Electronic Supplementary Material (ESI) for Journal of Materials Chemistry B.

Sensitive Detection of Clenbuterol by Hybrid Iridium/Silicon Nanowires-Enhanced Laser Desorption/Ionization Mass Spectrometry

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Abstract

There is an increasing demand in anti-doping drug monitoring in sports and food safety check by developing sensitive and fast analytical methods. Here we report the development of hybrid Ir/SiNW as a new MALDI matrix for detection of small molecules. This matrix is characteristic of sufficient UV absorption, low-noise background, and high efficiency in ionization of small molecules. Sensitive detection of clenbuterol (LOD: 0.18 pmol) and varieties of other small molecules have been achieved using Ir/SiNW matrix with a reproducible performance. Compared to the individual components separately, the matrix of hybrid Ir/SiNW synthesized via *in situ* growth can promote the MS signal intensity by up to 10 folds in the identical experimental conditions. We provide a unique mechanism for the high performance of hybrid Ir/SiNW matrix with the characteristic properties of hydrogen atom transferring and enhanced protonation at the interface of the hybrid nanostructures. Our approach of using hybrid Ir/SiNW matrix enables detection of clenbuterol quantitatively in complicated biological samples and *in vivo* experiments, promising a useful tool for food security and anti-doping drug monitoring in sports.

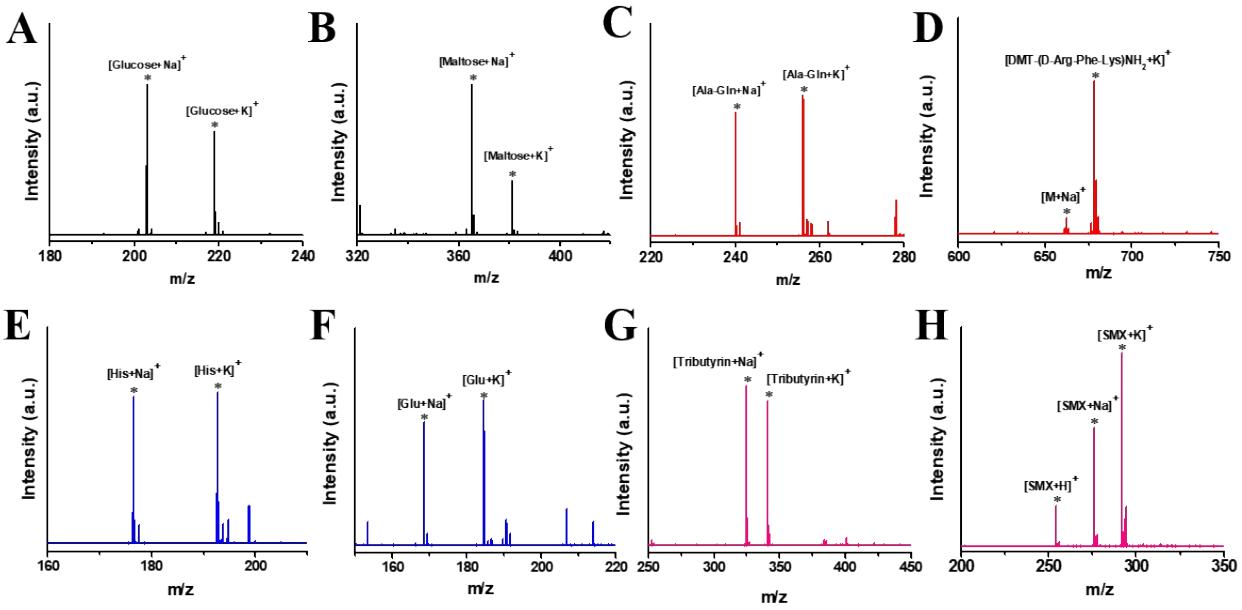

Fig. S1 Mass spectra of small molecular analytes in different categories using hybrid on Ir/SiNW matrix. (A) Glucose, (B) Maltose, (C) Ala-Gln, (D) DMT-[D-Arg-Phe-Lys]-NH_2, (E) Histidine, (F) Glutamate, (G) Tributyrin, (H) Sulfamethoxazole. Concentration: 100 mg/L. The relative laser power is 30 %. Each laser spot size is about 50 µm, each mass spectrum adds up to 3000 laser spots.

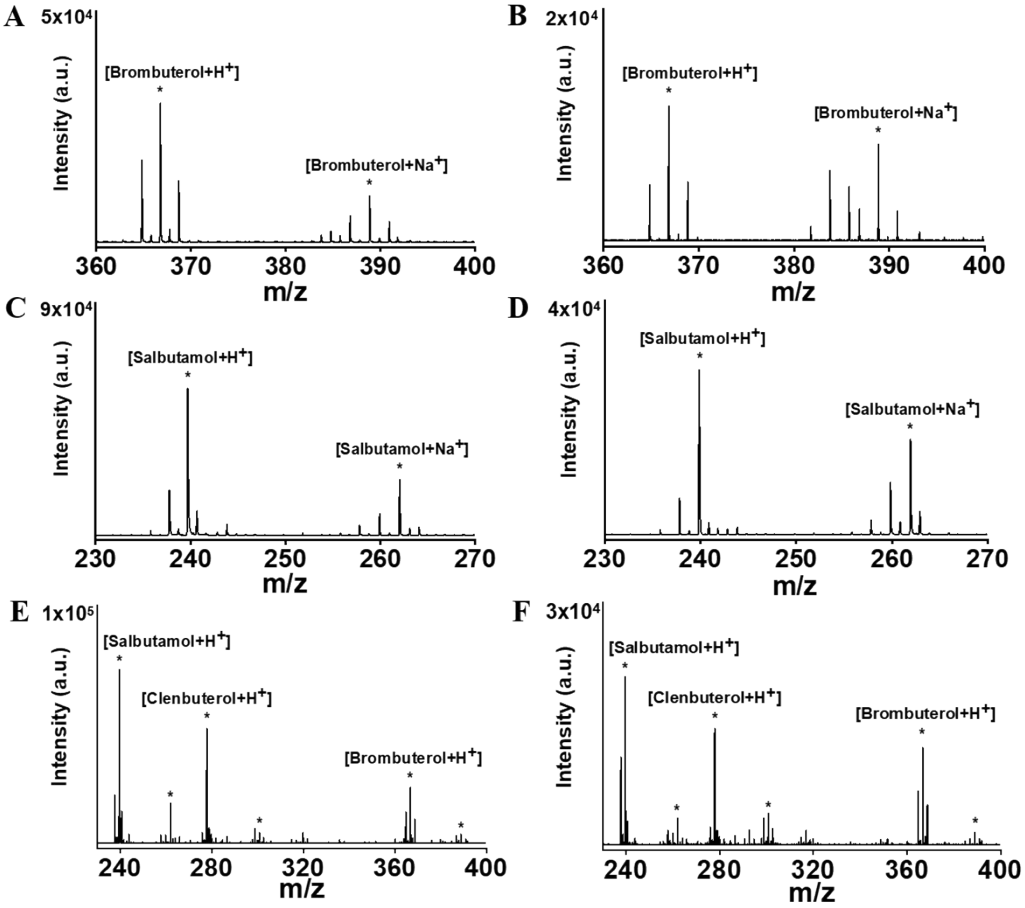

Fig. S2 Mass spectra of Brombuterol and Salbutamol using Ir/SiNW matrix. (A-B) Brombuterol, (C-D) Salbutamol, (E-F) Mixture of Brombuterol, Salbutamol and Clenbuterol. A, C and E prepared with DI water; B, D and F prepared with mouse serum. Concentration: 100 mg/L. Laser spot size: 50 μm. Accumulation: 3000 laser spots for each spectrum.

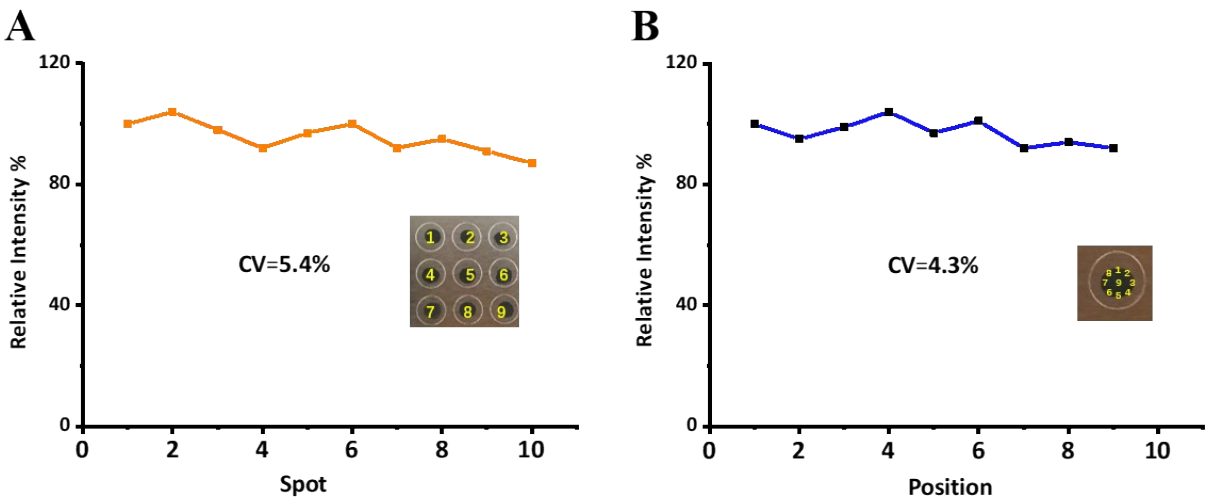

Fig. S3 Highly reproducible MS signal intensity by using the Ir/SiNW matrix. Analyte: clenbuterol. (A) 9 different spots in the 3 x 3 array. (B) 9 different positions in a single spot of analyte/ Ir/SiNW. The coefficient of variation (CV) values: only 5.4% spot-to-spot tests or 4.3% in the position-to-position tests. Insets: the photos of the spots deposited on the MALDI plate containing the analyte/matrix.

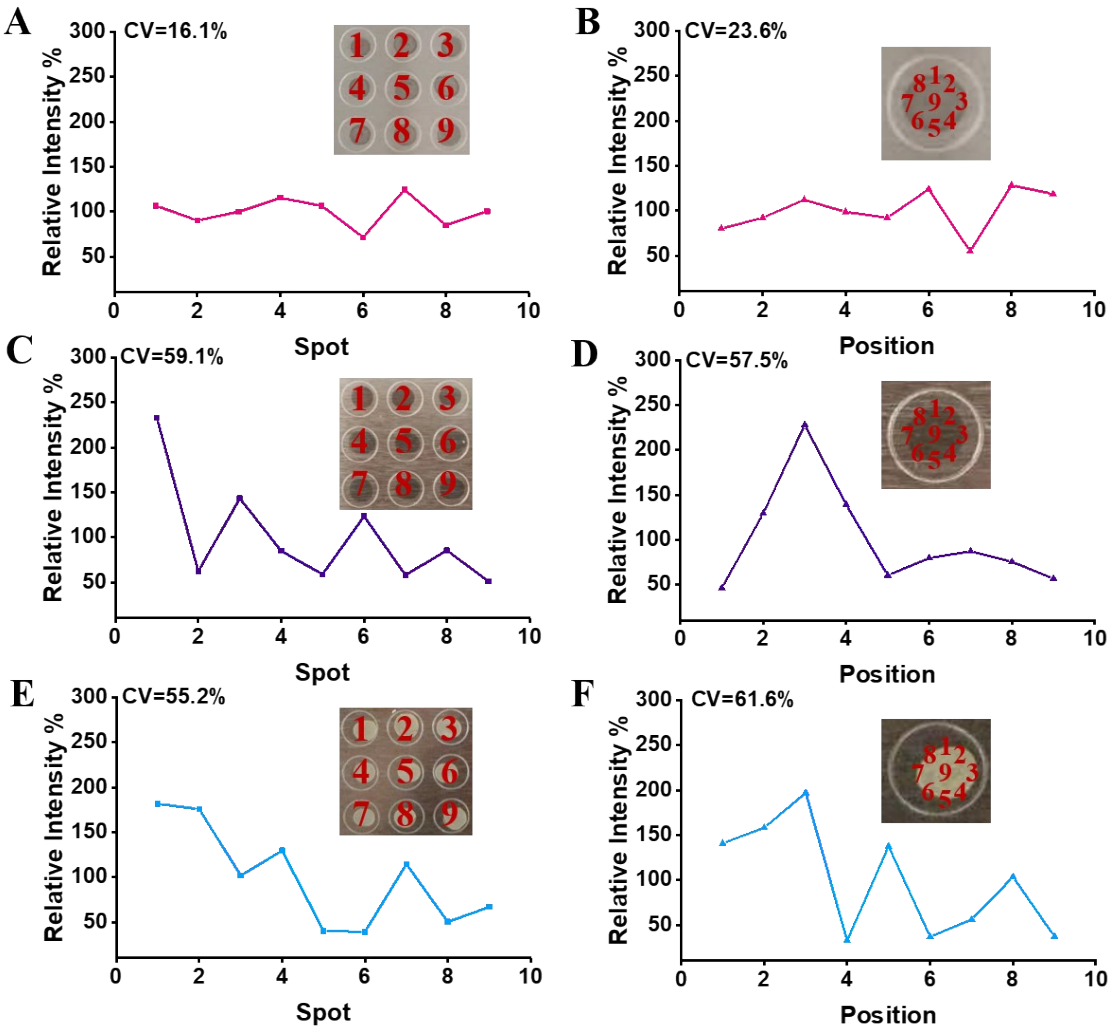

Fig. S4 Evaluation of MS signal reproducibility using different types of inorganic matrices for comparison. (A, C, E) 9 separate spots in the 3 × 3 array. (B, D, F) 9 different positions in a single spot of analyte/matrix. Insets: The photos of the spots deposited on the MALDI plate containing the analyte/matrix as specified. Matrices: Au nanoparticles (A, B), graphene oxide nanosheets (C, D), bare silicon nanowires (E, F). Analyte: clenbuterol.

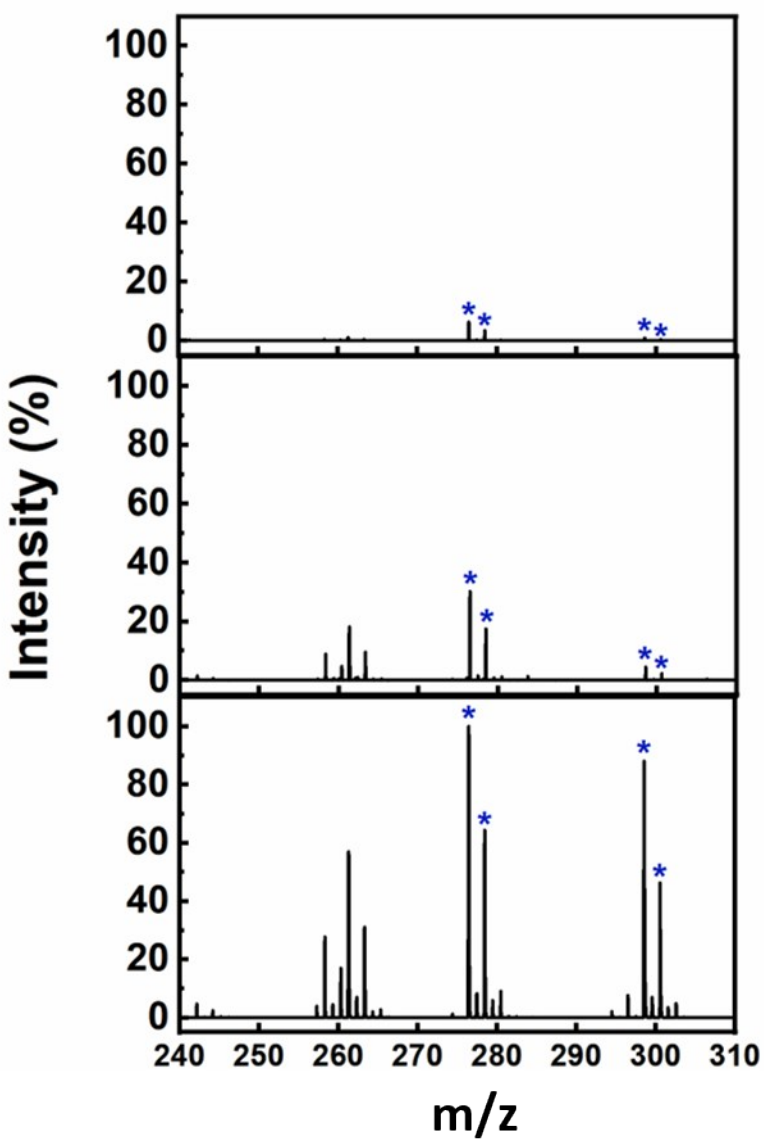

Fig. S5 Mass spectra of CL using Ir, SiNW, and Ir/SiNW matrices. The MALDI MS detection was performed in the positive-ion mode.

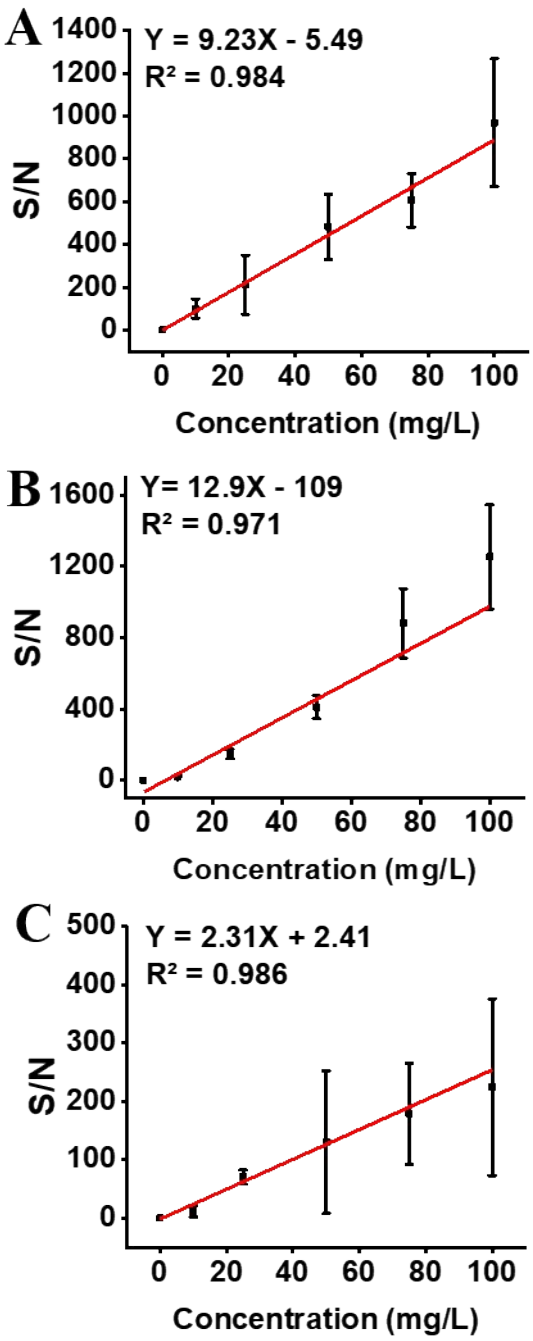

Fig. S6 Evaluation of organic matrices for the detection of CL, including (A) CHCA, (B) DHB, and (C) SA. Error bar: standard deviation (n=3).

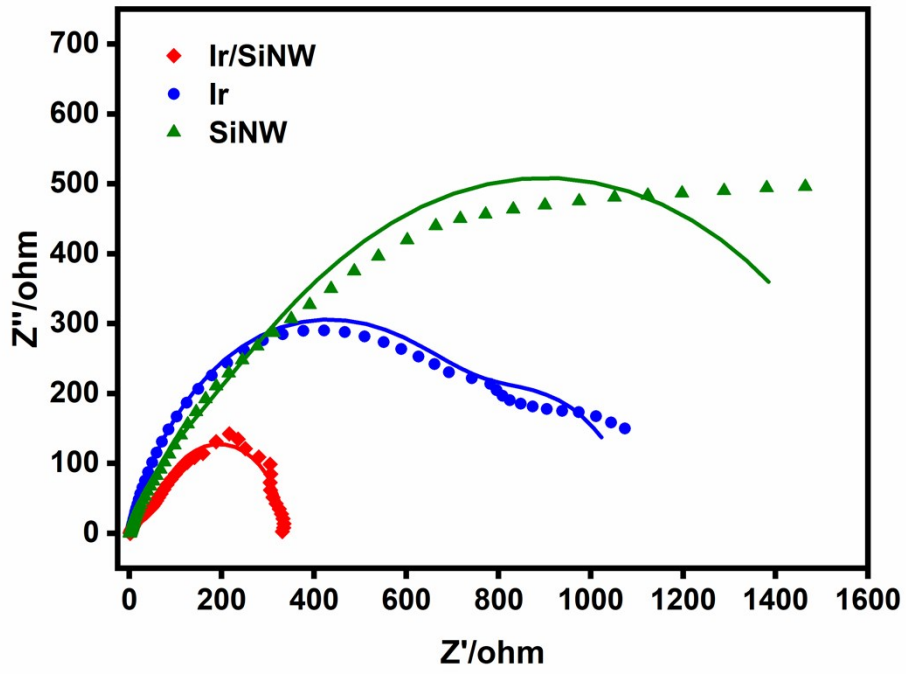

Fig. S7 Electrochemical impendence spectroscopy (EIS) analysis of Ir/SiNW, Ir nanoparticles, and bare SiNW. EIS measurements recorded between $1x10^5$ Hz and 0.1 Hz with a sinusoidal voltage perturbation of 5 mV amplitude.

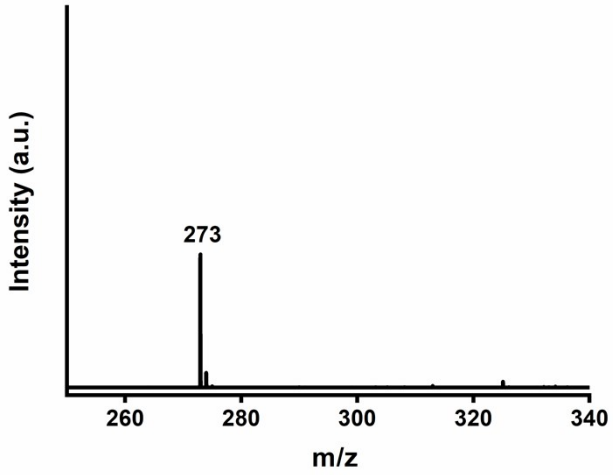

Fig. S8 Mass spectrum of the blank mouse blood sample without clenbuterol, after the identical procedure of sample pretreatment.

Table S1 Performance of Ir/SiNW matrix-assisted MALDI MS in comparison to other analysis techniques.

Method	Analyte	R^2	LOD*(pmol)	Concentration range (mg/L)	Internal standard	Sample Volume (μL)	Extraction procedure	Reproducibility
MALDI-TOF MS (our method)	clenbuterol	0.998	0.18	1-100	Clenbuterol-D9	1	3 steps	CV < 5.4%
HPLC[33]	clenbuterol	0.99	$2.8x10^{-3}$	$(1.38\text{-}5.52)\ x10^{-3}$	/	20	6 steps	CV: 4.5-8.5%
HPLC-MS[34]	ractopamine	0.999	0.507	5-1000	/	100	7 steps	CV > 5.8%
LC-ESI-TOF MS[35]	clenbuterol	0.998	$9.42\ x10^{-4}$	$(0.013\text{-}10)\ x10^{-3}$	Mabuterol	20	7 steps	CV: 1.3-7.0%
LC–MS/MS[36]	clenbuterol	0.999	$9.05\ x10^{-4}$	$(0.01\text{-}1)\ x10^{-3}$	Clenbuterol-D9	25	5 steps	CV: 0.7-17.9%
CE–UV[37]	clenbuterol	0.999	0.137	2-100	Terbutaline	40	8 steps	/
iEESI-MS[38]	Six β-agonists	0.999	/	/	/	100	/	RSD: 6.5-11.3%
Electrochemical detection aptasensor[39]	clenbuterol	0.991	0.181	$(0.1\text{-}500)\ x10^{-6}$	/	$5x10^3$	/	RSD: 2.09%

LOD*: limit of detection.

CV: coefficients of variation.

RSD: relative standard deviation.

/: Not Available.

Table S2 Performance comparison of silicon-based matrices and other inorganic nanomaterials for MALDI mass spectrometry

		Analyzed Molecules	LOD (S/N = 3)	Reproducibility	Mass spectra range	Concentration range (mg/L)
Silicon-based matrices	Ir/SiNW (This work)	clenbuterol	0.18 pmol	CV: ~ 5%	m/z 0-800	1-100
	Silicon nanopillar arrays[40, 41]	methadone	0.31 pmol	/	m/z 270-3000	0.02-2
	Silicon nanopowder[40, 42]	propafenone, verapamil et al.	33 fmol - 100 pmol	/	m/z 0-1000	0.003-455
	Periodic mesoporous organosilica (PMO) films[40, 43]	peptides	~ 0.6 pmol	/	m/z 500-1800	/
Other inorganic nanomaterials	Au NPs[44]	glutathione, angiotensin I, insulin	2 - 100 pmol	CV: 18-29%	m/z 300-1300	1.5-61.2
	Graphene Oxide[45]	tetracyclines	2 fmol	RSD: 2.33%	m/z 0-800	0.08-44.4
	Oxidized carbon nanotubes[46]	berberine, jatrorrhizine, palmatine	~ 3 fmol	RSD < 10%	m/z 0-3000	1-100
	Carbon nanodots[47]	amino acids, peptides et al.	2 fmol - 0.5 pmol	RSD < 4.2%	m/z 0-1000	90-1620