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Wet-chemically prepared low-dimensional ZnO/Al₂O₃/Cr₂O₃ nanoparticles for xanthine sensor development using an electrochemical method†

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A reliable xanthine (XNT) chemical sensor was fabricated using a facile wet-chemical method (by co-precipitation) to prepare ZnO/Al₂O₃/Cr₂O₃ nanoparticles (NPs) in an alkaline medium at low temperature. Powder X-ray diffraction (XRD), X-ray photoelectron spectroscopy (XPS), field emission scanning electron microscopy (FESEM), energy-dispersive X-ray spectroscopy (EDS), Fourier transform infrared spectroscopy (FTIR) and ultraviolet-visible spectroscopy (UV-vis) were implemented for detailed characterization of the NPs. To fabricate the working electrode as a XNT chemical sensor probe, a glassy carbon electrode (GCE) with a 0.0316 cm² surface area was coated with an ethanolic slurry of the prepared ZnO/Al₂O₃/Cr₂O₃ NPs to make a thin layer and used to analyse XNT in a phosphate buffer system. To evaluate the analytical performances of the XNT chemical sensor, the calibration curve of XNT was plotted as the relationship of current versus the concentration of XNT. The plotted calibration curve was found to be linear over the LDR (linear dynamic range) of 0.05 nM to 5.0 μM. The assembled XNT electrochemical sensor exhibited the highest sensitivity (70.8861 μA μM⁻¹ cm⁻²), the lowest detection limit (1.34 ± 0.07 pM), good reproducibility performance with high accuracy and long-term stability with standard results under ambient conditions. This is a simple route to selectively detect XNT with wet-chemically prepared co-doped ZnO/Al₂O₃/Cr₂O₃ nanomaterials using a reliable electrochemical method at a large scale for safety within healthcare fields.

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Introduction

Chemically, XNT is known as 3,7-dihydropurine-2,6-dione, and is an intermediate metabolized product of purine in the human body. Therefore, it is found in the human body at concentrations ranging from 0.5–2.5 μM in blood serum and 40–160 μM in urine.^{1,2} In the metabolism pathway of purine, XNT is oxidized to uric acid by an enzymatic reaction in the presence of XNT oxides (XOs). For excess XNT levels above the normal range, a number of pathological indicators such as hyperuricemia, tumour hyperthermia, xanthinuria, perinatal asphyxia, pre-eclampsia, leukemia, cerebral ischemia, and gout are recognized in the human body.^{3–5} The derivatives of XNT (caffeine and theobromine) are found as mild stimulants in drinks such as coffee and tea. To produce high quality foods,

the meat of fresh fish is used in food industries. Due to the degradation of ATP in dead fish, XNT is produced naturally.^{6,7} To determine XNT in human serum and food, a reliable and efficient method is needed for safety within the health and food sectors.^{8,9} HPLC (high-performance liquid chromatography),^{10,11} voltammetric and amperometric,^{12,13} and electrophoresis¹⁴ methods are extensively implemented to detect XNT quantitatively in an aqueous medium. In recent years, a number of research activities to detect XNT using electrochemical methods based on various metal oxides and hybrid materials have been reported.^{15–18} The aim of this research approach is to develop an electrochemical sensor using an electrochemical method based on ZnO/Al₂O₃/Cr₂O₃ NPs.

ZnO is a semi-conductive oxide with a 3.3 eV band gap energy, a 60 meV exciton binding energy, a high range of resistivity (10⁻³–10⁵ Ω cm) and transparency in the visible wave region.^{19–23} Therefore, ZnO shows good optical, electrical and piezo-electrical properties^{24,25} and these outstanding properties make ZnO a strong candidate in the field of sensor applications. As a sensor material, ZnO has been applied to detect many toxic chemicals such as acetone,²⁶ ethanol,²⁷ 4-aminophenol,²⁸ and bisphenol A²⁹ in an aqueous medium. With attractive photo-electronic characteristics, Al₂O₃ has also been applied as a chemical and biological sensor.^{30–32} Another active transition

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metal oxide Cr_2O_3 has also found use in catalysis, wear resistant materials, colorants, and optical and electronic devices.^{33–36} Besides this, the binary combination of $\text{ZnO}-\text{Al}_2\text{O}_3$ has found use as a sensor to detect catechol, hydroquinone³⁷ and methyl violet dye.³⁸ Moreover, $\text{ZnO}-\text{Cr}_2\text{O}_3$ has been reported as an efficient sensor material to detect ethanol³⁹ and LPG.⁴⁰

To execute this study, an electrochemical sensor was fabricated by deposition of $\text{ZnO}/\text{Al}_2\text{O}_3/\text{Cr}_2\text{O}_3$ NPs onto a GCE as a uniform thin layer with the help of a conducting Nafion binder. Thus, the resulting working electrode probe ($\text{ZnO}/\text{Al}_2\text{O}_3/\text{Cr}_2\text{O}_3$ NPs/binder/GCE) for XNT was implemented to detect XNT in an optimized phosphate buffer system using an electrochemical method under ambient conditions. This research approach might be a reliable and easy method to develop future sensitive chemical and biological sensors based on various doped or undoped ternary metal oxides.

Materials and methodology

Materials and methods

To prepare the ternary metal oxides, analytical grade chemicals such as $\text{Al}_2(\text{SO}_4)_3 \cdot 18\text{H}_2\text{O}$, $\text{Zn}(\text{NO}_3)_2 \cdot 6\text{H}_2\text{O}$, and $\text{Cr}(\text{NO}_3)_3 \cdot 9\text{H}_2\text{O}$ were purchased and used as received. As part of this investigation, various toxins namely 2,4-DNP (2,4-dinitrophenol), 2-APy (2-acetyl pyridine), BC (benzyl chloride), DEM (diethyl malonate),

EG (ethylene glycol), *M*-THyd (*M*-tolyl hydrazine hydrochloride), *M*-Xy (*M*-xylol), Zdehy (zimtaldehyde), and XNT were obtained from Sigma-Aldrich (USA). A Thermo-Scientific $\text{K}\alpha 1$ 1066 X-ray photoelectron spectroscopy (XPS) instrument with an excitation radiation source (A1 $\text{K}\alpha 1$, beam spot size = 300.0 μm , pass energy = 200.0 eV and pressure $\sim 10^{-8}$ torr) was used to study the binding energy and oxidation state of the elements existing in the synthesized $\text{ZnO}/\text{Al}_2\text{O}_3/\text{Cr}_2\text{O}_3$ NPs. To characterize their ability to absorb visible light, the prepared NPs were examined using a Thermo-Scientific 300 UV-vis spectrometer. A Thermo-Scientific NICOLET iS50 (Madison, WI, USA) FTIR spectrometer was used to identify the functional groups in the $\text{ZnO}/\text{Al}_2\text{O}_3/\text{Cr}_2\text{O}_3$ NPs. The elemental composition and structural morphology were inspected using FESEM analysis equipped with XEDS. The phase crystallinity and particle size of the prepared NPs were evaluated using powder X-ray diffraction (XRD) with an ARL™ X'TRA powder diffractometer. The electrochemical investigation was carried out using a Keithley electrometer (6517A, USA).

Synthesis of the $\text{ZnO}/\text{Al}_2\text{O}_3/\text{Cr}_2\text{O}_3$ NPs

To synthesise nanomaterials of transition metal oxides, the wet-chemical (co-precipitation process) method is an efficient, conventional method in an alkaline medium with pH 10.5. $\text{Al}_2(\text{SO}_4)_3 \cdot 18\text{H}_2\text{O}$, $\text{Zn}(\text{NO}_3)_2 \cdot 6\text{H}_2\text{O}$, and $\text{Cr}(\text{NO}_3)_3 \cdot 9\text{H}_2\text{O}$ are used

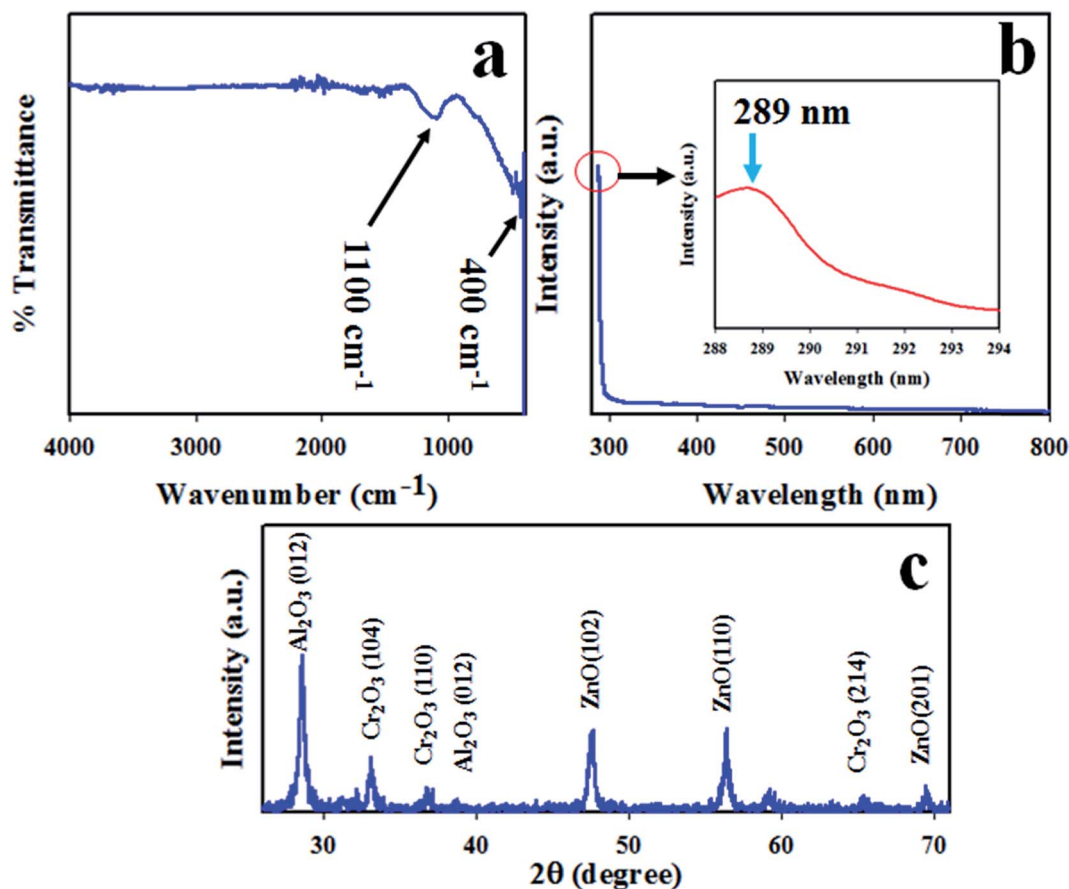
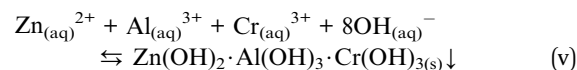
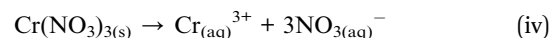
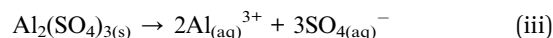
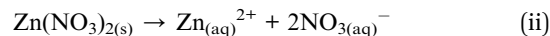
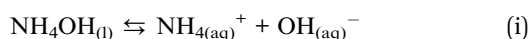


Fig. 1 The optical properties and crystallinity of the synthesized $\text{ZnO}/\text{Al}_2\text{O}_3/\text{Cr}_2\text{O}_3$ NPs. (a) FTIR analysis, (b) UV-vis spectrum, and (c) phase crystallinity.



to prepare a 0.1 M solution of each salt individually. 100.0 mL round bottom flasks with deionized water and 50.0 mL of each solution in a 250.0 mL conical flask were taken for the synthesis of the doped nanomaterials. Then, the conical flask was put on a hot plate at a temperature of 80 °C with continuous magnetic stirring. Consequently, a prepared 0.1 M NH₄OH solution was added dropwise into the mixture in the conical flask to gradually increase the pH of the solution up to 10.5. Due to the addition of ammonium hydroxide, the pH of the mixture was enriched slowly and the metal ions started to co-precipitate in the form of metal hydroxides and initiated the formation of the nuclei for crystal formation. At pH 10.5, all the metal ions had co-precipitated out quantitatively in the form of a Zn(OH)₂·Al(OH)₃·Cr(OH)₃·*n*H₂O crystal and with the temperature conditions and magnetic stirring, the process took several hours. A similar process for the formation of nanocrystals in an aqueous medium has been reported earlier.^{41–43} The reactions in the conical flask are proposed below:



Then, the precipitate was separated from the aqueous medium and washed with acetone and deionized water properly. After that, the resultant crystals were kept to dry inside an oven at a temperature of 110 °C overnight. Finally, the dehydrated Zn(OH)₂·Al(OH)₃·Cr(OH)₃(s) sample was subjected to calcination at a temperature of 500 °C for 6 hours in a high temperature muffle furnace in the presence of atmospheric oxygen. The metal hydroxides were converted to the metal oxides: ZnO·Al₂O₃·Cr₂O₃. The proposed reaction inside the muffle furnace is given as follows:

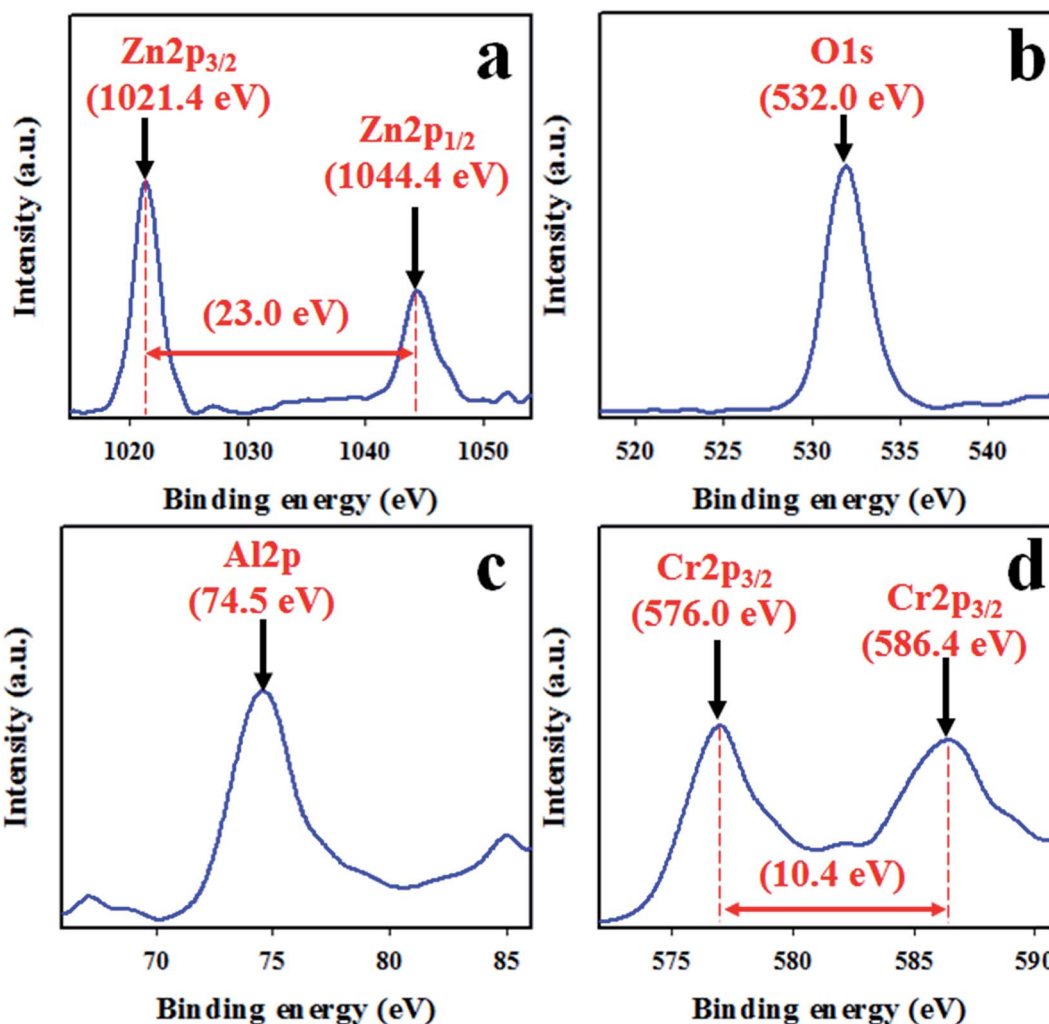
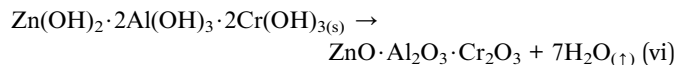


Fig. 2 High resolution XPS spectra of the ZnO/Al₂O₃/Cr₂O₃ NPs. (a) The core level XPS spectrum of Zn 2p, (b) O 1s orbitals, (c) Al 2p orbitals, and (d) the 3/2 spin orbitals of Cr 2p.





Fabrication of the GCE

The working electrode of the desired sensor was fabricated using a GCE. To do this, the slurry of ZnO/Al₂O₃/Cr₂O₃ NPs was prepared in ethanol and deposited onto the glassy carbon electrode in a very uniform thin layer. Then, the modified GCE was kept under ambient conditions for an hour to dry. To improve the binding strength between the NPs and the GCE, a drop of Nafion (5% Nafion suspension in ethanol) was added onto the modified GCE, which was put inside an oven at a temperature of 35 °C for a time adequate to dry the working electrode ZnO/Al₂O₃/Cr₂O₃ NPs/binder/GCE entirely. The desired sensor was assembled using an electrometer (a Keithley electrometer), where ZnO/Al₂O₃/Cr₂O₃ NPs/binder/GCE acted as working electrode and Pt-wire as a counter electrode. Depending on the concentration, a number of XNT solutions ranging from 0.05 mM to 0.05 nM were prepared and used as target analytes to evaluate the analytical performance of the anticipated XNT sensor. A curve was plotted (known as a calibration curve) as the relationship of current *vs.* the concentration of XNT. From the

maximum linearity (*r*²) of the calibration curve, the linear dynamic range (LDR) of the projected XNT sensor was estimated. Using the slope of the calibration curve, the sensitivity and detection limit (DL) of the XNT sensor were calculated. During the investigation, the buffer solution in the measuring beaker was kept at a constant 10.0 mL throughout the analysis. The Keithley electrometer was used as a simple two electrode system.

Results and discussion

Optical and structural properties of the ZnO/Al₂O₃/Cr₂O₃ NPs

Normally, metal oxides show a characteristic absorption peak in the region 400–800 cm⁻¹ in FTIR investigations. To study the FTIR spectrum of the synthesized ZnO/Al₂O₃/Cr₂O₃ NPs, FTIR analysis was implemented in the region 400–4000 cm⁻¹. As observed in Fig. 1(a), two major absorption peaks at 400 and 1100 cm⁻¹ were exhibited, which are associated with the stretching vibrations of the Zn–O and C–O functional groups, respectively.^{44–46} The photocatalytic activity of the ZnO/Al₂O₃/Cr₂O₃ NPs was investigated by the implementation of UV-vis analysis in the range of 280–800 nm as shown in Fig. 1(b). As shown in Fig. 1(b), a characteristic absorption band was observed at 289 nm.^{47–49} The band gap energy of the ZnO/Al₂O₃/Cr₂O₃ NPs was estimated using the following equation and is found to be 4.29 eV:

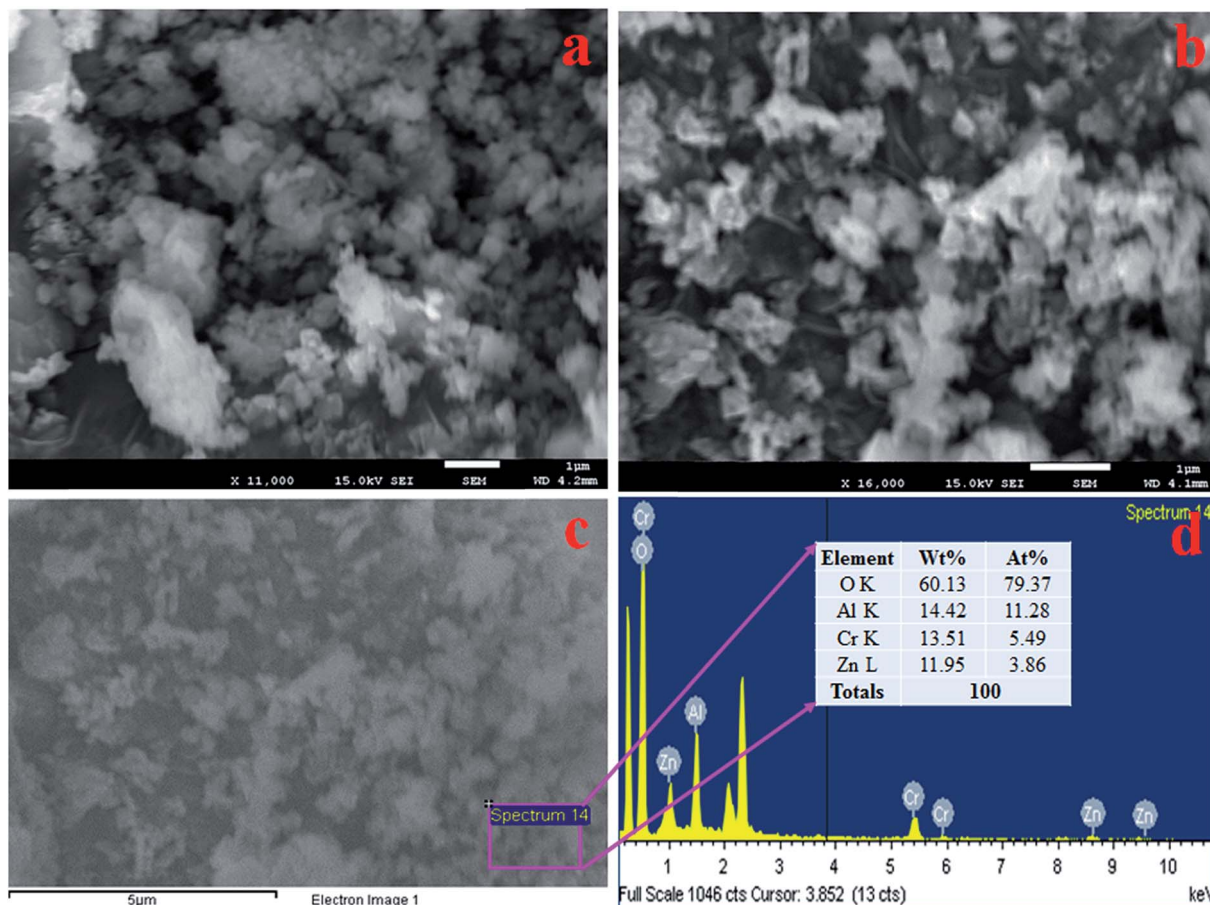


Fig. 3 Structural and compositional analysis of the prepared ZnO/Al₂O₃/Cr₂O₃ NPs. (a and b) Low and high magnification FESEM images and (c and d) elemental analysis with EDS.



$$E_{\text{bg}} \text{ (eV)} = 1240/\lambda \quad (\text{vii})$$

where E_{bg} is the band gap energy and λ is the maximum absorption wavelength.

The crystallinity of ZnO/Al₂O₃/Cr₂O₃ NPs was studied by execution of XRD analysis with a radiation source of Cu K α at 1.5406 Å. The resulting XRD pattern recorded over the 2θ range of 26–74° is shown in Fig. 1(c). As shown in Fig. 1(c), the observed peaks of ZnO are shown as (101), (102) and (201) planes, which are indicated by JCPDS no. 00-036-1451 and previous reports of ZnO.^{50–52} The diffracted peaks of Cr₂O₃ such as (104), (110), and (214) are also shown in Fig. 1(c) and have great similarity to JCPDS no. 01-089-6744 and those from previous authors.^{53,54} Besides this, the reflected XRD peaks (012) and (110) of Al₂O₃ match those of JCPDS no. 077-1716 and reports for Al₂O₃.^{55,56} Using the Scherrer equation, the crystal size of the NPs has been estimated from the Al₂O₃ peak (012) and is found to be 22.54 nm.

$$D = 0.9\lambda/(\beta \cos \theta) \quad (\text{viii})$$

where λ is the wavelength of the X-ray radiation (1.5418 Å) and β is the full width at half maximum (FWHM) of the peak at diffracted angle θ .

XPS analysis of the ZnO/Al₂O₃/Cr₂O₃ NPs

To measure the surface composition and oxidation state of the synthesized ZnO/Al₂O₃/Cr₂O₃ NPs, XPS analysis was performed as shown in Fig. 2. As demonstrated in Fig. 2, the XPS spectra show the peaks associated with Zn, O, Al and Cr only. The other peaks are due to the presence of the impurities. The high resolution XPS spectrum of Zn 2p presented in Fig. 2(a) shows two split spin orbitals centered at 1021.4 eV for Zn 2p_{3/2} and 1044.4 eV for Zn 2p_{1/2}. The spin energy separation is 23.0 eV, which is the characteristic value for the Zn²⁺ oxidation state.^{57–59} The O 1s spectrum shows a highly intense peak at 532.0 eV as shown in Fig. 2(b), which can be ascribed to lattice oxygen with an oxidation state of O²⁻ in the ZnO/Al₂O₃/Cr₂O₃ NPs.^{60,61} As shown in Fig. 2(d), the core level Cr 2p XPS spectrum shows two split spin orbitals at 576.0 eV for Cr 2p_{3/2} and 586.4 eV for Cr 2p_{1/2} corresponding to the Cr³⁺ oxidation state.^{62,63} The XPS peak positioned at

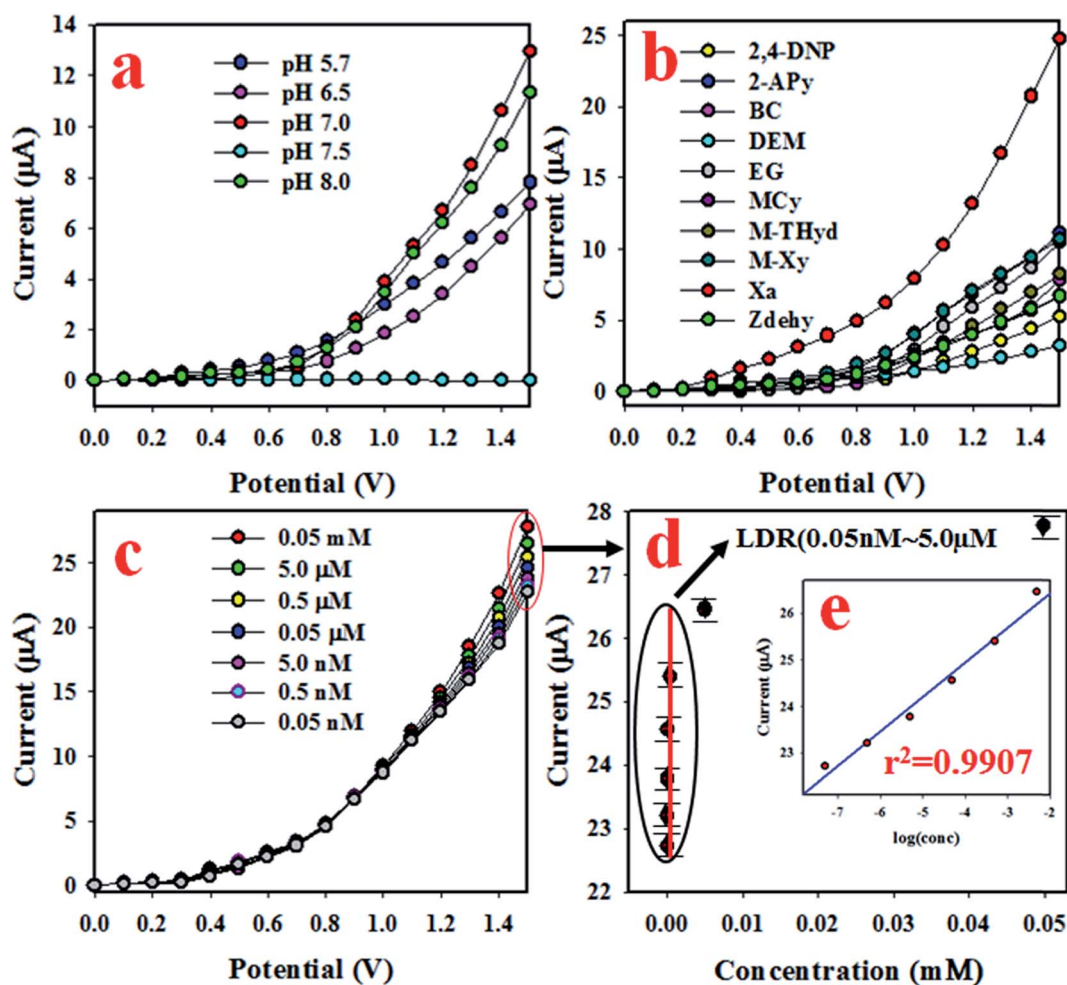


Fig. 4 The estimation of sensor analytical behavior and performance. (a) pH optimization, (b) estimation of the selectivity, (c) concentration variation from lower to higher range, and (d) the calibration curve [inset log(conc.) vs. current].



74.5 eV is related to the Al^{3+} state as represented in Fig. 2(c).^{64,65}

Morphological and elemental analysis of the $\text{ZnO}/\text{Al}_2\text{O}_3/\text{Cr}_2\text{O}_3$ NPs

FESEM equipped with EDS was implemented to identify the structural morphology of the synthesized $\text{ZnO}/\text{Al}_2\text{O}_3/\text{Cr}_2\text{O}_3$ NPs. As demonstrated in Fig. 3(a and b), both the low and high magnification FESEM images confirmed that the prepared $\text{ZnO}/\text{Al}_2\text{O}_3/\text{Cr}_2\text{O}_3$ oxides are aggregated nanoparticles in shape. An identical result was also observed from EDS analysis as shown in Fig. 3(c and d). The elemental composition of the mixed oxides was found to be 60.13% O, 14.42% Al, 13.51% Cr, and 11.95% Zn and is presented in Fig. 3(d). Therefore, EDS analysis established that the synthesized NPs contained O, Al, Zn, and Cr only and peaks associated with the presence of impurities were not observed.

Analytical performance of the XNT sensor

The synthesized $\text{ZnO}/\text{Al}_2\text{O}_3/\text{Cr}_2\text{O}_3$ NPs were used to fabricate the desired electrochemical sensor. To assemble the working electrode of this electrochemical sensor, the $\text{ZnO}/\text{Al}_2\text{O}_3/\text{Cr}_2\text{O}_3$

NPs were deposited onto a GCE as a uniform layer of thin film with a Nafion conducting binder. At the very beginning of this study, the assembled electrochemical (applying the I - V method) sensor was tested to find out the most desirable buffer system. To execute this testing, a number of buffer systems with various pH values ranging from 5.7–8.0 were analyzed as shown in Fig. 4(a). As can be observed in Fig. 4(a), the anticipated electrochemical sensor shows the highest I - V response at pH 7.0. Therefore, it can be concluded that the proposed sensor based on $\text{ZnO}/\text{Al}_2\text{O}_3/\text{Cr}_2\text{O}_3$ NPs/binder/GCE has maximum electrochemical activity at pH 7.0. To examine the selectivity of the assembled electrochemical sensor, environmental toxins were analyzed with micro-level concentrations at pH 7.0. The corresponding I - V data for 2,4-DNP, 2-APy, BC, DEM, EG, *M*-THyd, *M*-Xy, Zdehy, and XNT are presented in Fig. 4(b), for which the applied potential range of 0 to +1.5 V was used at pH 7.0. Obviously, XNT shows the best I - V response among these toxins. To estimate the analytical performance of the XNT electrochemical sensor, it was diluted in deionized water to make up a number of XNT solutions based on concentrations ranging from 0.05 mM to 0.05 nM which were applied as analytes to measure I - V responses (Fig. 4(c)). As shown in Fig. 4(c),

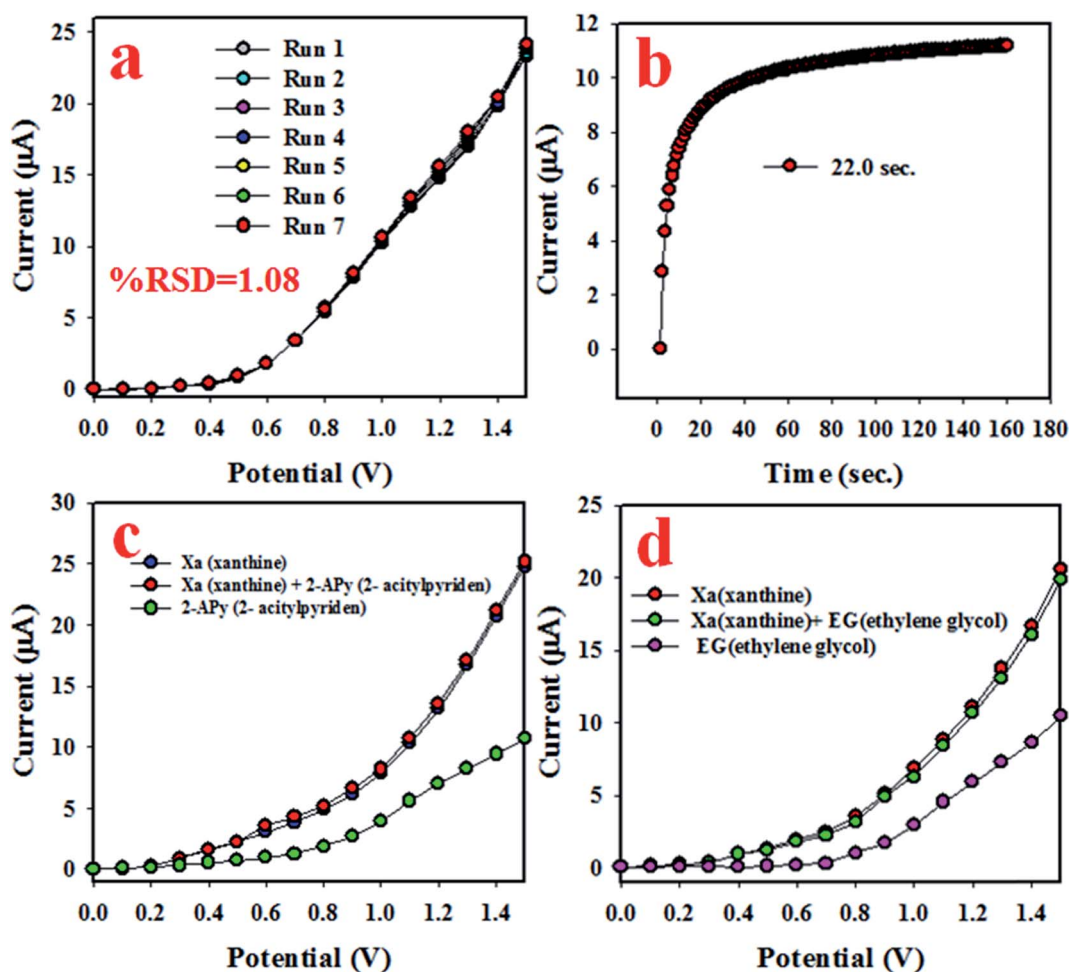


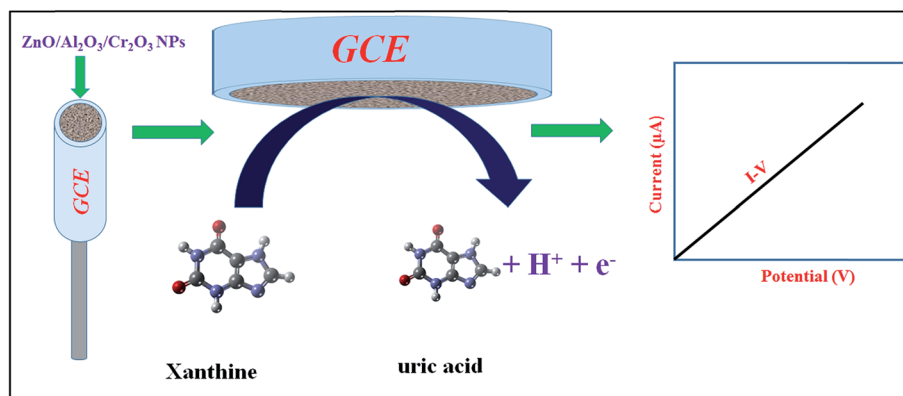
Fig. 5 Reliability investigations of the XNT sensor based on $\text{ZnO}/\text{Al}_2\text{O}_3/\text{Cr}_2\text{O}_3$ NPs/binder/GCE: (a) testing reproducible performance, (b) response time, and (c and d) interference tests.



Table 1 A comparison of the sensor performance with that of similar work based on different electrode fabrications using an electrochemical approach^a

Modified GCE	DL	LDR	Sensitivity	Ref.
Co/ZnO NPs/GCE	178.8 pM	5.0 nM to 0.05 mM	53.1 $\mu\text{A } \mu\text{M}^{-1} \text{cm}^{-2}$	66
ZnO/Al ₂ O ₃ /Cr ₂ O ₃ NPs/GCE	1.34 pM	0.05 nM to 5.0 μM	70.9 $\mu\text{A } \mu\text{M}^{-1} \text{cm}^{-2}$	This work

^a DL (detection limit) and LDR (linear dynamic range).

**Scheme 1** A prototype representation of the electrochemical oxidation of XNT in an aqueous medium using an electrochemical method.

were investigated as shown in Fig. 5(c and d). It can be summarized that the anticipated XNT sensor is highly selective toward XNT without any interference effects in the presence of other toxins.

As shown in Fig. 4(c), the I - V response varies with the corresponding concentration of XNT. The proposed XNT sensor with ZnO/Al₂O₃/Cr₂O₃ NPs/binder/GCE was implemented successfully to detect XNT in an optimized phosphate buffer system. A control experiment was performed (Fig. S1[†]) and is included in the ESI.[†] Here, a control experiment was performed based on different compositions of fabricated GCEs such as Al₂O₃, ZnO, Cr₂O₃, ZnO/Al₂O₃, Al₂O₃/Cr₂O₃, ZnO/Cr₂O₃, and ZnO/Al₂O₃/Cr₂O₃ nanoparticles. Based on these observations, the highest sensor response was exhibited with ZnO/Al₂O₃/Cr₂O₃ NPs/binder/GCE compared to those of other fabricated electrodes such as Al₂O₃, ZnO, Cr₂O₃, ZnO/Al₂O₃, Al₂O₃/Cr₂O₃, and ZnO/Cr₂O₃.

During the initial stages of the sensing study of the XNT sensor, the surface coverage on the anticipated working

electrode was smaller due to absorption of very few XNT molecules and the corresponding XNT oxidation reaction proceeded. With the increase in XNT concentration in the detecting system, both the surface coverage and rate of reaction increased gradually and approached steady state equilibrium conditions. With further enrichment of the XNT concentration, equilibrium current density was observed in the detecting system. This equilibrium current density is presented in Fig. 4(d) and the current data points are consistently distributed along the linear plot. Therefore, this investigation provides evidence of the reliability of the method. As presented in Fig. 5(b), the response time of the XNT sensor is 22 s and this amount of time is necessary for the XNT sensor to produce a steady state equilibrium I - V response. Therefore, the XNT sensor based on ZnO/Al₂O₃/Cr₂O₃ NPs/binder/GCE exhibited appreciable analytical performance characteristics such as good sensitivity (70.8861 $\mu\text{A } \mu\text{M}^{-1} \text{cm}^{-2}$), a broad linear dynamic range (0.05 nM to 5.0 μM), a very low detection limit (1.34 \pm 0.07 pM), a short response time (22 s), reproducibility with a constant I - V

Table 2 Analyses of real environmental samples with the ZnO/Al₂O₃/Cr₂O₃ NPs/binder/GCE sensor

Sample	Added XNT concentration (nM)	Measured melamine conc. ^a by ZnO/Al ₂ O ₃ /Cr ₂ O ₃ NPs/GCE (nM)			Average recovery ^b (%)	RSD ^c (%) ($n = 3$)
		R_1	R_2	R_3		
Industrial effluent	5.000	4.97128	4.96702	4.94034	99.18	0.34
PC-baby bottle	5.000	4.88659	4.92789	4.87152	97.91	0.60
PVC-water bottle	5.000	4.89598	4.93011	4.92118	98.32	0.36
PVC-food packaging bag	5.000	4.95423	4.95025	4.94347	98.99	0.11

^a Mean of three repeated determinations (signal to noise ratio of 3) with ZnO/Al₂O₃/Cr₂O₃ NPs/GCE. ^b The concentration of XNT determined/the concentration taken (unit: nM). ^c Relative standard deviation value indicates precision among three repeated measurements (R_1 , R_2 , R_3).



response, and high selectivity without interference effects. Also studied was the sensor performance based on various time spans such as intra-day and inter-day validations, which are presented in Fig. 6(a–d). A comparison of the XNT sensor performances was carried out and is included in Table 1. As indicated in Table 1, the XNT sensor based on ZnO/Al₂O₃/Cr₂O₃ NPs/binder/GCE shows better performance when comparing the sensitivity, detection limit and linear dynamic range.⁶⁶

Possible sensing mechanism of XNT

During the electrochemical analysis of XNT using the *I*–*V* method, the XNT molecules are adsorbed onto the surface of the working electrode based on ZnO/Al₂O₃/Cr₂O₃ NPs/binder/GCE, where the XNT molecules are oxidized to uric acid (Scheme 1). As illustrated in Scheme 1, due to oxidation of the XNT molecule using the *I*–*V* method, an electron is produced which is responsible for the higher conductivity of the sensing phosphate buffer medium. A similar pattern of electrochemical oxidation of XNT has been reported previously.^{15,16,67}

Validity of the XNT sensor with real environmental samples

To test the validity of the proposed XNT electrochemical sensor based on ZnO/Al₂O₃/Cr₂O₃ NPs/binder/GCE, environmental samples such as extracts from a PC-water bottle, a PC-baby bottle, a PVC food packaging bag and industrial effluent have been analyzed using a recovery method. The results of the analyses are presented in Table 2. In Table 2, the obtained results are quite reasonable and acceptable.

Conclusion

The electrochemical sensor was fabricated using wet-chemically prepared ZnO/Al₂O₃/Cr₂O₃ nanoparticles and implemented to selectively detect XNT in a phosphate buffer phase. The fabricated sensor shows good sensitivity, a wider linear dynamic range, a much lower detection limit, a quick response time, and excellent reproducibility performance. Besides this, it was found to be stable long-term in a phosphate buffer medium without any interference effects and able to successfully detect XNT in real environmental samples. This has introduced a new route for efficient detection of XNT using an electrochemical approach with ternary ZnO/Al₂O₃/Cr₂O₃ nanoparticles for safety within healthcare and biomedical fields.

Conflicts of interest

There are no conflicts to declare.

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