

Supporting Information

Accumulation, Distribution, and Toxicity of Black Phosphorus Nanomaterials Across Biological Systems: A Critical Review

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Table S1 Preparation methods of BPNMs

Methods		Preparation principle	Advantages	Disadvantages	Ref.
Top-down methods	Liquid-phase exfoliation	Exfoliation with the assistance of ultrasound in the solvent	Simple operation, high stripping efficiency, different morphologies, different layers for nanosheets	Environmentally unfriendly, low yield, prone to oxidation	1-3
	Mechanical exfoliation	Utilize external forces for exfoliation, such as tapes	Simple principle and operation	Consuming time, low yield, prone to oxidation	3-5
	Electrochemical exfoliation	Exfoliation with the assistance of electric field force in the solvent	Simple operation, high stripping efficiency, large output, direct conduction	Consuming energy	6-9
Bottom-up methods	Facile solvothermal synthesis	Direct preparation by utilizing the temperature, pressure of the closed reaction system and the catalytic effect of the solvent	Simple operation, low cost	Poor crystal form, thick BPNMs	10-12
	Pulsed laser deposition	Growth of thin film by using a laser to bombard the target and deposit the bombarded plasma on the substrate	Room temperature, adjustable process parameters	Slow rate, spraying small particles, low quality	13
	Chemical vapor deposition	Direct preparation by using the high-temperature gas-solid phase catalytic reaction	Simple operation, short time-consuming, low cost	Immaturity, impurities	14

Table S2 The toxic effects of BPNMs in vivo

BPNM types	Organisms	Lateral size /Thickness (nm)	Exposure dose	Experimental Time	Exposure Routes	Effects on different organs	Ref.
BP@PLEL hydrogel	Female Balb/c mice (6 weeks)	288.3 ± 122.4/23.4 ± 8.2	10 µg/mouse	20 d	Single subcutaneous injection	No apparent damage to normal liver, spleen, kidney, heart, and lung of the mice; high PTT efficacy to eliminate residual tumor tissues	15
BPNSs	Sprague Dawley male rats (6 weeks)	~200/~5.5	0.5 mg/kg	7 d	Single intravenous injection	No significant change of liver and kidney functions	16
DOX loaded BPNSs	Male Balb/c mice (5 weeks)	~200/~5.5	0.5 mg/kg	14 d	Single intravenous injection	No significant damage to normal tissues and high efficacy to inhibit tumor growth for synergistic photodynamic/photothermal/chemotherapy	16
BPNSs	Healthy and AKI ICR mice	225.8 ± 4.0/3.8–4.5	6 mg/kg	1 d and 2 h	Single injection	No obvious damage to major organs of healthy mice; high efficacy for curing AKI mice	17
BPNSs	Balb/c mice (8 weeks)	~500/5.3–5.9	20 mg/kg	7 and 21 d	Single and three intravenous injections (once every 2 days)	Single injection: no obvious toxicity to major organs except of liver function; Three injections: abnormal liver and renal functions after 7 days and recovery after 21 days	18
PEG-BPNSs	Female athymic nude mice (4 weeks)	~150/4–5	7.5, 15, and 30 mg/kg	21 d	Three intravenous injections (once every 3 days)	Selective killing of tumor tissue and safety to normal organs at 15 mg/kg, and abnormal liver and renal functions at 30 mg/kg	19
Bare BP and TiL ₄ @BP	Balb/c mice (8 weeks)	3.3/1.5	0.5 mg/kg	1, 7, and 28 d	Single intravenous injection	No obvious damage to major organs; inflammatory responses in peripheral blood, serum, and spleen induced by bare BP rather than TiL ₄ @BP at day 1 and recovery at day 7 and 21	20

BPQDs	Male C57BL/6 mice	2.7 ± 0.7/1.5 ± 0.8	340 µg/mouse	1, 7, and 30 d	Single intraperitoneal injection	No apparent pathological damages to all organs during the 30-day period; lipid peroxidation and reduction of catalase activity in liver, and DNA damage in bone marrows at 1 day, recovery at 7 days, and remained normal at 30 days	21
BPNSs	Balb/c mice (8 weeks)	100–1000/4–24	125, 250, and 500 µg/kg	7 d	Single intravenous injection	Slightly sparse hair and significantly weight reduction; a time-dependent reversible inflammatory response in peripheral blood	22

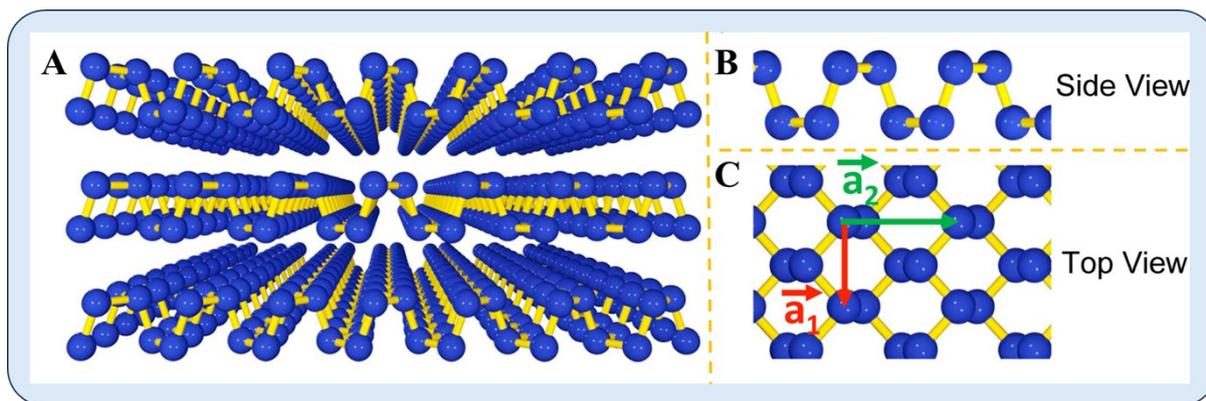


Figure S1. Crystal and band structure of few-layered phosphorene (FLP). (A) Perspective side view, (B) side view, and (C) top view of FLP. Adapted from Liu et al.,²³ with permission from American Chemical Society, Copyright 2014.

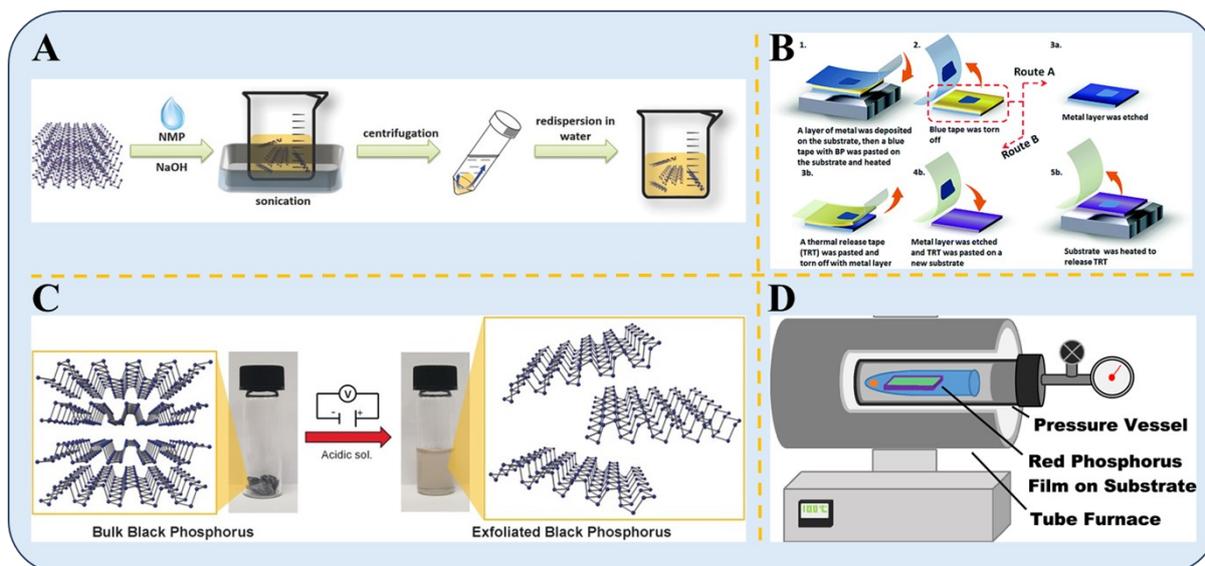


Figure S2. Synthetic processes of representative methods for BPNMs. (A) Schematic illustration of the fabrication process for basic-N-methyl-2-pyrrolidone-exfoliated phosphorene. Adapted from Guo et al.,² with permission from John Wiley and Sons, Copyright 2015. (B) Schematic illustration of the metal-assisted mechanical exfoliation process for few-layer BP. Adapted from Guan et al.,¹ with permission from Royal Society of Chemistry, Copyright 2018. (C) Experimental configuration for the electrochemical exfoliation of BPNs. Adapted from Ambrosi et al.,⁶ with permission from John Wiley and Sons, Copyright 2017. (D) Schematic of BP growth on a substrate from amorphous red phosphorus thin film within a pressure vessel reactor. Adapted from Smith et al.,¹⁴ with permission from IOP Publishing, Copyright 2016.

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