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Tailoring the electrocatalytic activity of porous carbon with heteroatom dopants for the quantification of acetaminophen in pharmaceuticals and biological samples

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1. Chemicals

Acetaminophen (ACAP) and glucose were purchased from Alfa Aesar. Boric acid, dopamine hydrochloride (DA), NaOH were bought from SRL chemicals. Tetraethyl orthosilicate (TEOS), phytic acid (PA) and DMF were purchased from Sigma-Aldrich. Phosphate buffer (0.1 M) was prepared by using NaH_2PO_4 and Na_2HPO_4 from Merck. All the chemicals were exploited as received without further purification. Ultra-pure milli-Q water (18 MΩ cm^{-1}) was utilized throughout the experiments.

2. Characterisations

Prior to electrochemical sensing, porous nature of the prepared materials was characterized by Talos F 200S High-Resolution Transmission Electron Microscope (HR-TEM). Elemental doping was confirmed by (MULTILAB 2000, Thermo Scientific) XPS analysis. The topology of the prepared porous carbon materials was analysed with Field-Emission Scanning Electronic Microscope (FE-SEM; performed with Carl Zeiss AG Supra 55 VP). XRD patterns were recorded on Bruker X-pert diffractometer with Cu Kα radiation. N_2 adsorption−desorption was determined by Brunauer−Emmett−Teller (BET) measurements using Autosorb iQ Station 1 analyzer. Raman spectra were taken by using RM 1000, Renishaw

UK Micro Raman Instrument and thermogravimetric analysis was taken by employing SDT Q600 V8.3 Build 101, TA instrument

2.1 Preparation of hard template- SBA-15

47 mL TEOS was added deliberately into a premixed solution of structure directing pluronic-123 polymer ($EO_{20}PO_{70}EO_{20}$) 20 g and 40 mL of HCl. The mixture is blended for about one day at 313 K. The product was kept in an oven at 373 K for 24 h followed by washing with copious amount of water and ethanol and dried. The as-synthesized SBA-15 was air-calcinated at 773 K for 4 h to eliminate structure directing surfactant.

2.2 Preparation of NP-MC

N, P dual-doped micro/mesoporous carbon was synthesized by pore-filling wet-impregnation process. Initially 1.25 g of glucose was dissolved in 5 mL of H_2O. For N and P doping, 0.4 g of DA and specific amount of phytic acid were mixed under stirring. Then, 1 g of SBA-15 was infused into the above mixture for impregnation up to 6 h. In addition, 0.14 g of H_2SO_4 was introduced dropwise with persistent stirring. Afterwards, two step hydrothermal treatment was done starting from 100 ºC (6 h), further by increasing 160 ºC (6 h). The mixture was taken out after cooling down to room temperature (RT). Separately, 0.8 g of glucose was dissolved with 5 mL water and 0.09 g of H_2SO_4 added to it. Finally, the prepared solution was mixed with the above cooled solution, further hydrothermal process carried out with the above-mentioned experimental procedure. The obtained product was washed, dried and transferred to alumina boat crucible and further pyrolyzed at 900 ºC about 4 h in a horizontal quartz tube under Ar atmosphere. The carbonized product was blended with 2 M NaOH solution and stirred to remove the SBA-15 template thoroughly. The resultant NP-MC product was washed and dried at 90 ºC. The NB-MC was synthesized by the same procedure with the addition of boric acid instead of phytic acid. The N-MC was prepared by the aforementioned procedure in the absence of phytic acid and the MC was synthesized without adding any N and P sources.

2.3 Electrochemical measurements

Prior to modification, glassy carbon working electrode (GCE) has been micro polished using alumina slurry (0.1, 0.03 and 0.05 micron), then cleaned ultrasonically with water and ethanol, respectively. Thereafter, 1 mg of synthesized carbon samples were dispersed into 200 µL of DMF and ultrasonicated up to 30 mins. Further, thin electroactive layer (3 µL) of dispersed sample with catalyst loading of 0.214 mg cm^{-2} were dropped on cleaned GC surface and sustained at RT until entire solvent vanished. The modified working electrodes were applied to detect ACAP by employing cyclic voltammetry (CV), differential pulse voltammetry (DPV) and chrono amperometry (CA) techniques.

Autolab electrochemical workstation (PGSTAT 302 N) controlled with NOVA 1.11 software was utilized to run electrochemical experiments with a conventional three-electrode cell. GCE was used as a working electrode. Pt wire and saturated calomel electrode (SCE) were employed as counter and reference electrode, respectively. DPV measurements were obtained for applied potential 0.1 V to 0.6 V with sweeping rate of 10 mV s^{-1}, pulse amplitude of 25 mV, modulation time at 0.2 s for electroanalytical operations.

2.4 Real sample analysis

Commercial acetaminophen pills (Cipla-500) were purchased from local drug store and pulverised with mortar. Specific amount of ACAP drug was weighed and dissolved in PBS (pH-7.5) followed by sonication and filtered through Whatman filter paper (Axiva-420R) [24]. Blood serum samples collected from healthy volunteer has been diluted (20 times) using PBS to minimize matrix effect [3]. For analysing exact quantification of ACAP, freshly prepared synthetic urine, saliva and sweat samples were used immediately as reported in the previous literature [25]. The freshly prepared ACAP solution has been spiked into the aforesaid real samples.

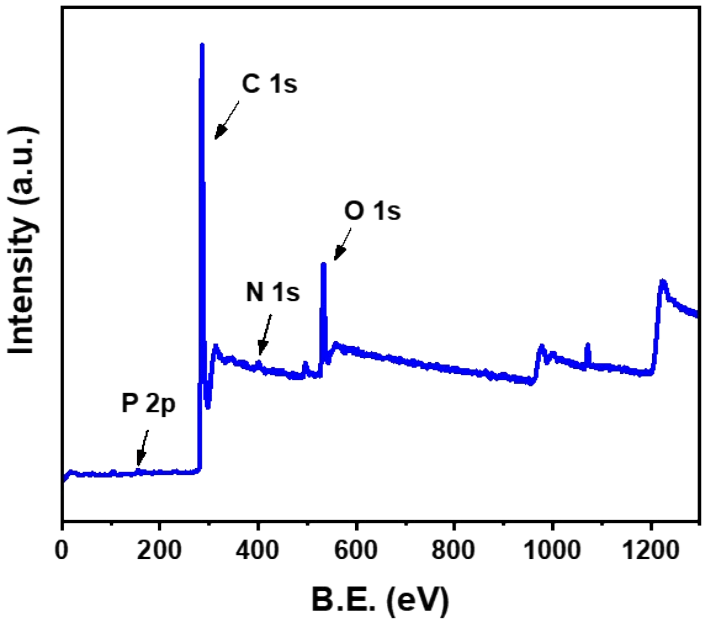

Figure S1: Survey spectrum of NP-MC.

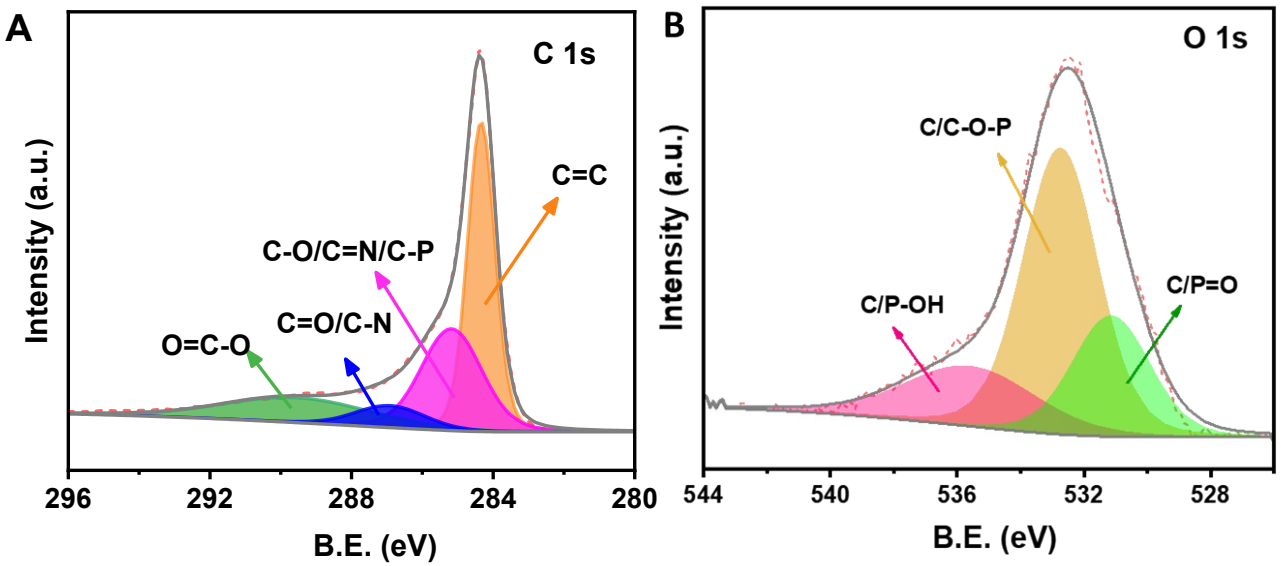

Figure S2: XPS spectra of C 1s (A) and O 1s (B) for NP-MC.

Table S1: Pore structure parameters of MC samples

S.No	Carbon samples	BET-Surface area (m^2/g)	Total pore volume (cm^3/g)	Pore size distribution (nm)
1	MC	1020	0.11	4.4
2	N-MC	797	0.132	3
3	NB-MC	808	0.169	4.3
4	NP-MC	970	0.171	3

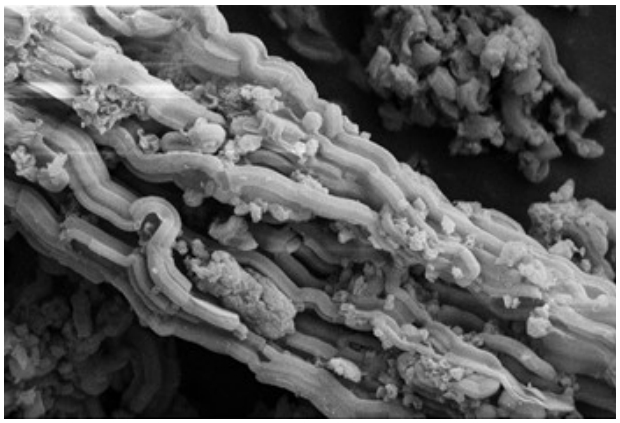

Figure S3: FESEM image of SBA-15

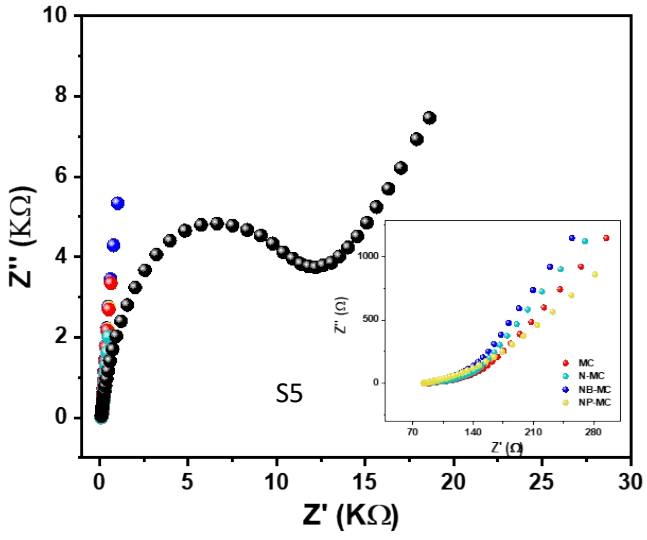

Figure S4: Nyquist plot of Bare GCE, MC, N-MC, NB-MC and NP-MC.

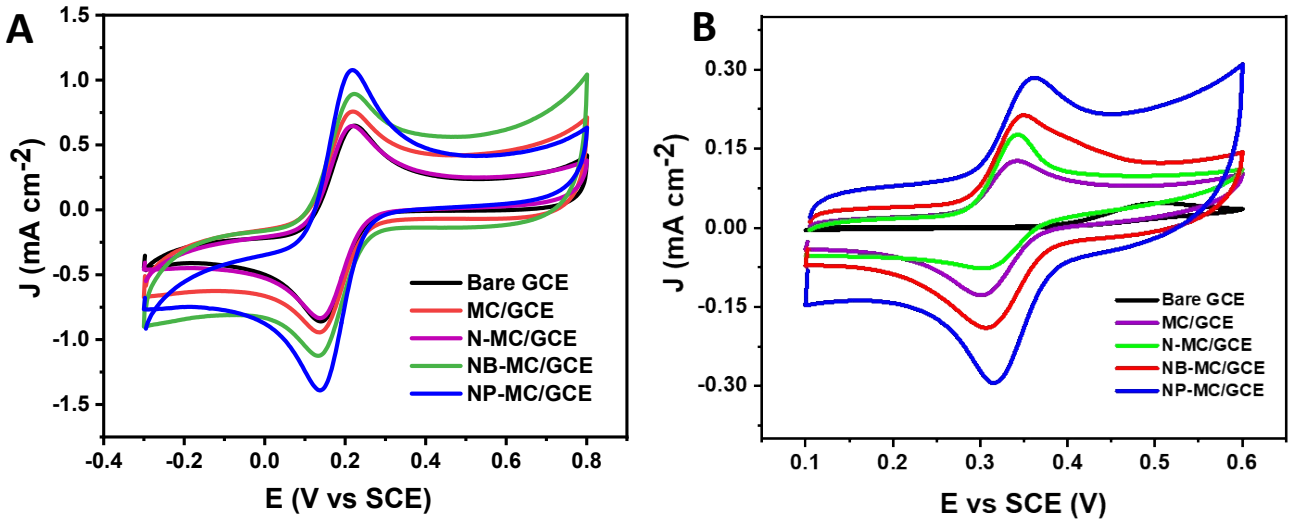

Figure S5: Cyclic voltammograms of modified electrodes at 25 mV s^{-1}; (A) $[Fe(CN)_6]^{3-/4-}$ redox system; (B) N_2-saturated 0.1 M PBS with 0.2 mM ACAP.

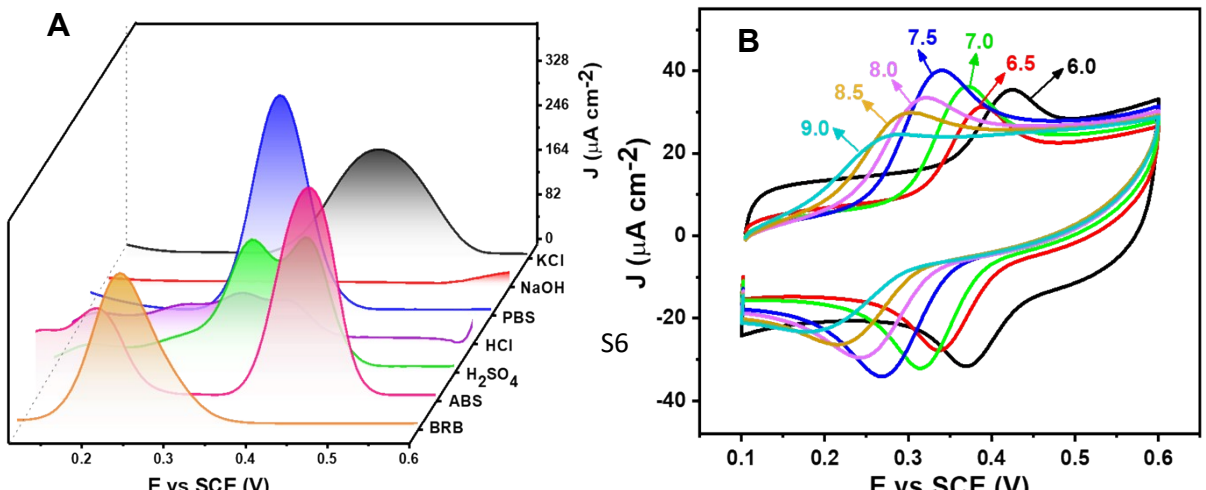

Figure S6: Cyclic voltammetric curves of NP-MC/GCE, (A) In different Supporting eletrolytes; (B) In different pH from 6.0-9.0.

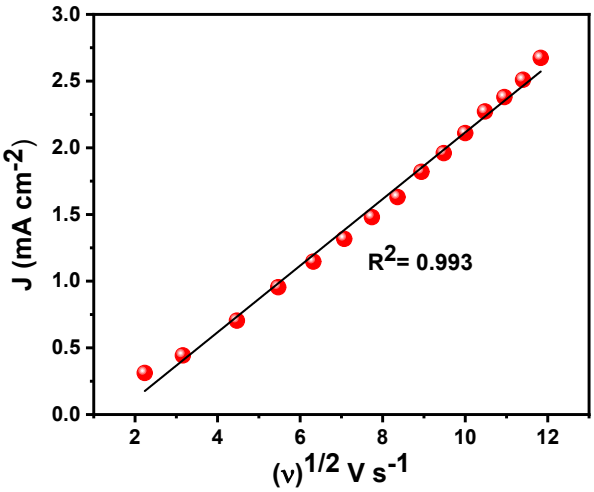

Figure S7: Plot of (Jpa) vs $(\upsilon)^{1/2}$ of NP-MC in 0.1 mM ACAP at different scan rates (5 to 140 mV s^{-1}).

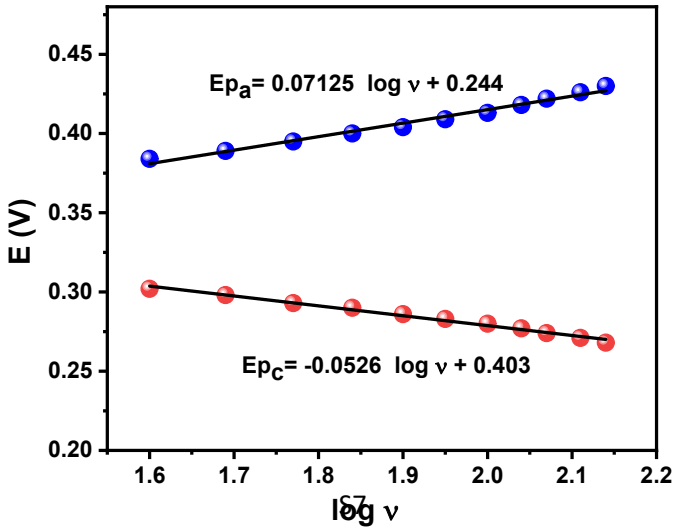

Figure S8: plot of E vs log (υ) of NP-MC in 0.1 mM ACAP at different scan rates from 5 to 140 mV s^{-1}.

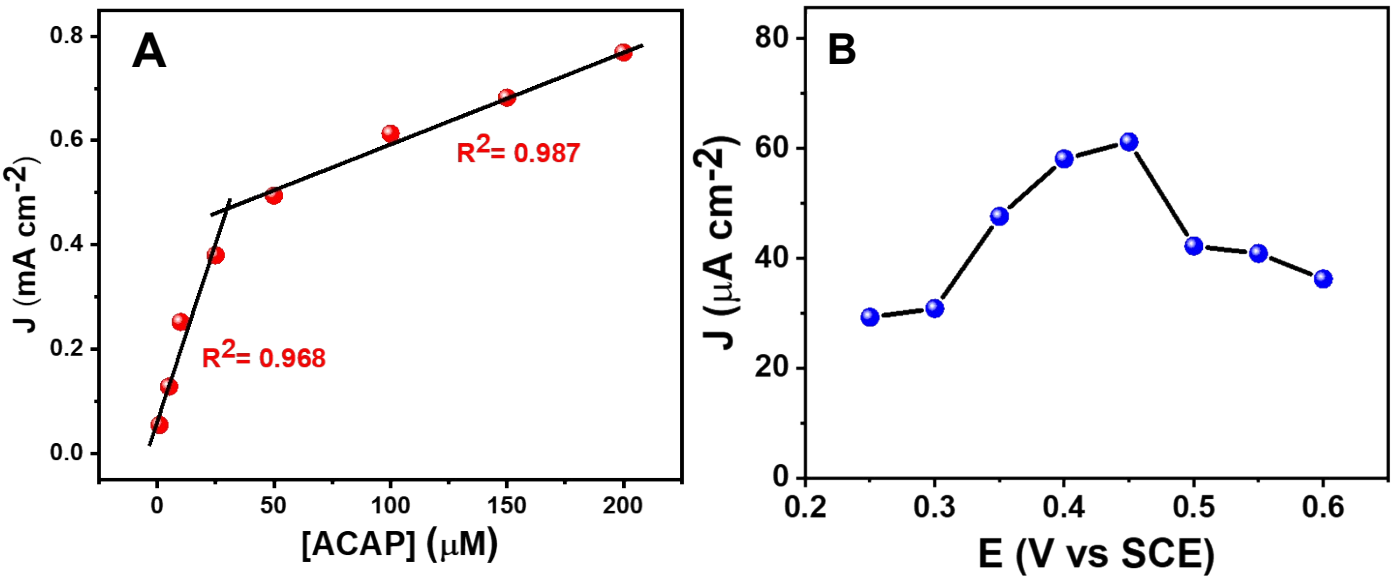

Figure S9: (A) linear calibration fit with different ACAP concentration in DPV (B) CA potential optimization study using an addition of 0.1 mM ACAP in 0.1 M PBS (pH-7.5) at various applied potential from 0.25 to 0.6 V over NP-MC/GCE.

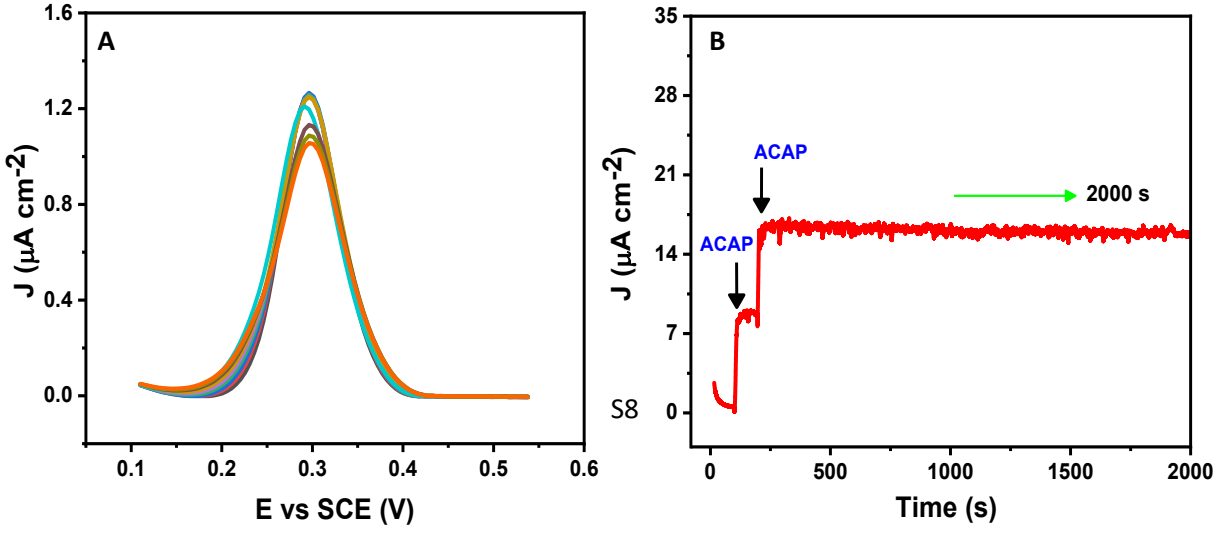

Figure S10: DPV interference effect of NP-MC with 10-fold NaCl, KCl, $CaCl_2$, $MgCl_2$, $CuSO_4$, glucose and biomolecules with 5- fold excess of uric acid (UA), dopamine (DA) and ascorbic acid (AA) and (B) Dynamic amperometric stability response of NP-MC upto 2000 s.

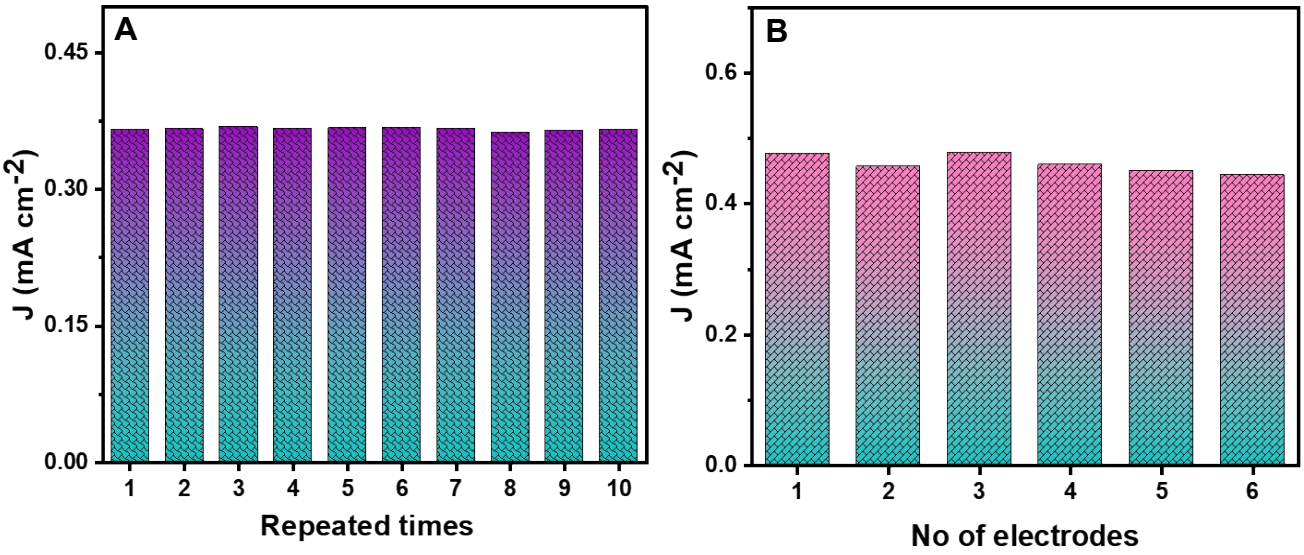

Figure S11: (A) Repeatability of NP-MC modified electrode for 10 times with a time interval of 3 min and (B) reproducibility of NP-MC modified electrode with 6 different electrodes in 0.1 mM ACAP.

Table S2: Comparison of analytical parameters of different modified electrode for the detection of ACAP.

S.No	Materials	Linear range	Electrochemical Technique	LOD (µM)	Sensitivity	ref
1	N-CMOS	0.1-80 µM	DPV	0.0303	1.971 µA μM^{-1} cm^{-2}	[1]
2	N-MWCNT	0.118–0.907 mM	CV	0.485	0.601 A M^{-1} cm^{-2}	[2]
3	Pd/POMs/NHCSs composite	0.02 µM - 0.083 mM	DPV	0.003	508.46 µA mM^{-1}	[3]
4	NP-CM	0.07 µM - 30 µM	DPV	0.04	19.3 µA $\mu M^{-1}cm^{-2}$	[4]
5	H–C/N@TiO_2	0.3–50 µM	DPV	0.05	NR	[5]
6	NCDs	0.5 - 600 µM 0.05 µM - 2.250 mM	DPV Amperometry	0.157 0.041	NR	[6]
7	NG-BDD	0.02−50 µM	DPV	0.005	NR	[7]
8	P-NC/GCE	3–110 µM	DPV	0.5	NR	[8]
9	NP-MC	1-200 µM 3-4000 µM	DPV Amperometry	0.038 0.027	13.21 µA μM^{-1} cm^{-2} 36.14 µA μM^{-1} cm^{-2}	This work

NR- Not reported; H–C/N@TiO_2 -Nitrogen-doped Carbon@TiO_2 double-shelled hollow spheres; N-CMOS - N-doped carbon dots/manganese oxide; N-MWCNT - Nitrogen-doped MWCNTs; Pd/POMs/NHCSs composite- Pd/Polyoxometalate/Nitrogen-doping Hollow Carbon Spheres; NP-CM- N, P-co-doped carbon microspheres; NCD- Nitrogen doped carbon dots; NG-BDD Graphite/Boron-Doped diamond; P-NC/GCE – Nitrogen rich porous carbon.

Table S3: Detection of ACAP in blood serum, pharmaceutical tablets and synthetic sweat, saliva and urine samples.

Samples	Added ACAP (µM)	Found ACAP (µM)	Recovery (%)	RSD
Human blood serum samples 	10 20 30	9.51 18.91 29.56	95.1 94.5 98.5	2.30 1.62 2.35
ACAP tablet 	10 20 30	10.5 19.71 29.2	105 98.5 97.3	3.51 2.65 2.39
Synthetic urine samples	10 20 30	9.85 18.63 28.65	98.5 93.15 95.5	4.10 3.62 2.98
Synthetic sweat samples	10 20 30	10.4 18.9 31.8	104 94.5 106	3.69 3.68 4.03
Synthetic saliva samples	10 20 30	9.68 21.0 29.6	96.8 105 98.6	2.78 4.32 1.63

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