

Supplementary information

Surface enhanced Raman scattering microtips for microenvironment pH determination of semi-solid preparations

Xiangxin Lu,¹ Yunqing Wang,² Rongchao Mei,³ Xiaomeng Chong,⁴ Lingxin Chen,² Baoming Ning,^{*4} Rongjin Zhang,^{*5} Xuming Zhuang^{*1}

1. College of Chemistry and Chemical Engineering, Yantai University, Yantai 264005, China
2. CAS Key Laboratory of Coastal Environmental Processes and Ecological Remediation, Yantai Institute of Coastal Zone Research, Chinese Academy of Sciences, Yantai 264003, China
3. School of Pharmacy, Binzhou Medical University, Yantai 264003, China
4. National Institutes for Food and Drug Control, Key Laboratory of National Medical Products Administration-Key Laboratory of Research and Evaluation of Chemical Drug Quality, Beijing 102629, China;
5. SCMPA Key Laboratory for Quality Research and Control of Chemical Medicine, Chengdu 610000, China

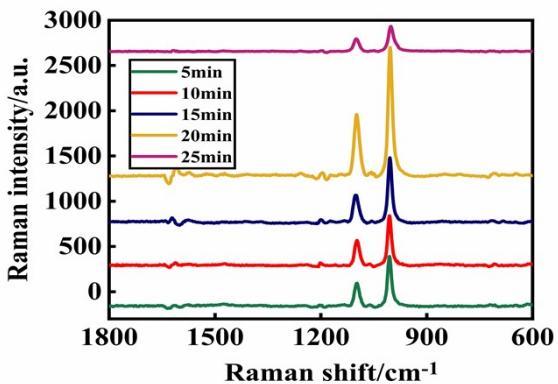


Figure S1. SERS spectra of microtips with different reaction times in Au^+ growth solution.

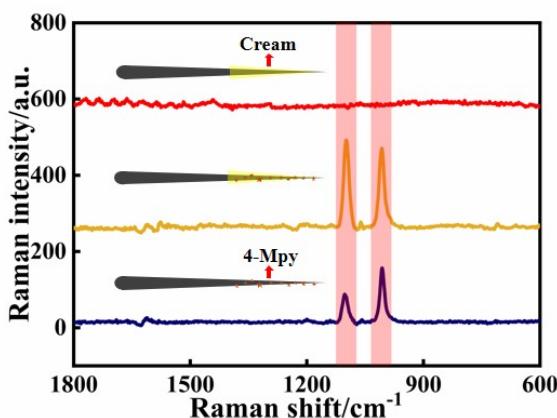


Figure S2. SERS signals of microtips at different conditions. Top: blank SERS microtip (no 4-Mpy) + cream; Middle: pH sensitive microtip + cream; Bottom: pH sensitive microtip.

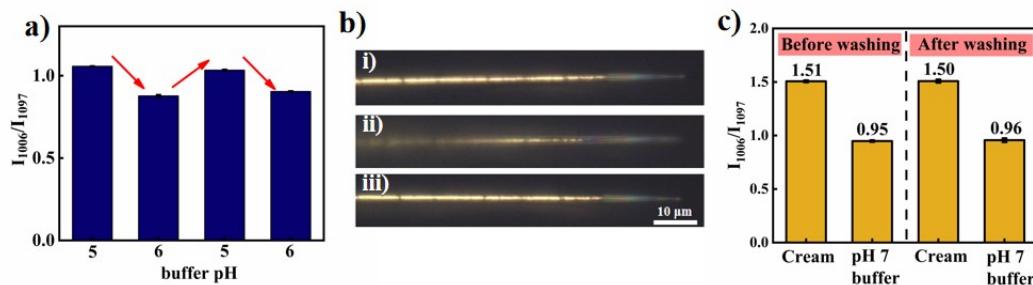


Figure S3. a) Histograms of I_{1006}/ I_{1097} changes of SERS microtips in different pH solutions; b) microscopic image of SERS microtip (i), SERS microtip with cream thin layer (ii), and the same SERS microtip after washing with ethanol (iii); (c) I_{1006}/ I_{1097} values of creams and pH 7 buffer solution by SERS microtips before and after ethanol washing, indicated that pH assay is reversible and the microtip can be reused.

Table S1. pH detection results of 8 brands of mupirocin ointment

Brand of cream	pH meter detection	SERS microtip detection (0-40 μm)
Benevolence	7.46	8.22
	7.53	8.49
	7.60	7.88
		8.20
		7.85
Pitbond	5.81	4.12
	5.87	3.88
	5.80	4.64
		3.82
		4.52
Mo Meishu	6.82	6.97
	6.93	6.27
	7.11	7.42
		6.03
		6.22
Aoqi	6.73	6.98
	6.84	7.23
	6.96	6.56
		7.72
Aegis	7.03	7.98
	7.18	7.83
	7.33	7.87
		7.64
		7.33
Baiduobang	6.93	7.93
	7.14	7.77
	7.23	8.11
		7.74
		7.77
Metdoxin	7.10	7.30
	7.05	7.24
	7.10	7.29
		8.13
		7.12
Kang Libang	7.10	6.33
	7.12	7.76
	7.15	7.47
		7.25
		7.05

Table S2. pH detection results of 7 brands of econazole nitrate creams

Brand of cream	pH meter detection	SERS microtip detection (0-40 μm)
Hengjian	3.70	3.87
	3.71	4.83
	3.67	5.59
		5.74
		5.55
Xuanqing1	3.53	1.71
	3.59	1.71
	3.62	1.80
		2.33
		2.57
Wei Danin	6.40	5.74
	6.34	6.65
	6.29	7.13
		7.23
		7.51
Xuanqing2	3.86	3.87
	3.76	4.05
	3.77	4.13
		3.91
		4.07
Benevolence1	7.03	5.45
	6.96	6.41
	6.98	5.31
		7.42
		7.80
Baiyun Mountain	3.50	3.00
	3.46	5.31
	3.43	5.74
		4.79
		5.12
Benevolence2	7.02	7.23
	6.98	5.37
	7.02	7.81
		7.32
		7.57

Table S3. pH detection results of 4 brands of metronidazole hydrogel

Brand of gel	pH meter detection	SERS microtip detection (0-40 μm)
Liv	4.64	3.68
	4.70	3.32
	4.71	4.11
		5.09
		5.11
Hardcore doctor	7.30	6.07
	7.23	6.03
	7.26	6.39
		7.23
		7.48
Hi Liaoto	5.44	3.93
	5.42	3.92
	5.50	5.56
		5.80
		5.51
Boom	5.48	4.52
	5.47	4.03
	5.45	5.28
		5.61
		5.44

Table S4. pH detection results of 4 brands of terbinaphthol hydrochloride hydrogel

Brand of gel	pH meter detection	SERS microtip detection (0-40 μm)
999	5.59	3.15
	5.65	3.62
	5.68	4.81
		4.07
		5.71
Vantone	4.85	5.74
	4.84	5.12
	4.80	5.93
		6.23
		6.88
Wei Danin	4.86	4.00
	4.91	4.50
	4.88	5.32
		5.19
		5.03
Better	5.05	4.49
	5.04	4.31
	5.00	4.64
		5.91
		5.64