Electronic Supplementary Information

Lithium-rich composite metal oxide used as SALDI-MS matrix for the determination of small biomolecules

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Experimental Section

Chemicals and Materials.

MnO₂ nanoparticles (99.9% pure grade, 325 mesh), NiO nanoparticles (99% pure grade, 325 mesh), Co₃O₄ nanoparticles (99.7% pure grade, 2-6 micron) were obtained from Alfa Aesar (Ward Hill, MA USA). Methanol was purchased from Concord Technology Co., Ltd. (Tianjin, China). Ethyl acetate was purchased from Beijing Tongguang Fine Chemicals Co., Ltd.(Beijing, China). Purified water was obtained from Hangzhou Wahaha Group Co., Ltd. (Zhejiang, China). The standards of gliclazide and glipizide were purchased from the National Institute for the Control of Purmaceutical and Biological Products (Beijing, China). Trifluoroacetic acid (TFA) and Substance P were obtained from J&K Technologies Inc., China. Lipid standards were purchased from Avanti Polar Lipids (Alabaster, AL). Lys-bradykinin and Neaurotensin were purchased from Shanghai Apeptide Co., Ltd. (Shanghai, China). PEG4000, PEG6000, PEG 8000 were purchased from Beijng Yili Fine Chemicals Co., Ltd. (Beijng, China). Unless otherwise stated, all chemicals including Acetonitrile, 2,5-dihydroxylbenzoic Acid (DHB), α- cyclodextrin, β- cyclodextrin, γ-cyclodextrin, three maltoses, bradykinin, were all purchased from Sigma-Aldrich (St. Louis, MO, USA).

Stainless steel MALDI target plate and conductive ITO coated glass slides were purchased from Bruker Daltonik (Bremen, Germany).

Synthesis and characterization of lithium-rich composite metal oxide.

The lithium-rich composite metal oxide prepared sol-gel method was by а using ethylenediaminetetraacetic acid (EDTA) and citric acid as chelating agents, which have been reported previously. Briefly, stoichiometric amounts of lithium acetate, manganese acetate, nickel acetate and cobalt acetate were dissolved in water, then mixed with EDTA and citric acid solution and adjusted to pH ~8 with ammonia. The mixture was heated under constant stirring at 90°C for 12h until a gel formed, then heated at 450°C for 6 h to remove residual organics, and finally calcined at 900°C for 24h to obtain the final oxide powder.

The morphologies and microstructures of the material were examined by a cold field emission scanning microscopes (FE-SEM, S4800) operating at 10 kV.

Room temperature optical absorption spectra of the material powder was detected by Schimadzu UV-VIS-NIR recording spectrophotometer (UV-3100) with intergrating-sphere photometer.



Figure S1 UV-vis absorption spectra of the lithium-rich composite metal oxide

SALDI-MS analysis.

SALDI-MS spectra were acquired with an Ultraflex MALDI TOF/TOF mass spectrometer (Bruker Daltonics, Bremen, Germany) operating under reflection and positive mode and equipped with pulsednitrogen laser (337 nm). The accelerating voltage was set at 25 kV with a 70 ns extraction delay. Laser fluence was optimized between 20% and 40%. Each mass spectrum was generated by an average of 400 laser shots. The matrices were prepared with water at a matrix concentration of 1 mg/mL and 0.1% TFA(v/v). Analytes were added to the matrix solution and subsequently vortexed. Given their monodispersed state in solution, the lithium-rich composite metal oxide materials typically form homogeneous crystals with the analytes. Finally, 1 μ L of the mixture solution was pipetted onto the MALDI target plate and air-dried for subsequent MS analysis.

DHB matrix was prepared in CH₃CN/water (2:1, v/v) at a concentration of 30 mg/mL. For the traditional analysis, 1μ L of analyte solution was first spotted onto the plate and air-dired, followed by 1μ L DHB solution.

All the experiment were conducted on stainless steel target except the analysis of drug and synthetic molecules, which was carried out on glass target, for the reason that glass target is absolutely neat before use.



Figure S2 SALDI mass spectra of α- cyclodextrin (5 pmol) obtained using different matrices (a) MnO₂, (b) NiO, (c) Co₃O₄, (d) Lithium-riched composite metal oxide (# represent for [M+Li]⁺; • represent for [M+Na]⁺; * represent for [M+K]⁺).



Figure S3 The effect of different concentration of matrix (mg/mL): (a) 0.5, (b) 1, (c) 2, (d) 3 for the detection of α-cyclodextrin (5 pmol).



Figure S4 SALDI-MS spectrum of peptides (4 pmol): (a) Bradykinin fragment, (b) Neurotensin, (c) Lysbradykinin, (d) Substance P.



Figure S5 The SALDI-MS spectra of olive oil (50 µg/mL): (a) with DHB as matrix, (b) with inorganic material as matrix

Analysis results were compared between DHB matrix and lithium-rich composite metal oxide matrix. In this exploration, better signals were obtained with inorganic matrix (Figure S4), due to the homogeneous co-crystallization of analytes and inorganic matrix. More peaks with better intensities were observed with inorganic matrix. Peak identification were conducted by weight matching with theoretical values. However, no lithium-adduct ions were matched, that may due to the analytes properties. In this case, the lithium-rich composite metal oxide acted only as energy mediator.

Table S1 Signals obtained for the detection of olive oil			
m/z	Identification		
865.7	$[PtPtL+K]^+$		
881.4	$[OLL+H]^+$	$[OOLn+H]^+$	[POO+Na] ⁺
891.4	[SSS+H]+	$[PtLL+K]^+$	$[PLLn+K]^+$
907.4	[OOO+Na] ⁺	[SOL+Na] ⁺	
923.4	$[OOO+K]^+$	$[SOL+K]^+$	

P: palmitic acid; Pt: palmitoleic acid; O: oleic acid; S: stearic acid; L: linoleic acid; Ln: linolenic acid. (the lipids were confirmed by accurate molecular weight)