Electronic Supplementary Information

h-FBN Assisted Negative Ion Paper Spray for Sensitive Detection of Small Molecules

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Contents

1. Chemicals and materials

h-BN was purchased from Sigma-Aldrich (St. Louis, MO). L-Proline (L-Pro), L-Valine (L-Val), 2-Naphthalene sulfonic acid, Maltotetraose, Maltopentaose, scutellarin and fluorin boric acid were from MACKLIN (Shanghai, China), Bisphenol A (BPA) was purchased from Energy Chemical (Shanghai, China). Bisphenol S (BPS), Vancomycin and Glucose (Glu) were bought from Aladdin (Shanghai, China). Salicylic acid (SA) was from Sinopharm Chemical Reagent Co., Ltd (Shanghai, China). Three TCM chemicals, emodin, baicalin and amygdalin were bought from HENOWNS (Tianjin, China). Grade 1 chromatography paper was from Whatman (Maidstone, England). Unless otherwise stated, all commercially available solvents are analytical grade or of the highest purity.

2. Structure characterization

Transmission electron microscopy (TEM) was carried out with JEM-2100F field emission electron microscope. X-ray photoelectron spectroscopy (XPS) was conducted using an Escalab250Xi instrument. The scanning electron microscopy (SEM) images and Mapping images were taken with JEOL JSM6700F SEM. Hydrophobicity of nanomaterials was measured by Contact Angle measuring instrument.

3. Experimental details

Preparation of few-layer h-BN. h-BN (0.5 g) was suspended in isopropanol (50 mL), followed by mechanical agitation combined with ultrasonic dispersion for 24 h. Then the dispersion was centrifuged at 4000 r/min for 5 min for collecting the supernatant. And the supernatant was further centrifuged at 10000 r/min for 30 min, and the obtained few-layer h-BN was dried at 60 ℃.

Synthesis of fluorine doped few-layer h-BN (h-FBN). 0.05 g of the prepared few-layer h-BN and HBF_4 (5 mL) were mixed and stirred for 8 h at 50 ℃. The mixture was cooled down to room temperature and centrifugation. The precipitate was washed four times with deionized water. The obtained h-FBN were dried at 60 ℃ for further use.

Preparation of h-BN/h-FBN coated paper. Grade 1 chromatography paper was cut into isosceles triangles (base 5 mm, height 7 mm), and put in the solutions of h-BN or

h-FBN (both 1 mg/mL) for 1 h to load the nanomaterials. The coated papers were dried at room temperature for next usage.

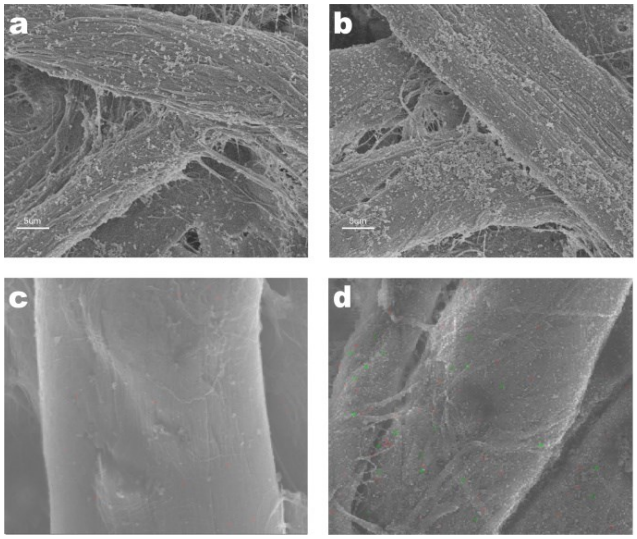

Figure S1. SEM images of (a) h-BN coated paper and (b) h-FBN coated paper. Mapping images of (c) h-BN coated paper and (d) h-FBN coated paper. The red dots are B element, and the green dots are F element.

Mass spectrometry analysis. BPA solution (5 μM, 20 μL) was dropped on the prepared h-FBN or h-BN coated paper, followed by drying under 30 ℃. Then the paper with analyte was clamped on a copper clamp. For PS-MS experiment, the distance between paper spray tip and MS inlet was 5 mm. A high negative voltage of -3.5 kV was applied and the elution solvent methanol/water (v/v=9:1) was supplied to elute the ionized molecules for MS detection. An LCQ fleet ion trap mass spectrometer (Thermo Scientific, San Jose, CA, U.S.A.) in negative ion mode was used to record the MS signals. MS/MS ion scans were generated through collision-induced dissociation (CID).

4. Background spectra of three kinds of papers

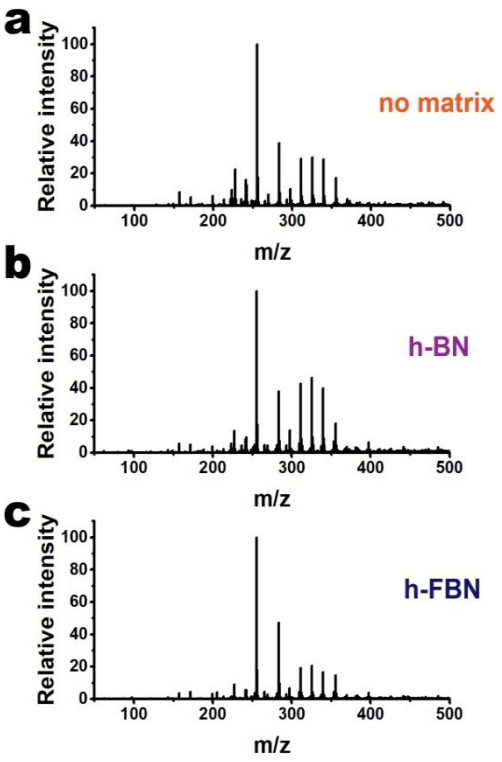

Figure S2. Background spectrum of (a) pristine paper, (b) h-BN coated paper and (c) h-FBN coated paper.

5. Optimization of detecting conditions

There are many factors affecting paper spray, including spray voltage, spray solvent, paper-based materials, distance between paper tip and mass spectrometry inlet, etc. In addition to changing the paper-based materials, we mainly optimized the spray voltage and spray solvent. The distance between the paper tip and the mass spectrometry inlet and the shape of the paper base have been described in the text experiment. The most commonly used mass spectrometry solvent for elution was methanol and water. So under the same experimental conditions, the condition optimization was realized by changing the ratio of methanol to water (5:1、7:1、9:1、10:1, voltage was 3000 V) or changing the voltage (2500 V、3000 V、3500 V、4000 V, elution solvent was methanol: water = 9:1 (v/v)).

Under the optimized conditions, several other compounds were also detected with negative ion mode, including L-proline (L-Pro, 2.5 nmol), L-valine (L-Val, 1.25 nmol), salicylic acid (SA, 200 pmol), glucose (Glu, 2.5 nmol), 2-Naphthalene sulfonic acid (50 pmol), Bisphenol S (BPS, 50 pmol), Maltotetraose (250 pmol), Maltopentaose (250 pmol), Vancomycin (250 pmol), emodin (12.5 pmol), baicalin (500 pmol) and amygdalin (50 pmol).

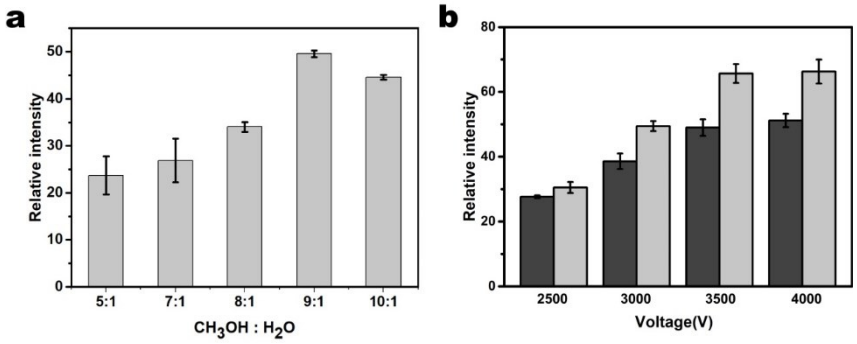

Figure S3. (a) Optimization of elution solvent. (b) Optimization of spray voltage (The dark gray is h-BN and the light gray is h-FBN).

6. Standard curve of BPA

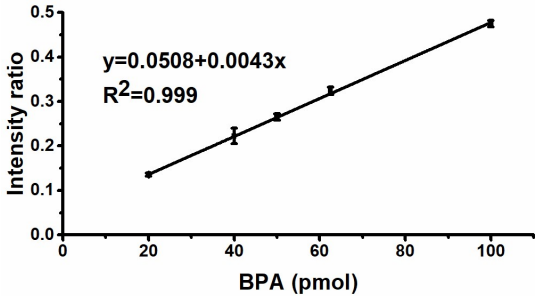

Figure S4. Standard curve of BPA.

7. Detections of TCMs in serum and whole blood samples

For three Traditional Chinese medicines (TCM) in serum, the high abundance protein in serum was removed by methanol at a ratio of 1:5. Technically, 50 μL methanol solution containing baicalin was mixed with serum (10 μL) and oscillated1 min. After storage at room temperature for 30 min, the sample was centrifuged for 10 min at 4℃ (12000 r/min) and the supernatant was collected for the next step. For whole blood sample, 75 μL methanol containing baicalin was added to 425 μL whole

blood sample, which was used directly in PS-MS analysis.

To obtain standard curves, scutellarin ($C_{21}H_{18}O_{12}$, MW=462.37) was selected as the internal standard. For serum sample, serum solutions (5 μL) containing baicalin and internal standard (final concentration of scutellarin: 0.25 mM, final concentration of baicalin: 0.33 mM、0.27 mM、0.17 mM、0.13 mM、0.08 mM、0.07 mM) was added to h-FBN coated paper and dried at room temperature for PS-MS detection. For whole blood sample, the solutions (1 μL) containing baicalin and internal standard (baicalin: 0.1 mM、0.125 mM、0.2 mM、0.25 mM、0.5 mM, scutellarin: 0.25 mM,) were applied for PS-MS detection following the same procedure to the serum sample.

8. Calculations of S/N ratio and LOD

The S/N was calculated based on the following equation:

$$S/N=I_{peak}/\sigma_{STD\ of\ the\ noise}$$

where I_{peak} is the peak intensity of the analyte (above the average of the noise) and $\sigma_{STD\ of\ the\ noise}$ is the standard deviation of the noise. For each spectrum, the noise region was selected a few m/z before or after the analyte peak, and the noise region does not include any detectable ion peak.[1]

Calculation of LOD is based on the following formula:

$$LOD = (3 \times S)/k$$

where S is the standard deviation of the intercept and k is the slope of the calibration curve.[2]

9. Detections of several other molecules

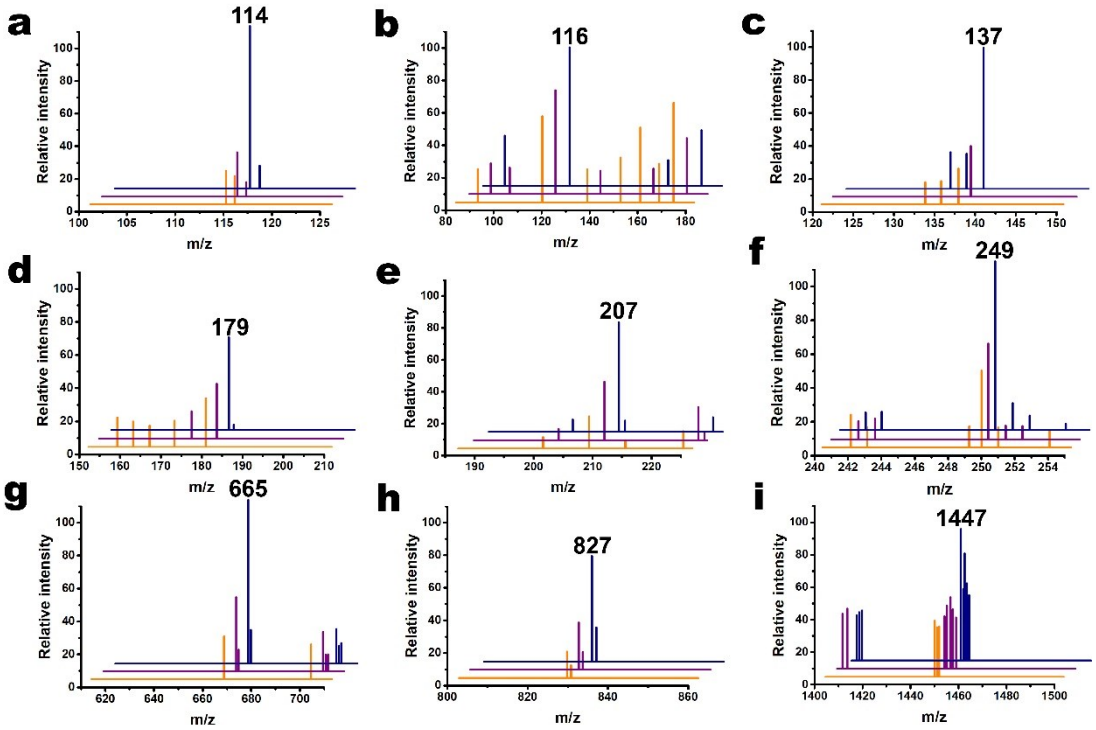

Figure S5. Negative ion mode PS-MS spectra of (a) L-Pro, (b) L-Val, (c) SA, (d) Glu, (e) 2-Naphthalene sulfonic acid, (f) BPS, (e) Maltotetraose, (h) Maltopentaose and (i) Vancomycin, by using h-FBN coated (blue), h-BN coated (purple) and pristine papers (orange).

10. Detections of TCM molecules

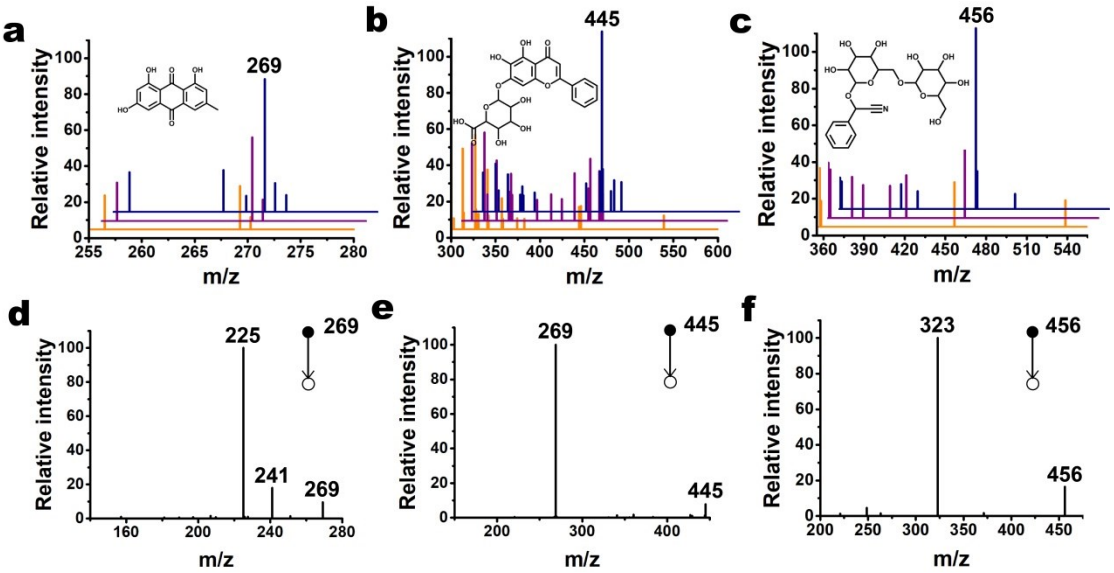

Figure S6. Negative ion mode PS-MS spectra of (a) emodin, (b) baicalin and (c) amygdalin using h-FBN coated (blue), h-BN coated (purple) and pristine paper (orange). Relative MS/MS spectra

of (d) emodin, (e) baicalin and (f) amygdalin.

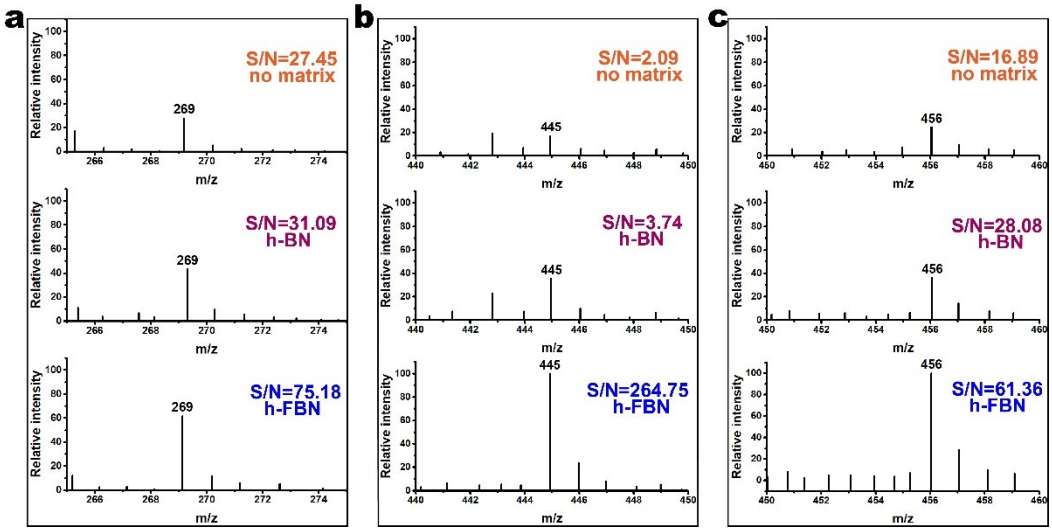

Figure S7. MS spectra and signal-to-noise ratio (S/N) of (a) emodin (b) baicalin and (c) amygdalin (orange: blank paper, purple: h-BN, blue: h-FBN).

11. Extract ion chromatogram of TCMs and background noises

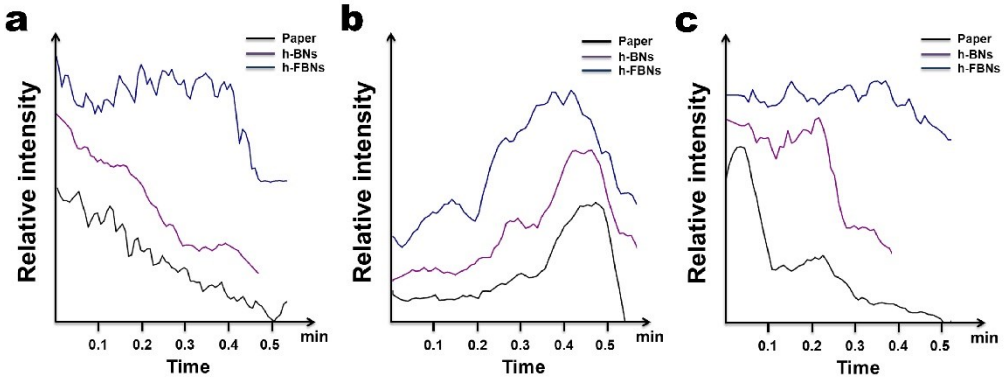

Figure S8. Extract ion chromatogram of (a) emodin, (b) baicalin, (c) amygdalin.

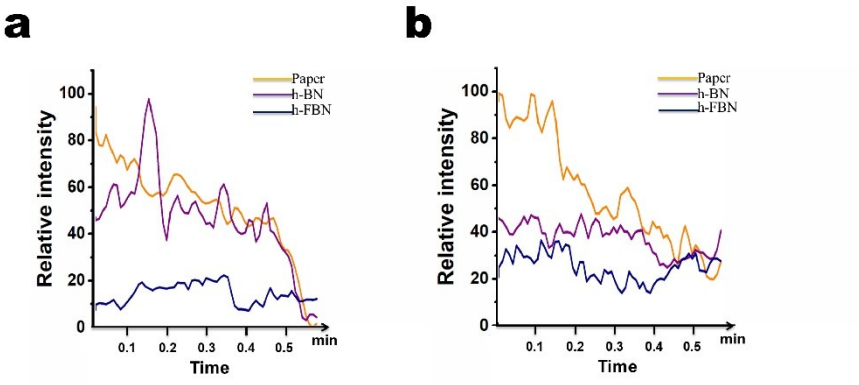

Figure S9. Extract ion chromatogram of background noise (m/z 325) in (a) baicalin and (b) amygdalin tests.

12. Calculations of S/N ratio for baicalin in blood samples

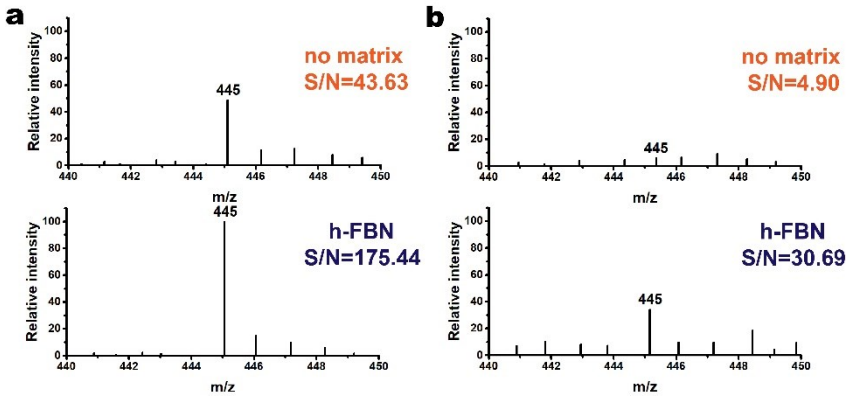

Figure S10. Negative ion mode PS-MS spectra of baicalin in (a) serum and (b) whole blood.

13. The performance compared with other studies

Table S1 The analytical performance of h-FBNs-assisted negative ion mode PS-MS compared with other studies

Molecules	Matrix	Amount	Ion Mode	Mass spectrometer
Amino acids	Graphene[3]	500 pmol	Positive	MALDI MS
Amino acids	gNG,[4] g-C_3N_4,[5] h-BN[6]	500 pmol	Negative	MALDI MS
Amino acids	GO/MWCN,[7] O−P,N-Doped Carbon/Graphene[8]	1 nmol	Positive/Negative	MALDI MS
Glucose	GO/MWCN[7]	1 nmol	Positive/Negative	MALDI MS
Glucose	O−P,N-Doped	1 nmol	Positive	MALDI MS

Glucose	Carbon/Graphene[8] paraffin barriers[9]	28 nmol (LOD)	Positive	PSI MS
BPA	g-C_3N_4[5]	1 nmol	Negative	MALDI MS
Salicylic acid	h-BN[6]	500 pmol	Negative	MALDI MS
Salicylic acid	urea-modified paper substrate[10]	109 pmol (LOD)	Negative	PSI MS
Amino acids	h-FBN	2.5 nmol	Negative	Our work
Glucose	h-FBN	2.5 nmol	Negative	Our work
BPA	h-FBN	1.7 pmol (LOD)	Negative	Our work
Salicylic acid	h-FBN	200 pmol	Negative	Our work

14. Contact Angles of h-BN and h-FBN

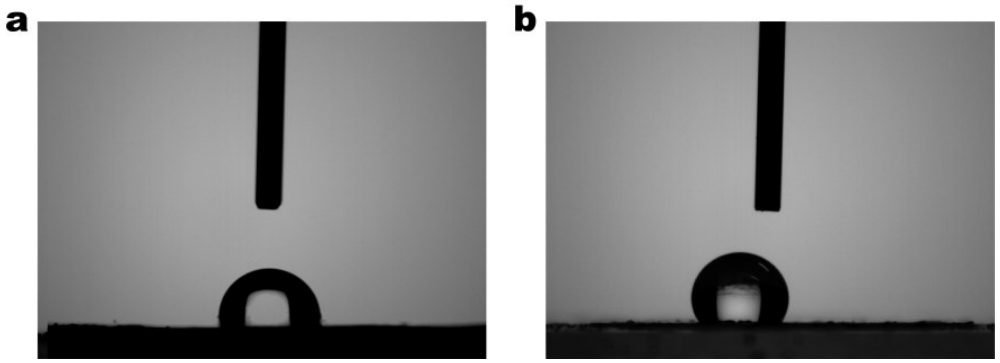

Figure S11. The contact angle measurements of (a) h-BN and (b) h-FBN.

15. Theoretical Modeling by Density Functional Theories

The theoretical modeling calculations were conducted at density functional theories (DFT) level that are implemented in the Vienna ab initio simulation package (VASP).[11,12] Projector-augmented wave (PAW)[13] potentials were used to describe the electron–ion interactions, while the electron exchange–correlation interactions were calculated using the generalized gradient approximation (GGA)[14] in the form of a Perdew–Burke–Ernzerhof (PBE) scheme. A plane-wave cutoff of 500 eV was used for Kohn-Sham electron wave function in all the calculations. Structurally, we

considered F-doping on h-BN monolayer which contain 3×3, 4×4 and 5×5 primitive cell. The corresponding F-doping ratio is 2~5.56%. Two F-doping on B and N atoms were considered. All the atomic positions and lattice vectors were fully optimized using a conjugate gradient algorithm to obtain the ground-state configuration. Atomic relaxation was performed until the change in total energy was smaller than 0.01 meV and all the Hellmann–Feynman forces on each atom were less than 0.01 eV/Å-1, which could guarantee fully relaxed structures.

16. Bader Charge Analysis

To quantitatively probe the different hydrophobicity of h-BN and h-FBN, we analyzed the surface polarization of these two nanomaterials by calculating the atomic charges. As shown in Fig. S12, Bader charge analysis[15] showed that there were +2.18 and -2.18 net charges on B and N atoms in h-BN which was well consistent with previous studies,[16, 17] revealing the high polarization of h-BN surface. For h-FBN, the net charge of F was only -0.80. For the nearest N atoms around F, the net charge also decreased to -2.04. Although the B connecting with F has a larger net charge of +2.26, it is sp^3 hybridized and spatially surrounded by four neighbors thus does not directly interact with the analyte molecules. Combining these data, the surface of h-FBN becomes more hydrophobic than h-BN.

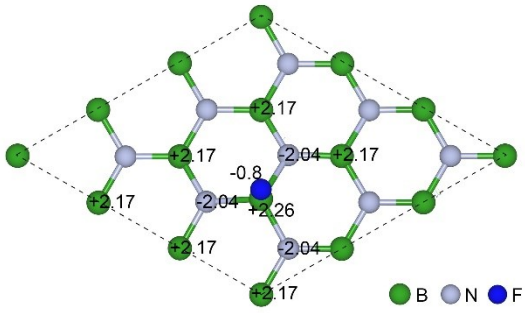

Figure S12. Net charges of h-FBN atoms in 3×3 supercell from Bader charge analysis.

17. References

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