamma ray, and an alpha particle, allowing the destruction of target tumor tissues.

v. **DDS Evaluated Molecular Dynamics Simulations:**[36] The delivery of the drug on-site should limit the side effects of the drug. The interactions of different anticancer drugs and h-BN nanosheet as a carrier system have been further calculated in Molecular Dynamic (MD) simulations and Density Functional Theory (DFT). The orbital energy and density of state (DOS) measurements show decreasing the HOMO to the LUMO energy gap of h-BN nanosheet upon the adsorption of anticancer drugs.

XIII. CONCLUSION

A 2D type h-BN structure's anticipated capabilities allow the researchers to create novel nanoscale materials. The integration of various biological and inorganic building elements on this 2D substrate has enabled these advancements. Expert material researchers have partially validated the noteworthy manipulation tactics of h-BN for a range of biomedical applications. Compared to most studies using graphene oxide (GO) to deliver anticancer drugs, the novel class h-BN (white graphene) has an even more appealing plat shape. This allows the therapeutic gene or anticancer medication, such as doxorubicin, to release at the desired location. Therefore, it is expected that h-BN laden with anticancer drugs will soon be used in advanced cancer therapy.

XIV: REFERENCES

1. Sharker SM. Hexagonal boron nitrides (white graphene): a promising method for cancer drug delivery. International Journal of Nanomedicine, Dec. 19, 2019; 9983-93.
2. Wen W, Song Y, Yan X, Zhu C, Du D, Wang S, Asiri AM, Lin Y. Recent advances in emerging 2D nanomaterials for biosensing and bioimaging applications. Materials Today, Mar. 1, 2018; 21(2): 164-77.
3. Çiçek N. *Ultrasound stimulated hexagonal boron nitrides as cancer drug nanocarriers* (Doctoral dissertation).
4. Chen Y, Tan C, Zhang H, Wang L. Two-dimensional graphene analogues for biomedical applications. Chemical Society Reviews, 2015; 44(9): 2681-701.
5. Lu T, Wang L, Jiang Y, Huang C. Hexagonal boron nitride nanoplates as emerging biological nanovectors and their potential applications in biomedicine. Journal of materials chemistry B., 2016; 4(36): 6103-10.
6. Ciofani G, Danti S, Genchi GG, Mazzolai B, Mattoli V. Boron nitride nanotubes: Biocompatibility and potential spill-over in nanomedicine. Small, May. 27, 2013; 9(9-10): 1672-85.

7. Jedrzejczak-Silicka M, Trukawka M, Dudziak M, Piotrowska K, Mijowska E. Hexagonal boron nitride functionalized with Au nanoparticles—properties and potential biological applications. Nanomaterials, Aug. 9, 2018; 8(8): 605.
8. Gao W, Zhao Y, Yin H. Lateral size selection of liquid exfoliated hexagonal boron nitride nanosheets. RSC advances, 2018; 8(11): 5976-83.
9. Wang G, Zhao D, Spring DJ, DePinho RA. Genetics and biology of prostate cancer. Genes & development, Sep. 1, 2018; 32(17-18): 1105-40.
10. Das BC, Chokkalingam P, Masilamani P, Shukla S, Das S. Stimuli-responsive boron-based materials in drug delivery. International Journal of Molecular Sciences, Feb. 1, 2023; 24(3): 2757.
11. Feng S, Ren Y, Li H, Tang Y, Yan J, Shen Z, Zhang H, Chen F. Cancer cell–membrane biomimetic boron nitride nanospheres for targeted cancer therapy. International Journal of Nanomedicine, Mar. 11, 2021: 2123-36.
12. Çiçek N. *Ultrasound stimulated hexagonal boron nitrides as cancer drug nanocarriers* (Doctoral dissertation).
13. Jasim SA, Al-Lami MS, Shather AH, Aldhalmi AK, Taki AG, Ahmed BA, Al-Hamdani MM, Saraswat SK. Nanostructures of boron nitride: A promising nanocarrier for anti-cancer drug delivery. Micro and Nanostructures, Jan. 1, 2024; 185: 207708.
14. Mehta, S., Shah, V., Patel, G. *et al.* A holistic review of recent advances in nano-based drug delivery systems for the treatment of triple-negative breast cancer (TNBC). *J Nanopart Res.*, 2024; 26: 87. https://doi.org/10.1007/s11051-024-06000-8
15. Waheed S, Li Z, Zhang F, Chiarini A, Armato U, Wu J. Engineering nano-drug biointerface to overcome biological barriers toward precision drug delivery. Journal of Nanobiotechnology, Aug. 31, 2022; 20(1): 395.
16. Metselaar JM, Lammers T. Challenges in nanomedicine clinical translation. Drug delivery and translational research, Jun. 2020; 10: 721-5.
17. Rasul MG, Kiziltas A, Arfaei B, Shahbazian-Yassar R. 2D boron nitride nanosheets for polymer composite materials. npj 2D Materials and Applications, May 17, 2021; 5(1): 56.
18. Liu Z, Dibaji A, Li D, Mateti S, Liu J, Yan F, Barrow CJ, Chen Y, Ariga K, Yang W. Challenges and solutions in surface engineering and assembly of boron nitride nanosheets. Materials Today, Apr. 1, 2021; 44: 194-210.
19. Lu, W., Deng, Q., Liu, M. et al. Coaxial Wet Spinning of Boron Nitride Nanosheet-Based Composite Fibers with Enhanced Thermal Conductivity and Mechanical Strength. Nano-Micro Lett., 2024; 16: 25. https://doi.org/10.1007/s40820-023-01236-w
20. Ren J, Innocenzi P. 2D boron nitride heterostructures: recent advances and future challenges. Small Structures, Nov. 2021; 2(11): 2100068.
21. Đorđević S, Gonzalez MM, Conejos-Sánchez I, Carreira B, Pozzi S, Acúrcio RC, Satchi-Fainaro R, Florindo HF, Vicent MJ. Current hurdles to the translation of nanomedicines from bench to the clinic. Drug delivery and translational research, Mar. 2022: 1-26.
22. Li H, Qiao W, Shen Y, Xu H, Fan Y, Liu Y, Lan Y, Gong Y, Chen F, Feng S. Biomimetic boron nitride nanoparticles for targeted drug delivery and enhanced antitumor activity. Pharmaceutics, Apr. 18, 2023; 15(4): 1269.
23. Lingyu Wu, Kai Wu, Chuxin Lei, Dingyao Liu, Rongni Du, Feng Chen and Qiang Fu, Surface modifications of boron nitride nanosheets for poly(vinylidene fluoride) based film capacitors: advantages of edge-hydroxylation; journal of materials chemistry A., 2019; 7: 7664-7674.
24. Surendran, V.S., Bindhu, B., Indulal, C.R. et al. Surface Modification of Boron Nitride Nanosheets for Effective Heat Transfer Applications. Chemistry Africa, 2022; 5: 761–770. https://doi.org/10.1007/s42250-022-00352-1.
25. Rasul MG, Kiziltas A, Arfaei B, Shahbazian-Yassar R. 2D boron nitride nanosheets for polymer composite materials. npj 2D Materials and Applications, May 17, 2021; 5(1): 56.
26. Rajendran, S., Ravi, S.N., Nair, V.M. et al. Recent Development and Future Aspects: Nano-Based Drug Delivery System in Cancer Therapy. Top Catal, 2024; 67: 203–217. https://doi.org/10.1007/s11244-023-01893-6
27. Sharker SM, Alam MA, Shill MC, Rahman GS, Reza HM. Functionalized hBN as targeted photothermal chemotherapy for com plete eradication of cancer cells. Int J Pharm., 2017; 534(1–2): 206–212. doi:10.1016/j.ijpharm.2017.10.025
28. Khatti Z, Hashemianzadeh SM. Boron nitride nanotube as a delivery system for platinum drugs: drug encapsulation and diffusion coeffi cient prediction. Eur J Pharm Sci., 2016; 88: 291–297. doi:10.1016/j. ejps.2016.04.011
29. Roosta S, Hashemianzadeh SM, Ketabi S. Encapsulation of cisplatin as an anti-cancer drug into boron-nitride and carbon nanotubes: molecular simulation and free energy calculation. Mater Sci Eng C., 2016; 67: 98–103. doi:10.1016/j.msec.2016.04.100
30. Onsori S, Alipour E. A computational study on the cisplatin drug interaction with boron nitride nanocluster. J Mol Graphics Modell, 2018; 79: 223–229. doi:10.1016/j.jmgm.2017.12.007
31. Vatanparast M, Shariatinia Z. Hexagonal boron nitride nanosheet as novel drug delivery system for anticancer drugs: insights from DFT calculations and molecular dynamics simulations. J Mol Graphics Modell, 2019; 89: 50–59. doi:10.1016/j.jmgm.2019.02.012.
32. Sharker SM, Alam MA, Shill MC, Rahman GS, Reza HM. Functionalized hBN as targeted

photothermal chemotherapy for com plete eradication of cancer cells. Int J Pharm., 2017; 534(1–2): 206–212. doi:10.1016/j.ijpharm.2017.10.025.

33. Zhang Y, Guo R, Wang D, Sun X, Xu Z. Pd nanoparticle-decorated hydroxy boron nitride nanosheets as a novel drug carrier for chemo-photothermal therapy. Colloids Surf, B., 2019; 176: 300–308. doi:10.1016/j.colsurfb.2019.01.015.
34. Ferreira T, Miranda M, Rocha Z, Leal A, Gomes D, Sousa E. An assessment of the potential use of BNNTs for boron neutron capture therapy. Nanomaterials, 2017; 7(4): 82. doi:10.3390/nano7040082.
35. El Khalifi M, Bentin J, Duverger E, Gharbi T, Boulahdour H, Picaud F. Encapsulation capacity and natural payload delivery of an anticancer drug from boron nitride nanotube. Phys Chem Chem Phys., 2016; 18(36): 24994–25001. doi:10.1039/C6CP01387B.
36. Vatanparast M, Shariatinia Z. Hexagonal boron nitride nanosheet as novel drug delivery system for anticancer drugs: insights from DFT calculations and molecular dynamics simulations. J Mol Graphics Modell, 2019; 89: 50–59. doi:10.1016/j.jmgm.2019.02.012.