Development of a Nonenzymatic Colorimetric Sensor for the Detection of Uric Acid Based on Ionic Liquid-Mediated Nickel Nanostructures

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ABSTRACT: Uric acid (UA) is a metabolic byproduct of purine nucleotides and is excreted as a urine component. Abnormalities in UA metabolism cause localized inflammation due to crystal deposition and can lead to various diseases. In the current study, we successfully fabricated a biosensor based on 1-H-3-methylimidazolium acetate (ionic liquid, IL)-capped nickel nanoparticles (NiNPs) for the detection of uric acid in test samples. The structures of IL-capped NiNPs and their precursors were characterized by Fourier transform infrared spectroscopy, scanning electron microscopy, and X-ray diffraction. The IL-capped NiNPs possessed intrinsic peroxidase-like properties and displayed selective UA quenching after interacting with 3,3′,5,5′-tetramethylbenzidine (TMB) solution. Different parameters such as pH, time, IL, TMB, and UA concentration were optimized to obtain the best results for the proposed sensor. The UA biosensor shows good responses in the linear range from $1 \times 10^{-8}$ to $2.40 \times 10^{-6}$ M, with a lower limit of detection of $1.30 \times 10^{-7}$ M, a limit of quantification of $4.3 \times 10^{-7}$ M, and an $R^2$ value of 0.9994. For the colorimetric detection of UA, the proposed sensor gave a short time response of 4 min at room temperature and pH 7.5. The proposed sensing probe detects UA in real serum samples and could be used as a selective sensor for UA in the real sample detection.

1. INTRODUCTION

In humans, uric acid (UA), one of the most important metabolic byproducts of purine nucleotides, is excreted in the urine. Overproduction of UA, generated from purine metabolism via xanthine oxidase, has been proven to play triggered roles in human disease onset. A precise increase in the serum UA level is directly associated with the disease severity and progression. At normal physiological pH, UA acts as a weak acid ($pK_a$ 5.8) and exists as urate salt, which upon excess deposition leads to UA crystal formation as monosodium urate (MSU). The normal UA reference level in human blood is 2.5 to 7 mg/dL in men and 1.5 to 6 mg/dL in women. The normal physiological amount of UA in body fluids is balanced between excretion and generation. However, in diseased conditions such as Lesch–Nyhan syndrome, hyperuricemia, gout, and renal failure, UA has been proposed as a key diagnostic marker.

Normally, UA concentration is measured in urine, blood plasma, and exhaled breath condensate. Determination of UA concentration has been performed by uricase analysis,7 chemiluminescence (CL),8 capillary electrophoresis (CE)9,10 high-performance liquid chromatography (HPLC),11 electrochemistry, dry chemistry systems, biosensor methods, and so forth. Generally, for the detection of UA, chromatographic techniques such as CE and HPLC make great contributions but require expensive instruments and complicated sample preparation procedures. However, for the detection of UA in real samples with a lower limit of detection and high accuracy, chemiluminescence and electrochemistry-based analytical methods are still preferred. Nevertheless, for the accurate determination of UA, a simple, fast, and effective method is still required. As a prerequisite of low cost, feasibility, and simplicity of no need for sophisticated techniques, nonenzymatic chemosensor-based colorimetric biosensor development has gained great attention. Colorimetric detection of UA reported by Zhao et al.7 has shown the development of...
intrinsic peroxidase-like catalytic activity of BSA-stabilized Au nanoclusters. Although the sensor shows high sensitivity, it possesses less specificity due to its strong affinity toward Au and Ag nanoparticles.\[15,16\] Pal et al. reported a nonenzymatic platform for the colorimetric detection of UA based on Ni@MnO$_2$.\[17\] The results presented are encouraging, but in their work, Ni nanostructures alone did not show any sensing activity. Tripathi et al. reported that using Ni thin films deposited by glancing angle deposition (GLAD) shows colorimetric sensing of UA in a nonenzymatic manner.\[18\] However, in their work, they showed that Ni alone does not show any considerable sensing response toward UA sensing.

Recently, our group has successfully shown the application of an ionic liquid (IL) in enhancing the sensing properties of nanomaterial-based sensing platforms for the detection of various analytes.\[19,20\] Owing to the emerging applications and versatile properties of ILs, we hypothesized the functionalization of NiNPs with 1-H-3-methylimidazolium acetate.

In sensing applications, metal–organic frameworks (MOFs) have gained great attention. Due to their huge surface areas, stability, variable architectures, exposed metal sites, and high and controllable pore size, they represent a novel class of porous organic–inorganic hybrid materials.\[21\] Although MOFs based on colorimetric sensors have achieved some success, the development of MOFs as enzyme mimics for bioanalysis applications is still required. Although these MOFs show excellent lattice stability, a small pore structure with a high density of active catalytic centers, and an easy synthesis process.\[22\] These characteristics of MOFs avoid the interference of other molecules in biological samples and become suitable for catalytic applications. However, their colorimetric detection application is still far from fully developed and is in its infancy stage.\[23\]

In this study, nickel nanoparticles (NiNPs) were prepared by using benzyl di-ethylene tri-amine as the stabilizing and reducing agent. Characterization of the prepared NiNPs was carried out with standard spectroscopic techniques, including X-ray diffraction (XRD), Fourier transform infrared (FTIR) spectroscopy, and scanning electron microscopy (SEM). After the synthesis and characterization, these NiNPs were tuned with an IL as a colorimetric biosensor for UA detection. To achieve the optimum performance of these IL-capped NiNPs, different-effecting parameters, such as pH, temperature, incubation period, amount of Ni/IL, TMB, and UA concentrations were optimized. Finally, for the qualitative and quantitative detection of UA, we developed a simple and cost-effective biosensor method that can be observed by naked eyes and UV–vis spectroscopy, respectively. Furthermore, the proposed sensor was practically applied for the determination of UA in real human serum samples.

2. MATERIALS AND METHODS

2.1. Chemicals and Reagents. All the chemicals and reagents used in this study were of analytical grade and were acquired from Sigma Aldrich. These include nickel nitrate hexahydrate (Ni(NO$_3$)$_2$·6H$_2$O, 97%), uric acid (C$_5$H$_4$N$_4$O$_3$, 98%), 1-methylimidazole (C$_4$H$_6$N$_2$), 3,3',5,5'-tetramethylbenzidine (TMB) sodium chloride (NaCl, 99%), acetic acid (CH$_3$COOH, 97%), and sodium acetate (CH$_3$COONa, 99%). Methanol and ethanol (Sigma Aldrich) were used as solvents for washing purposes. All the solutions were prepared in double-distilled water, and high-quality Pyrex glass was used throughout the experiment.

2.2. Instrumentation. The distinctive peaks of the prepared NiNPs were identified using an FTIR MX-300 system (Agilent Technologies, Danbury, Conn, USA), and the desired functional group spectrum within the range of 500–4000 cm$^{-1}$ with 256 scans per sample at 4 cm$^{-1}$ resolution was recorded. A scanning electron microscope (JSM-5910, Japan) equipped with an energy-dispersive X-ray (EDX) system was
used for the size, morphology, and elemental analyses of the prepared nanoparticles. The crystal structure of the prepared nanoparticles was studied by using an XRD-6100 system (Bruker Smart Apex CCD) equipped with monochromatic CuKα radiation (λ = 0.15418 nm). A quartz cuvette double beam UV−vis spectrophotometer (Shimadzu, UV-1800, Germany) was used for absorption spectra acquisition.

2.3. Preparation of Nickel Nanoparticles. To synthesize the desired NiNPs, a modified protocol was used as reported recently by our group. Briefly, 0.02 and 0.004 M solutions of nickel nitrate hexahydrate (Ni(NO₃)₂·6H₂O) and benzyl diethylene tri-amine were prepared in 50 mL double-distilled (dd) water, respectively. The 0.004 M solution of benzyl diethylene tri-amine was added dropwise to the nickel nitrate solution and thoroughly stirred for about 60 min at room temperature until the color of the mixture was changed from pale blue to black. The synthesized NiNPs were pelleted out by centrifugation at 4000 rpm for 10 min at 37 °C and oven-dried for 4 h at 50 °C after washing with ethanol twice. Finally, the synthesized NiNPs were stored in 2 mL Eppendorf tubes at room temperature for further use. The synthesis scheme of NiNPs is summarized in Figure 1A.

2.4. Synthesis of ILs. The synthesis of IL was carried out as per our published protocol. Briefly, 0.01 M acetic acid and 0.01 M 1-methylimidazole were mixed with an equal ratio in two-neck flasks with constant stirring for 6 h under cooling. A concentrated yellow color solution of IL was obtained by a rotary evaporator and was stored at room temperature for further use (Figure 1B).

2.5. Capping of NiNPs with ILs. A china dish was used to soak roughly 6 mg of the produced NiNPs in 1 mL of IL (1-H-3-methylimidazolium acetate) for capping. Maceration of the IL-capped NiNPs was done for roughly 25 min with the use of a mortar and pestle to produce the desired dispersion, as shown in Figure 1C. Furthermore, the capping of the nanoparticles and IL was confirmed using FTIR analysis, as shown in Figure 2B, Section 3.1.

2.6. Colorimetric Nonenzymatic Detection of Uric Acid. Double-distilled water was used for the preparation of all solutions used. Briefly, 40 μL of capped NiNPs was mixed with TMB (0.08 M, 150 μL), H₂O₂ solution (0.04 M, 90 μL), PBS (0.06 M, 550 μL), and UA (2.4 × 10⁻⁶ M, 100 μL) and was incubated at ambient temperature for 4 min. A greenish color appeared before UA addition, which turned transparent after UA addition. The subsequent colorimetric change was observed by naked eyes, further confirmed by UV−vis spectrum (500−800 nm) analysis using a spectrophotometer.

3. RESULTS AND DISCUSSION

3.1. FTIR Study of the Prepared Nickel Nanoparticles. The FTIR spectrum-based functional group analysis of the prepared NiNPs is shown in Figure 2A. The key participating molecules involved in the synthesis of NiNPs were investigated. The respective spectrum absorption bands are shown in Figure 2A. The presence of the amine group is indicated by the N−H peaks at 3444 and 1640 cm⁻¹, which were acquired from benzyl diethylene tri-amine used in the reduction of NiNPs. The 1466 cm⁻¹ peak was assigned to the sp² vibration of the C≡H (alkene) bond. The existence of N−H peaks suggested that the amine group is bound to the surface of NiNPs. The C−H bending was observed at 1370 cm⁻¹. The IL-capped NiNP FTIR spectra have been shown in Figure 2B.

Along with new peaks, peak shifting was observed at 1466 and 1370 to 1260 and 1230 cm⁻¹ of amine-coated NiNPs, which confirms the capping of theionic liquid 1-H-3-methylimidazolium acetate with the Ni nanoparticles.

3.2. XRD Profile of the Synthesized Ni Nanoparticles. The XRD spectrum profile of the prepared NiNPs shows sharp peaks at 20−80° that indicate its crystalline nature, as shown in Figure 3. No impurity peaks were found in the diffraction pattern, suggesting the ultrapure phase of their synthesis. The presence of five sharp and prominent diffraction peaks at 2θ values of 37.5°, 43.25°, 62.75°, 75.25°, and 80° corresponds to the crystal planes of (111), (200), (220), (222), and (311), respectively, corresponding to JCPDS Card No. 73-1523. The synthesized NiNP planes are face-centered cubic, with a lattice constant of 4.17 Å, agreeing well with the standard card data. Using the standard Debye-Scherrer equation, the average crystal size was calculated to be 35 nm, as determined from the corresponding X-ray spectral peak. 27,28

3.3. SEM Analysis of the Prepared Ni Nanoparticles. To investigate the size and structure morphology of the prepared NiNPs, SEM was used, as shown in Figure 4. The acquired SEM image shows irregular NiNP agglomerates with void spaces. The microstructures are not very clear, which have been confirmed by the Scherrer equation, as given in Section
3.2. This agglomeration of NiNPs is due to the increase in surface area-to-volume ratio that leads to an increase in attractive forces among the particles to form spherical shapes. 29

3.4. IL-Capped NiNP-Based Colorimetric Detection of Uric Acid. The prepared NiNPs tuned with IL were used for the colorimetric detection of uric acid, as shown in Figure 5. The desired detection analysis was done by adding uric acid (2.4 μM, 100 μL) after 4 min of incubation to the colorimetric mixture having NiNPs (40 μL), TMB (8 mM, 150 μL), H₂O₂ (4 mM, 90 μL), and PBS (6 mM, 550 μL) solutions. The colorimetric change (greenish to transparent) was observed by naked eyes, further confirmed by absorption spectrum analysis (Figure 5). The same colorimetric mixture composition without UA was used as a normal control with a good absorption peak in the 550−700 nm range (Figure 5A). No absorption peak was seen in the test sample having UA (Figure 5B).

3.5. Proposed Mechanism for IL-Capped NiNP-Based Uric Acid Detection. The prepared IL-capped NiNPs act as a biocatalyst by producing hydroxide radicals from H₂O₂ reduction that oxidize the TMB solution. In the presence of uric acid, the oxidized TMB (blue-green) solution reverts to a colorless reduced TMB product. Meanwhile, UA is converted into intermediate Allontoin molecules that revert to UA in the presence of water molecules, as shown in Scheme 1.

3.6. Optimization of the Proposed Sensor. To investigate the potential biosensing role of the proposed IL-capped NiNPs, different key parameters were optimized before being tested in real blood samples. These are given below.

3.6.1. Optimization of IL-Capped NiNPs. As a key component of the proposed biosensor, different concentrations of the ionic liquid-tuned NiNPs (10−70 μL) were tested in a reaction mixture having the same composition as we
mentioned in Section 3.2. Briefly, 40 μL of IL-capped NiNPs was enough to produce an optimum response. The reaction progress (blue-greenish to transparent) can be noticed easily via naked eyes. Further confirmations were done by absorption spectrum analysis by using a spectrophotometer, as shown in Figure 6A.

3.6.2. Effect of TMB Concentration. As the main colorimetric reporter component of the proposed biosensor, different TMB concentrations (2−14 mM, 150 μL) were tested in a reaction mixture having the same composition as we mentioned in Section 3.2. Briefly, (8 mM, 150 μL) TMB solution was enough to produce an optimum color response in the absence of UA. In the presence of UA, the reaction progress (blue-greenish to transparent) can be noticed easily via naked eyes. Further confirmation was done by absorption spectrum analysis by using a spectrophotometer, as shown in Figure 6B. Irrespective of its previously reported 0.8 mM concentration, in our current finding, the TMB solution shows the optimal result at 8 mM concentration only. The main possible reason for these 1000× detection limit differences may be the nature, composition, and oxidizing power of the different nanostructures.

3.6.3. Optimization of \( \text{H}_2\text{O}_2 \). \( \text{H}_2\text{O}_2 \) is the gold standard oxidizing reagent for the reporter TMB solution. Therefore, optimal \( \text{H}_2\text{O}_2 \) concentration (4 mM, 90 μL) was determined by using different \( \text{H}_2\text{O}_2 \) (1−7 mM) concentrations. The
proposed biosensors (IL-capped NiNPs) showed a maximum response at this optimal (4 mM:90 μL) H₂O₂ concentration in the reaction mixture, as shown in Figure 6E. Meanwhile, the reported H₂O₂ concentration (8 mM:500 μL) was not suitable for our current (IL-capped NiNPs) biosensors. The possible reasons may be its purity, sensitivity, reaction mixture composition, their peroxidase-like activities, and so forth.

3.6.4. pH Effect on the Proposed Biosensor. In the physiological system, pH is one of the most influential factors responsible for the onset of prohibition of a chemical reaction. The desired biosensor (IL-capped NiNPs) was calibrated at different pH modules (1−13) using hydrochloric acid (HCl) and sodium hydroxide (NaOH) solutions. The optimal result for the IL-capped NiNP biosensor was found at pH 7.5, as shown in Figure 6C. However, in a normal enzymatic scenario, the reaction occurs at pH 4.

3.6.5. Effect of Time on the Proposed Biosensor. Time is one of the most influential factors in numerous biochemical reactions. Therefore, the desired biosensor (IL-capped NiNPs) was optimized at different time intervals (0−8 min). The optimal result was achieved after 4 min, irrespective of the previously reported 15 min intervals. The desired time-based response (colorimetric change) was noticed by visual observation and confirmed by UV−vis spectrum analysis, as shown in Figure 6D.

3.6.6. Steady-State Kinetic Analysis. The Michaelis–Menten equation was used to calculate the Michaelis constant (Km) and maximum velocity (Vmax) for the proposed sensing platform (IL-capped NiNPs). As can be seen in Table 1, the proposed platform demonstrates a very low Km value of 0.017 for TMB and 0.01 for H₂O₂. The lower value is desirable as it indicates that the IL-capped NiNPs have a greater affinity for the substrates. Moreover, when compared with the literature, the Vmax value of IL-capped NiNPs is higher, as can be seen in Table 1.

In comparison to the values obtained for other catalysts, it is clear that IL-capped NiNPs demonstrate good catalytic behavior for the oxidation of TMB in the presence of H₂O₂.

3.6.7. Analytical Characteristics of the Proposed IL-Capped NiNP Biosensor. For the colorimetric detection of UA concentration, the key biosensing features of the proposed IL-capped NiNP biosensor were studied using standard calibration curves, as shown in Figure 7. Under optimized conditions, the proposed colorimetric sensing probe was tested in the uric acid concentration range of 1 × 10⁻⁸−2.4 × 10⁻⁶ M. It exhibited peroxidase-like activity in a wide linear range. The uric acid concentration in the reaction mixture was inversely proportional to the absorption peak that can be noticed from the reduction of the UV−vis spectral peak at 652, as shown in Figure 7. The proposed biosensor shows a good linear response in the range of 1 × 10⁻⁸−2.4 × 10⁻⁶ M, with an LOQ of 4.3 × 10⁻⁸ M, an LOD of 1.30 × 10⁻⁷ M, and an R² value of 0.9994. These values were calculated by using the formulas (10σ/slope) for LOQ and (3σ/slope) for LOD. The slope value was derived from the linear curve, while σ shows the blank sample standard deviation. The proposed IL-capped NiNP biosensor shows a good limit of detection (LOD) of 1.3 μM and an R² value of 0.995 compared to that of the literature-reported UA sensor. Similarly, the analytical efficiency of the proposed IL-capped NiNP biosensor was good, as shown in Table 2, compared with that of the already reported biosensors.

3.7. IL-Capped NiNP Biosensor Interference Profile Studies. To investigate the potential UA detection selectivity with the peculiar sensitivity of IL-capped NiNP biosensor, interference profile studies were done. The absorbance response of the proposed biosensor was measured in the presence of other coexisting species, including ethanol, methanol, dopamine, urea, Ca²⁺, K⁺, ascorbic acid, glutathione, and UA, as shown in Figure 8. Except for UA, none of the coexisting species were found to reduce the oxidized TMB

![Figure 7. IL-capped NiNP-based UA biosensing. Different UA concentrations (1 × 10⁻⁸−2.4 × 10⁻⁶ M) were mixed with an optimized reaction mixture. (A) Upper top right shows colorimetric change with respect to different concentrations of UA and the bottom graph represents the respective UV−vis spectra. (B) Calibration plot of UA concentration versus absorbance.](https://doi.org/10.1021/acsomega.2c04070)

Table 1.Comparison of Kinetic Parameters of IL-Capped NiNPs and HRP

| catalysts       | substrate | Vₘₐₓ (10⁻⁸ M·s⁻¹) | Kₘ (mM) | ref   |
|-----------------|-----------|-------------------|---------|-------|
| HRP             | TMB       | 17.19             | 0.424   | 32    |
| HRP             | H₂O₂      | 10.55             | 3.240   |       |
| IL-capped NiNPs | TMB       | 32                | 0.017   | this work |
| IL-capped NiNPs | H₂O₂      | 45                | 0.01    |       |

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solution (greenish to transparent) in the presence of IL-capped NiNP biosensor. Thus, the obtained results demonstrate high selectivity and good sensitivity of IL-capped NiNP biosensors for UA detection. The results indicate that the coexistence of these interfering substances does not affect the detection of UA. Thus, the proposed biosensor shows great potential to be tested for UA detection in real serum samples.

### 3.8. Clinical Applications of IL-Capped NiNP Biosensors

The proposed IL-capped NiNP biosensor was tested in real serum samples using the same experimental conditions, except for uric acid addition. Instead of direct UA addition, human serum samples (100 µL) were added to the reaction mixtures. Different UA concentrations of 0.295, 0.692, and 1.37 µM were spiked into the real serum samples by using the standard UA calibration method, as shown in Figure 9. Thus,

**Figure 8.** IL-capped NiNP biosensor interference profiling. The interference to the IL-capped NiNP biosensor by the coexisting species at 2.40 × 10^{-6} M concentrations including (A) ethanol, (B) K^+, (C) urea, (D) dopamine, (E) methanol, (F) Ca^{2+}, (G) ascorbic acid, (H) glutathione, and (I) uric acid.

**Figure 9.** Real serum sample UA profile. IL-capped NiNP biosensor-based UV−vis spectra of the real blood serum samples at optimized reaction mixture conditions having different UA concentrations. However, the concentration of A is (3 × 10^{-7} M), B is (7 × 10^{-7} M), and C is (1.4 × 10^{-6} M).

### Table 2. Comparative Analysis of the Proposed IL-Capped NiNP Biosensor for Uric Acid Detection

| s. no | materials used | linear range (µM) | limit of detection (µM) | ref |
|-------|----------------|-------------------|-------------------------|-----|
| 1     | luminol−K_3[Fe(CN)_6] | 4.8–179 | 3 | 33 |
| 2     | uricase/AuNP/MWCNT Au electrode | 10–800 | 10 | 34 |
| 3     | TMB−Cu^{2+}−uricase | 1–100 | 640 | 35 |
| 4     | CdTe nanoparticles | 0.22–6 | 100 | 36 |
| 5     | uricase/BSA-stabilized Au nanoclusters | 2.0–200 | 0.36 | 7 |
| 6     | uricase/HRP−CdS quantum dots | 125–1000 | 125 | 37 |
| 7     | nanocrystalline cobalt selenide TMB | 2.0–40 | 500 | 39 |
| 8     | Ni GLAD film | 15–500 | 3.3 | 18 |
| 9     | Ni@MnO_2 | 1–40 | 0.24 | 17 |
| 8     | IL-capped NiNPs | 0.01–2.40 | 0.13 | this work |
by using different UA concentrations under the same optimized conditions, the unknown serum UA concentration was calculated based on a previously established calibration plot. The % recovery algorithm was used to calculate the findings, as displayed in Table 3. Finally, the proposed IL-capped NiNPs biosensor was tested for multiple serum samples’ UA detection. The proposed biosensor was able to detect UA in serum samples with the highest sensitivity and selectivity.

Recovery% = UA found/UA added × 100

4. CONCLUSIONS

In the present study, we synthesized IL-capped NiNPs as efficient uric acid biosensors under normal physiological conditions. The proposed biosensor was confirmed by using standard spectroscopic techniques. Different parameters such as pH, time, TMB, and H2O2 solution were optimized. Under optimized conditions, the sensing probe for uric acid detection was tested successfully in a wide linear range, which gave a low limit of detection and low limit of quantification. This newly explored IL-tuned NiNP biosensor shows numerous advantages, including low cost, facile preparation, good stability, and high catalytic efficiency with peculiar selectivity in a minimal timeframe detection. The desired biosensor was able to detect UA with the highest sensitivity and selectivity, irrespective of the presence of coexisting molecules’ hindrances. Even more, with the same sensitivity and selectivity, UA was determined in real serum samples, suggesting their potential diagnostic role shortly. Therefore, we predict that soon the proposed IL-capped NiNP biosensor would be used for the selective detection of uric acid in multiple diverse sample analyses.

Table 3. IL-Capped NiNP Biosensor-Based Detection of Uric Acid in Human Serum Samples

| samples | detected (µM) | uric acid added (µM) | uric acid found (µM) | recovery (%) | RSD (%) |
|---------|--------------|----------------------|----------------------|--------------|--------|
| 1       | 0.003        | 0.571                | 0.594                | 101.69       | 0.838  |
| 2       | 0.008        | 0.692                | 0.7                  | 101.15       | 1.009  |
| 3       | 0.03         | 1.37                 | 1.4                  | 102.18       | 0.459  |

Notes

The authors declare no competing financial interest.

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**REFERENCES**

(1) Maiuolo, J.; Oppedisano, F.; Gratteri, S.; Muscoli, C.; Mollace, V. Regulation of uric acid metabolism and excretion. Int. J. Cardiol. 2016, 213, 8.
(2) Lakhmi, D.; Whitcombe, M. J.; Davis, F.; Sharma, P. S.; Prasad, B. B. Electrochemical detection of uric acid in mixed and clinical samples: a review. Electroanalysis 2011, 23, 305.
(3) Lu, J.; Xiong, Y.; Liao, C.; Ye, F. Colorimetric detection of uric acid in human urine and serum based on peroxidase mimetic activity of MIL-53 (Fe). Anal. Methods 2015, 7, 9894.
(4) Bravo, R.; Hsueh, C.; Brajer-Toth, A.; Jaramillo, A. Possibilities and limitations in miniaturized sensor design for uric acid. Analyst 1998, 123, 1625.
(5) Shi, K.; Shiu, K. K. Determination of uric acid at electrochemically activated glassy carbon electrode. Electroanalysis 2001, 13, 1319.
(6) Miland, E.; Ordieres, A. M.; Blanco, P. T.; Smyth, M.; Fagain, C. Poly (o-aminophenol)-modified bienzyme carbon paste electrode for the detection of uric acid. Talanta 1996, 43, 785.
(7) Zhao, H.; Wang, Z.; Jiao, X.; Zhang, L.; Lv, Y. Uricase-based highly sensitive and selective spectrophotometric determination of uric acid using BSA-stabilized Au nanoclusters as artificial enzyme. Spectros. Lett. 2012, 45, 511.
(8) Li, Z.; Feng, M.; Lu, J. KMnO4–octylphenyl polyglycol ether chemiluminescence system for flow injection analysis of uric acid in urine. Microchem. J. 1998, 59, 278.
(9) Boughton, J. L.; Robinson, B. W.; Strein, T. G. Determination of uric acid in human serum by capillary electrophoresis with polarity reversal and electrochemical detection. Electrophoresis 2002, 23, 3705.
(10) Zinellu, A.; Sotgia, S.; Deiana, L.; Carru, C. Field-amplified sample injection combined with pressure-assisted capillary electrophoresis UV detection for the simultaneous analysis of allantoin, uric acid, and malondialdehyde in human plasma. Anal. Bioanal. Chem. 2011, 399, 2855.
(11) Li, Q.; Qiu, Y.; Han, W.; Zheng, Y.; Wang, X.; Xiao, D.; Mao, M.; Li, Q. Determination of uric acid in biological samples by high performance liquid chromatography-electrospray ionization-tandem mass spectrometry and study on pathogenesis of pulmonary arterial hypertension in pulmonary artery endothelium cells. RSC Adv. 2018, 8, 25808.
(12) Vishnu, N.; Gandhi, M.; Rajagopal, D.; Kumar, A. S. Pencil graphite as an elegant electrochemical sensor for separation-free and
simultaneous sensing of hypoxanthine, xanthine and uric acid in fish samples. Anal. Methode 2017, 9, 2265.

(13) Zhang, Z.; Yin, J. Sensitive detection of uric acid on partially electro-reduced graphene oxide modified electrodes. Electrochim. Acta 2014, 119, 32.

(14) Burgess, I. B.; Lončar, M.; Aizenberg, J. Structural colour in colourimetric sensors and indicators. J. Mater. Chem. C 2013, 1, 6075.

(15) Wang, S.; Chen, W.; Liu, A. L.; Hong, L.; Deng, H. H.; Lin, X. H. Comparison of the peroxidase-like activity of unmodified, amine-modified, and citrate-capped gold nanoparticles. ChemPhysChem 2012, 13, 1199.

(16) Liu, D.; Wang, Z.; Jiang, X. Gold nanoparticles for the colorimetric and fluorescent detection of ions and small organic molecules. Nanoscale 2011, 3, 1421.

(17) Pal, J.; Pal, T. Enzyme mimicking inorganic hybrid Ni@MnO$_2$ for colorimetric detection of uric acid in serum samples. ACS Adv. 2016, 6, 83738.

(18) Tripathi, A.; Harris, K. D.; Elias, A. L. Peroxidase-Like Behavior of Ni Thin Films Deposited by Glancing Angle Deposition for Enzyme-Free Uric Acid Sensing. ACS Omega 2020, 5, 9123.

(19) Nishan, U.; Gul, R.; Muhammad, N.; Asad, M.; Rahim, A.; Shah, M.; Iqbal, J.; Uddin, J.; Shujah, S. Colorimetric based sensing of dopamine using liquid functionalized drug mediated silver nanostructures. Microchem. J. 2020, 159, No. 105382.

(20) Nishan, U.; Haq, S. U.; Rahim, A.; Asad, M.; Badshah, A.; Ali Shah, A.-U.-H.; Iqbal, A.; Muhammad, N. Ionic-Liquid-Stabilized TiO$_2$ Nanostructures: A Platform for Detection of Hydrogen Peroxide. ACS Omega 2021, 6, 32754.

(21) Kumar, P.; Deep, A.; Kim, K.-H. Metal organic frameworks for sensing applications. TRAC, Trends Anal. Chem. 2015, 73, 39.

(22) Yu, T. A.; Le, G. H.; Dao, C. D.; Dang, L. Q.; Nguyen, K. T.; Nguyen, Q. K.; Dang, P. T.; Tran, H. T.; Duong, Q. T.; Nguyen, T. V. Arsenic removal from aqueous solutions by adsorption using novel MIL-53 (Fe) as a highly efficient adsorbent. RSC Adv. 2015, 5, 5261.

(23) Valvakens, P.; Vermoortele, F.; De Vos, D. Metal–organic frameworks as catalysts: the role of metal active sites. Catal. Sci. Technol. 2013, 3, 1435.

(24) Nishan, U.; Niazi, A.; Muhammad, N.; Asad, M.; Khan, N.; Khan, M.; Shujah, S.; Rahim, A. Non-enzymatic colorimetric biosensor for hydrogen peroxide using lignin-based silver nanoparticles tuned with ionic liquid as a peroxidase mimic. Arabian J. Chem. 2021, 14, No. 103164.

(25) Nishan, U.; Sabba, U.; Rahim, A.; Asad, M.; Shah, M.; Iqbal, A.; Iqbal, J.; Muhammad, N. Ionic liquid tuned titanium dioxide nanostructures as an efficient colorimetric sensing platform for dopamine detection. Mater. Chem. Phys. 2021, 262, No. 124289.

(26) Motlagh, M. K.; Youzbashi, A.; Sabaghzadeh, L. Synthesis and characterization of Nickel hydroxide/oxide nanoparticles by the complexion-precipitation method. Int. J. Phys. Sci. 2011, 6, 1471.

(27) Wu, S.-H.; Chen, D.-H. Synthesis and characterization of nickel nanoparticles by hydrazine reduction in ethylene glycol. J. Colloid Interface Sci. 2003, 259, 282.

(28) Qiao, H.; Wei, Z.; Yang, H.; Zhu, L.; Yan, X. Preparation and characterization of NiO nanoparticles by anodic arc plasma method. J. Nanomater. 2009, 2009, No. 795928.

(29) Mohammadyani, D.; Hosseini, S.; Sadrezaehad, S. Characterization of nickel oxide nanoparticles synthesized via rapid microwave-assisted route. Int. J. Mod. Phys. Conf. Ser. 2012, 5, 270.

(30) Pan, Y.; Yang, Y.; Pang, Y.; Shi, Y.; Long, Y.; Zheng, H. Enhancing the peroxidase-like activity of ficin via heme binding and colorimetric detection for uric acid. Talanta 2018, 185, 433.

(31) Kumar, S.; Bhushan, P.; Bhattacharya, S. Development of a paper-based analytical device for colorimetric detection of uric acid using gold nanoparticles–graphene oxide (AuNPs–GO) conjugates. Anal. Methods 2016, 8, 6965.

(32) Xue, W.; Cheng-Ling, T.; Jia-Jun, L.; ZHANG, H.-Z.; Jian, W. Ultra-small CuS nanoparticles as peroxidase mimics for sensitive and colorimetric detection of uric acid in human serum. Chin. J. Anal. Chem. 2018, 46, No. e1825.