Journal Pre-proofs

A Simple Sonochemical Assisted Synthesis of Porous $NiMoO_4$/chitosan Nanocomposite for Electrochemical Sensing of Amlodipine in Pharmaceutical Formulation and Human Serum

Bih-Show Lou, Umamaheswari Rajaji, Shen-Ming Chen, Tse-Wei Chen

PII: S1350-4177(19)31180-0
DOI: https://doi.org/10.1016/j.ultsonch.2019.104827
Reference: ULTSON 104827

To appear in: *Ultrasonics Sonochemistry*

Received Date: 27 September 2019
Revised Date: 8 October 2019
Accepted Date: 11 October 2019

Please cite this article as: B-S. Lou, U. Rajaji, S-M. Chen, T-W. Chen, A Simple Sonochemical Assisted Synthesis of Porous $NiMoO_4$/chitosan Nanocomposite for Electrochemical Sensing of Amlodipine in Pharmaceutical Formulation and Human Serum, *Ultrasonics Sonochemistry* (2019), doi: https://doi.org/10.1016/j.ultsonch.2019.104827

A Simple Sonochemical Assisted Synthesis of Porous $NiMoO_4$/chitosan Nanocomposite for Electrochemical Sensing of Amlodipine in Pharmaceutical Formulation and Human Serum

Bih-Show Lou[a,b], Umamaheswari Rajaji[c], Shen-Ming Chen[c,*], Tse-Wei Chen[c]

[a]Chemistry Division, Center for General Education, Chang Gung University, Taoyuan 333, Taiwan.

[b]Department of Nuclear Medicine and Molecular Imaging Center, Chang Gung Memorial Hospital, Taoyuan 333, Taiwan.

[c]Department of Chemical Engineering and Biotechnology, National Taipei University of Technology, No. 1, Section 3, Chung-Hsiao East Road, Taipei 106, Taiwan, Republic of China.

Corresponding Author: *E-mail: smchen78@ms15.hinet.net (S-M Chen), Phone: +886-2270-17147. Fax: +886-2270-25238.

Abstract

In this investigation, a facile sonochemical route has been developed for the preparation of porous nickel molybdate nanosheets/chitosan nanocomposite ($NiMoO_4$/CHIT) by using ammonium molybdate and nickel(II) acetate tetrahydrate and as nickel and molybdate precursor, respectively (ultrasonic power 60 W/cm^2 and frequency 20 kHz). The ultrasonic based materials preparation as a fast, convenient and economical approach has been widely used to generate novel nanomaterials. Herein, we report an efficient voltammetric sensor for amlodipine drug by using porous nickel molybdate nanosheets/chitosan nanocomposite ($NiMoO_4$/CHIT). Its structure and properties were characterized by x-ray diffraction pattern, scanning electron

microscope, transmission electron microscope, elemental analysis and mapping. The electrochemical studies are indicated the $NiMoO_4$/CHIT modified glassy carbon electrode (GCE) exhibited the good performance towards electrocatalytic sensing of amlodipine drug. Consequently, a linear correlation between the anodic peak current with sensor concentration 0.025 to 373.6 μM with a detection limit and sensitivity of 4.62 nM and 4.753 $\mu A.\mu M^{-1}.cm^{-2}$, respectively. A voltammetry based drug analysis was found to be high sensitive and reproducible, which able to detect nanomolar concentration. Furthermore, the fabricated electrochemical sensor was applied in drug and biological samples.

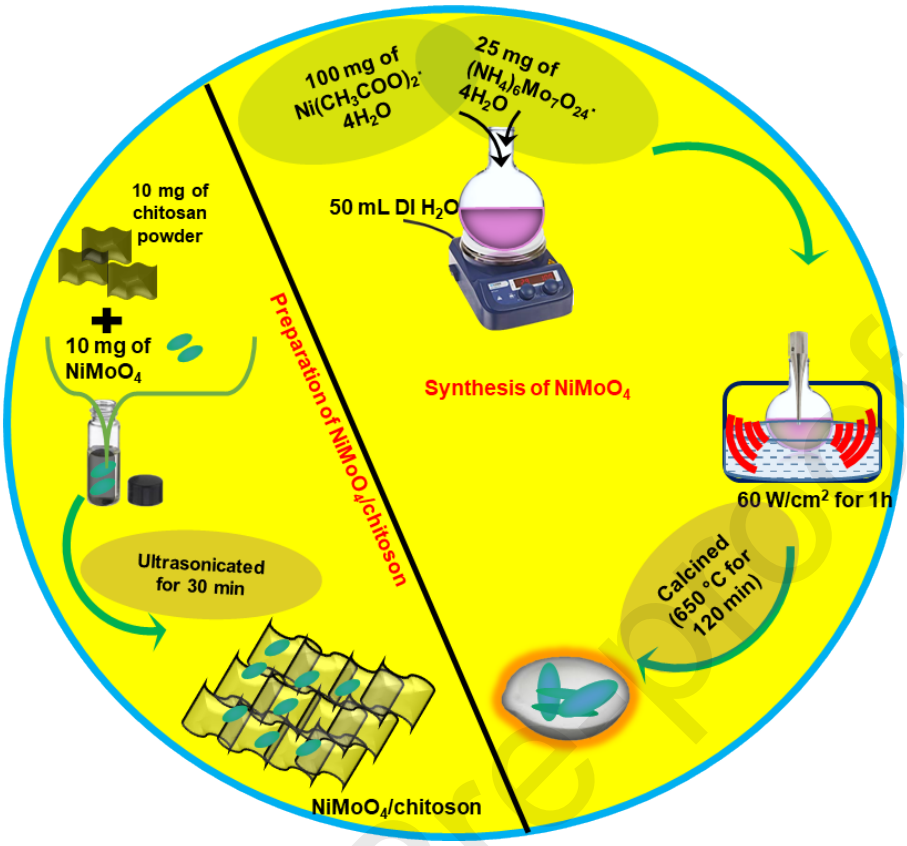
Keywords: Sonochemical synthesis; Bimetal oxide; Electrochemical detection; Drug analysis; Biological samples.

1. Introduction

Amlodipine is a dihydropyridine type drug, which inhibits the several disease such as high blood pressure and coronary artery disease in human and animal [1-4]. So, it has been widely used to treat hypertension; due to its relatively low cost and strong effective [5-7]. However, an excessive intake of amlodipine has side effects in form of abdominal pain, swelling, feeling tired, and nausea [8-11]. Therefore, it is necessary to develop rapid and effective method to determine the level of amlodipine in biological system. So far, HPLC (high performance liquid chromatography) [12], spectrophotometry, GC-TMS (gas chromatography- tandem mass spectrometry) [13, 14], fluorescence sensor [15], capillary zone electrophoresis and electrochemical sensor [16] techniques were used to determine the amlodipine. However, the results in considerable determination of amlodipine sensing in biological samples. Nevertheless,

it has drawbacks on the selectivity, over time consuming and expensive [17, 18]. Recently, electrochemical techniques are provide relatively low cost, facile, easy to operate, good sensitivity and excellent selectivity. Therefore, the fabrication of modified electrodes have been focused more interest in the research and medical development field.

Recently, bimetal oxide is providing exciting new capabilities for research and development in physical and chemical science [10, 19, 20]. In particular, transition series has recently emerged as a promising area in various applications such as supercapacitor [21], photo-degradation [22], batteries [23], hydrogen storage [24], electrochemical sensors [25], CO_2 and CO reduction [26]. $NiMoO_4$ has attracted widespread interests due to the ever-increasing demand for electrocatalytic materials. Here, $NiMoO_4$ for electrochemical sensor due to their excellent features, including intrinsic properties and electrical conductivity [27]. However, the practical applications of $NiMoO_4$ in electrochemical sensor are still hinder due to the moderate of sensing ability and stability [28-33]. Hitherto, various electrode materials including conducting biopolymer, carbonaceous materials, and transition metals have been used to develop superior electrocatalytic performances [7, 33-36]. From the past decades, chitosan, a biopolymer has attracted more interest in electrochemical, biocompatible and biodegradable properties [37, 38]. It has been well-established that biomedical applications and generally show higher electrocatalytic activity than other biopolymer materials due its unique features including excellent electrical conductivity, thermal stability, flexibility and large active surface area to anchor and ability to fast electron transfer [17, 39-42]. Therefore, the choice has been made with biopolymer to enhance the performance of nanomaterial in electrochemical sensor.



Scheme 1. Sonochemical synthesis of $NiMoO_4$/CHIT nanocomposite

Herein, we present our research in developing low-cost, simple and environmental friendly sonochemical-assisted method to prepare $NiMoO_4$/CHIT for drug sensing. Our study describes the strategies for improving the reproducibility and sensitivity voltammetry method to usability of drug sensing by $NiMoO_4$/CHIT modified glassy carbon electrode (Scheme 1 and 2). However, literature reports on the application of $NiMoO_4$/CHIT for electrochemical detection of drug are rare. Herein, we report for a novel and sensitive sensor for the electrochemical detection of amlodipine using $NiMoO_4$/CHIT nanocomposite modified electrodes, which exhibit remarkable sensitivities and desirable detection limits. In addition, the practicality and feasibility ability of $NiMoO_4$/CHIT modified glassy carbon electrode toward drug sensor in tablet and human serum samples.

2. Experimental part

2.1. Sonochemical assisted synthesis of $NiMoO_4$/CHIT

$NiMoO_4$ nanosheets was synthesized by sonochemical technique [43]. The synthesis, 0.2 g of ammonium molybdate ($(NH_4)_6Mo_7O_{24}\cdot 4H_2O$) and 0.1 g of nickel(II) acetate tetrahydrate ($Ni(CH_3COO)_2\cdot 4H_2O$) were dissolved in 50 ml of deionized water (chemicals and methods are given in supporting information). Then the above solution was heated at 75°C for 30 min under stirring. Then the reaction temperature was increased to 90°C and then treated by ultrasonic irradiation 60 W power and 20 kHz frequency (Misonix S-4000). Finally, the yellow-green product was obtained by washed with deionized water and ethanol and dried. The $NiMoO_4$/CHIT was prepared by the chitosan biopolymer assisted sonochemical exfoliation of $NiMoO_4$/CHIT. First, the chitosan biopolymer was dissolved in the ethanol. The 10 mg of $NiMoO_4$ nanoparticles was added into 10 mL of chitosan and dispersed in deionized water and directly used for the electrochemical applications.

2.2. Fabrication of $NiMoO_4$/CHIT/GCE

Prior to modification, the glassy carbon electrode (0.071 cm^2, Gaoss Union Co. Ltd., China) was polished with 0.05 μm alumina powder and then the electrode was sonicated in re-distilled water for 5 min. After that, the dispersed $NiMoO_4$/CHIT solution was (eight μL) drop casting onto the clean surface of glassy carbon electrode. The drop casted glassy carbon electrode was dried out at room temperature and the modified $NiMoO_4$/CHIT/glassy carbon electrode was used to the further all-electrochemical studies.

3. Results and discussions

3.1. XRD analysis

The XRD pattern of $NiMoO_4$/CHIT showed several diffraction peaks, which are originate from the (112), (220), (222), (200), (330), (204), (510), (150) and (530) phases of $NiMoO_4$ nanosheets (figure 1). The phase of $NiMoO_4$ is similar to its cubic phase structure with JCPDS labeled number of 13-0128 [44, 45]. Hence, the formation of $NiMoO_4$/CHIT was conformed in the XRD analysis.

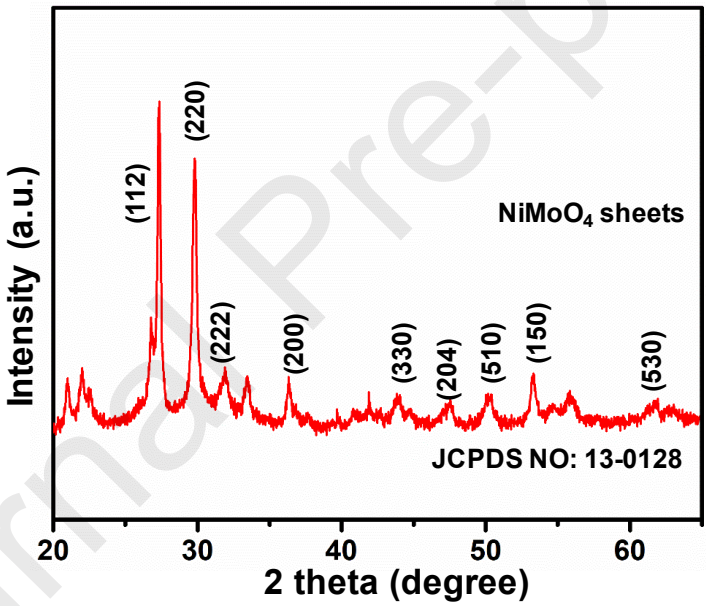


Figure 1. XRD analysis of $NiMoO_4$/CHIT nanocomposite.

3.2. Structural and morphological studies

Next, the morphological aspect of the nanocomposite was studied by TEM (figure 2A). The micrograph of $NiMoO_4$ displays mostly nanosheets, while the TEM image of $NiMoO_4$ is featured with the characteristic sheet-like morphology (figure 2B). However, the SEM image of $NiMoO_4$/CHIT nanocomposite shows the presence of $NiMoO_4$ nanosheets well distributed with

CHIT (figure 2C). A good electrostatic-attractive interaction between $NiMoO_4$ sheets and CHIT are possibly stabilizing them in the nanocomposite form. The EDX spectrum of $NiMoO_4$/CHIT revealed signals for the expected elements, such as carbon, nitrogen, oxygen, nickel and molybdenum signals (figure S1). The elemental mapping of $NiMoO_4$ nanosheets displayed the homogeneous distribution of nickel (D), molybdenum (E) and oxygen (F) in the $NiMoO_4$/CHIT (figure 2D-F).

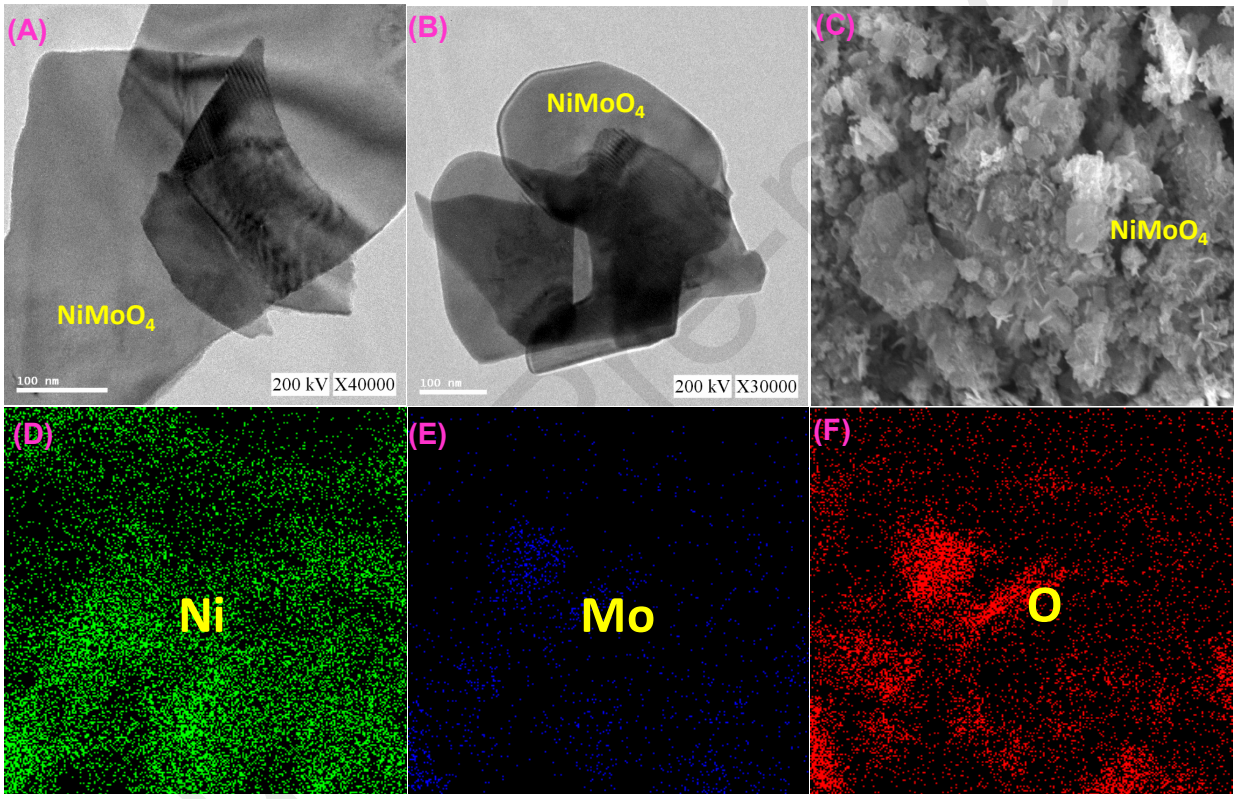


Figure 2. TEM images of $NiMoO_4$ nanosheets (A-B) and SEM image of $NiMoO_4$ (C). Elemental mapping analysis of $NiMoO_4$/CHIT (D-F).

3.3. Electrochemical analysis of amlodipine at $NiMoO_4$@CHIT modified GCE

Under optimum condition, the electrochemical sensor performance of $NiMoO_4$/CHIT/GCE and unmodified GCE were analyzed by cyclic voltammetry (CV). The cyclic voltammograms of unmodified GCE (b) and $NiMoO_4$/CHIT/GCE (c) toward 100 µM

amlodipine in phosphate buffer (pH = 7.0) are shown in figure 3A. A feeble oxidation peak was observed at potential of 0.83 V at unmodified GCE, indicates the electrode is incapability to catalyze the oxidation reaction of amlodipine drug. The CV of $NiMoO_4$/CHIT modified GCE exhibited good oxidation peak at lower potential of 0.78 V with high intensity of current. On the other hand, $NiMoO_4$/CHIT/GCE shows a sharp peak compare to the bare GCE. Notably, the result indicates that $NiMoO_4$/CHIT/GCE has excellent electrocatalytic and sensing ability towards oxidation of amlodipine drug. The electrochemical oxidation (ECO) of amine group to pyridine position, the reaction is involving with $-2e^-$ and $-2H^+$ process and the mechanism is shown in Scheme 2. Moreover, its irreversible process based on the modified electrode surface. After the electrochemical oxidation, the pyridine position is more stable. Therefore, the reversible reduction process is not possible in pH 7.0. In figure 3A, it indicates that the $NiMoO_4$/CHIT/GCE has 2.8 folds larger than that at unmodified GCE. Moreover, the superior electrochemical performance of $NiMoO_4$/CHIT/GCE is due to the excellent synergic effect between $NiMoO_4$ and CHIT toward amlodipine sensing.

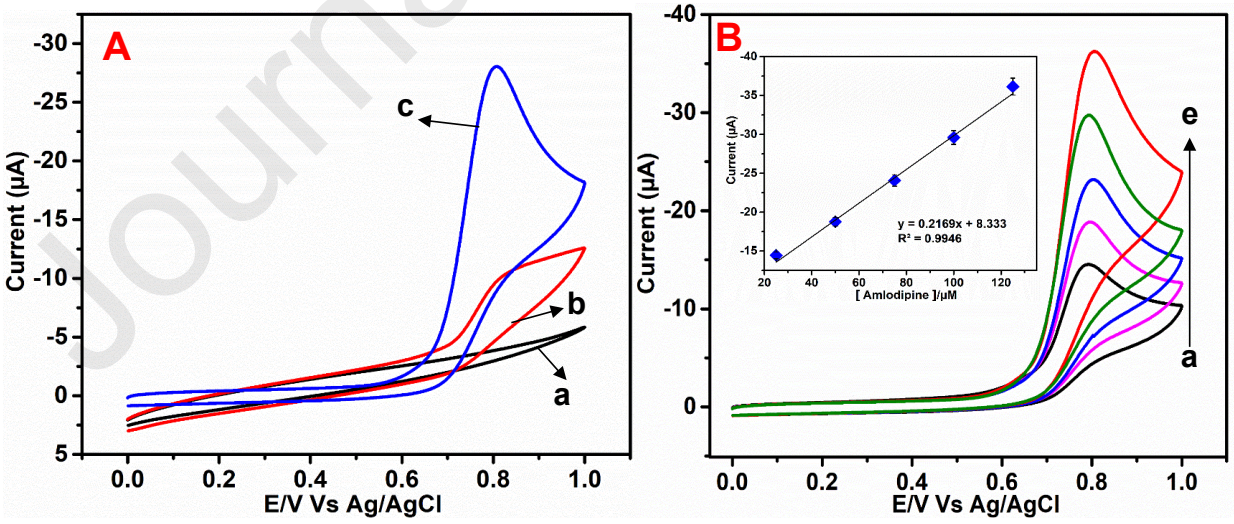
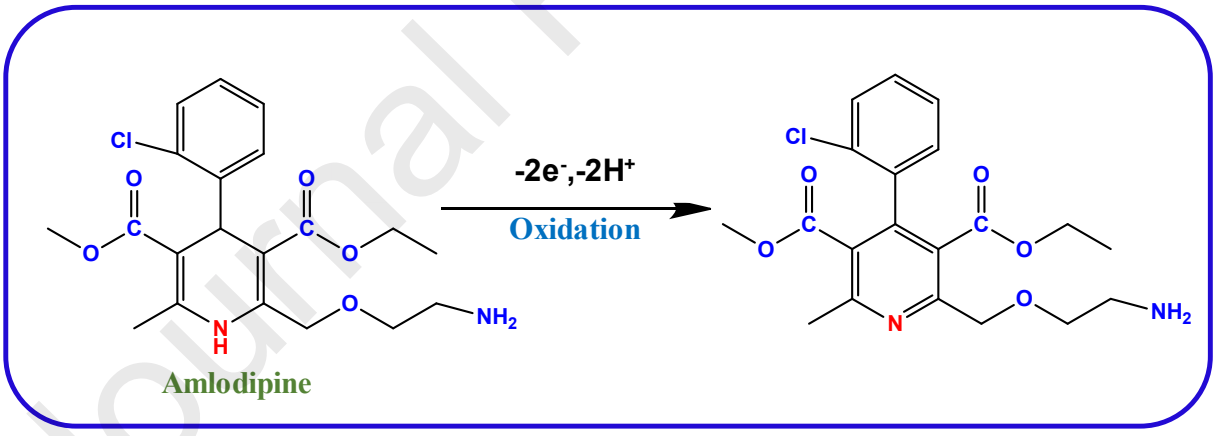


Figure 3. (A) CV responses of $NiMoO_4$/CHIT (c) modified and unmodified (b) GCE in phosphate buffer (0.05 M; pH 7.0) at 50 mV/s in the presence of 100 µM amlodipine and the absence of amlodipine (a) (n=3). (B) CVs of oxidation of amlodipine at $NiMoO_4$/CHIT/GCE for different concentration (25 to 125 µM) and (inset) the calibration plot of anodic peak current vs. [amlodipine]/µM.

In figure 3B, shows the CVs of $NiMoO_4$/CHIT/GCE towards different concentrations of amlodipine drug. When the concentration of amlodipine drug increase, the peak current is also increases linearly from 25 to 125 µM without any fouling. In figure 3B, inset shows the plot between peak current and corresponding concentration of amlodipine drug, its exhibits good linearity, thus the $NiMoO_4$/CHIT nanocomposite modified electrode holds superior electrochemical sensing ability towards drug sensing.



Scheme 2. Systematic mechanism of the electrocatalytic oxidation of amlodipine drug**.**

3.4. Effect of scan rate and various pHs

The influence of scan rate on $NiMoO_4$/CHIT/GCE in 0.05 M phosphate buffer at a scan rate of 50 mV/s containing 100 µM of amlodipine was examined by electrochemical studies,

figure 4A shows the CV results by means of increasing with the scan rate from 20 to 160 mV/s and oxidation peak current density increases and anodic current potential has the ability to shift towards higher positive value, such that the corresponding linear regression equation was acquired to be I_{pa} = 51.103x + 13.452 (R^2 = 0.9909) with excellent linear relationship between scan rate and oxidation peak currents shown in figure 4B. Therefore, these results indicate that the oxidation of amlodipine drug based on $NiMoO_4$/CHIT/GCE is diffusion-controlled process. Moreover, the electrochemical peak potential was shifted to negative direction when the scan rate was increased which can be attributed to the fast electron transfer process of totally irreversible electrode reaction.

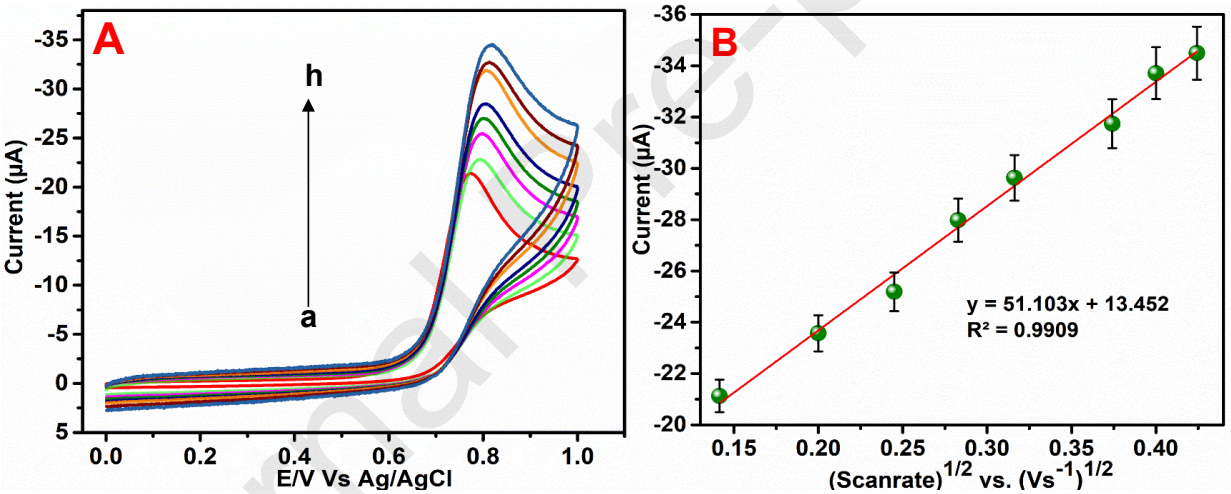


Figure 4. (A) CVs of oxidation of amlodipine at $NiMoO_4$/CHIT/GCE for different scan rate (20 to 160 mV/s). (B) The calibration plot of anodic peak current vs. square root of the scan rate.

The pH value was optimized by measuring the CV responses of modified electrodes in 100 µM amlodipine at the scan rate of 50 mV/s. Different ranges of supporting electrolyte was investigated. The phosphate buffer with maximum efficacy on the oxidation peak current response was selected. The effect of 0.05 M phosphate buffer pH on the DPV determination of

amlodipine drug was studied in the range of 3.0 to 11.0. In figure 5A, shows that the pH increasing pH from 3.0 to 11.0, the oxidation peaks potential shifts toward more negative value. The pH 7.0 is high current responses according to figure 5A and B with correlation coefficient of (R^2) 0.9945. Due to pH 7.0 being the normal pH in human and animal biological fluids and the sensitivity of this sensor, pH 7.0 was chosen for use as the supporting electrolyte in all subsequent analytical experiments.

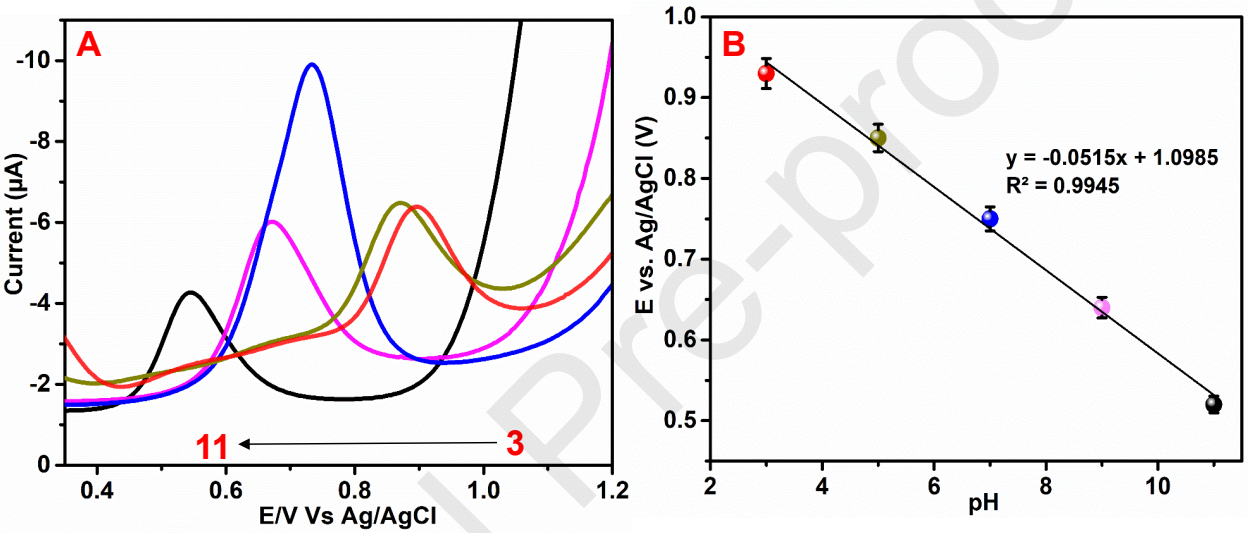


Figure 5. (A) CV responses of 100 μM of amlodipine in various pH ranging from 3.0 to 11.0 at $NiMoO_4$/CHIT/GCE (n=3) and (B) calibration plot for anodic peak current/μM vs. pH.

3.5. Electrocatalytic determination of amlodipine based on $NiMoO_4$/CHIT/GCE by DPV

The analytical behavior of $NiMoO_4$/CHIT/GCE to different additions of amlodipine was investigated also by differential pulse voltammetry (DPV) experiments in 0.05 M phosphate buffer at a scan rate of 50 mV/s (figure 6A). The DPV current response at $NiMoO_4$/CHIT modified GCE attained for different concentration of amlodipine drug from 0.025 to 373.6 μM in 0.05 M phosphate buffer at a scan rate of 50 mV/s. The DPV peak responses shown how it is sensitive even at very low concentration (nanomolar). The calibration plot shows that the results

in figure 6B. According to the DPV results, the anodic current intensity is increases linearly towards lower to higher concentration of amlodipine drug. It is evidently seen that the oxidation peaks current of amlodipine increases (0.025 to 373.6 µM). In figure 6B shows a good linearity between the anodic peak current and concentration of drug with a correlation coefficient (R^2) of 0.9941 from the linear regression equation of I_{pa} = 0.3375x – 0.241. The limit of detection (LOD) is expressed with $3*S_b/g$ (S_b is the standard deviation of blank sample and g is the slop of the calibration curve). The LOD was obtained 4.62 nM. Furthermore, the sensitivity was evaluated to be 4.753 $\mu A.\mu M^{-1}.cm^{-2}$. The electrochemical sensor performance of $NiMoO_4$/CHIT modified GCE was compared with previously reported sensor and results are given in Table 1. The limit of quantification (LOQ) of the enhanced sensor was calculated (24.65 nM) using the equation, $LOQ=3*S_b/g$. It can be seen that our NiMoO4/CHIT proposed sensor in this work shows improved electrochemical performance of the sensor compared to some of those recently reported electrochemical amlodipine sensors. Compared with conventional electrodes, our modified sensors present several advantages as they are highly versatile, cost-effective, user-friendly, and can be use in on-site detection.

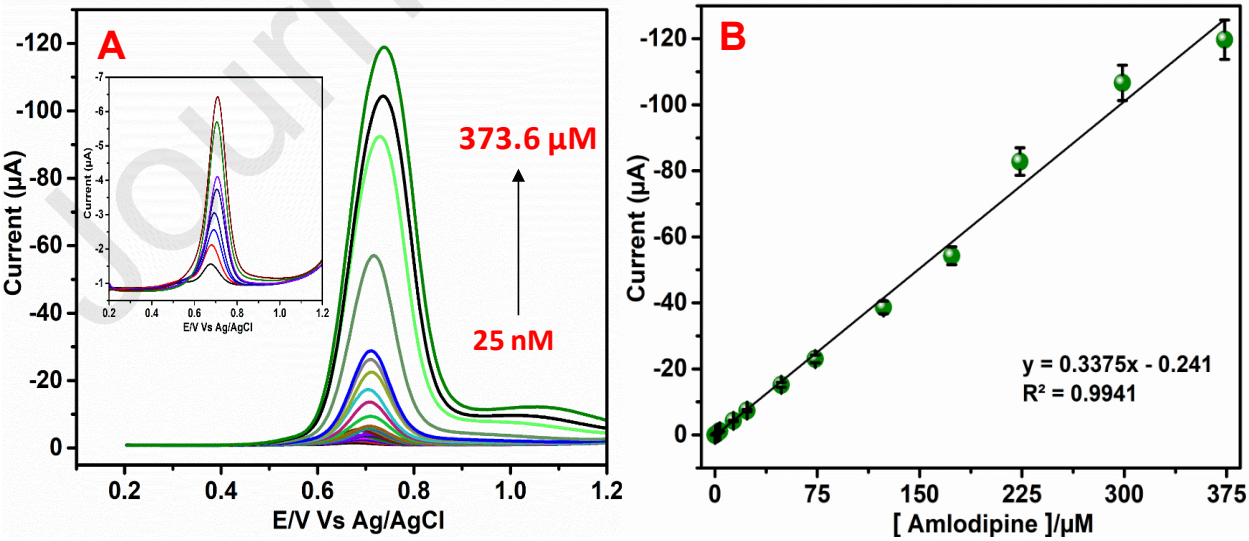


Figure 6. (A) DPV responses of $NiMoO_4$/CHIT/GCE in phosphate buffer with different concentration of amlodipine. (B) Calibration plot of peak current/μA vs. [amlodipine]/μM.

Table 1. Comparison between the sensor performance of $NiMoO_4$/CHIT modified GCE with other previously reported towards amlodipine sensor.

Electrodes	Linear range	Limit of detection	References
MWCNT/GCE	0.017–0.52 μM	0.009 μM	[46]
Carbon nanotubes/GCE	4.3–170 μM	1.7 μM	[47]
MWCNT/gold electrode	24–34 μM	4.2 μM	[48]
boron-doped diamond electrode	6–38 μM	0.07 μM	[49]
EPPGE	0.005–1 μM	0.001 μM	[50]
GCE	8.1–41 μM	0.12 μM	[51]
Fe_3O_4@SiO_2/MWCNT/GCE	0.25–500 μM	0.08 μM	[52]
Nickel hydroxide/GCE	13.9–167 μM	7.9 μM	[4]
$NiMoO_4$/CHIT/GCE	0.1 to 374.5 μM	12.74 nM	This work

3.6. Selectivity analysis of amlodipine sensor based on $NiMoO_4$/CHIT/GCE

To investigate the selectivity of the proposed method, an important parameter for the newly developed electrochemical sensor and the effect of some interfering analyte on the determination of drug was evaluated by DPV method. Selectivity of the $NiMoO_4$/CHIT modified

electrode to detect amlodipine (ALP) in presence of potential possible interferents such as, dopamine (DA), ascorbic acid (AA), folic acid (FA), uric acid (UA), glucose (Glu), K^+, Na^+, Fe^{2+} and H_2O_2 has been studied via DPV method. In figure 7A displays the calibration plot of $NiMoO_4$/CHIT modified electrode toward 100 µM of amlodipine and 0.5 mM of aforementioned interfering species. As shown in figure 7A, the electrode quickly responded to the low concentration amounts of amlodipine, while it was not responding to other species even at high concentrations, suggests excellent selectivity of the electrode. The corresponding histogram is also reflect the same observation in a more clear way (Figure 7A). Moreover, figure 7A shows the modified electrode was tested in presence of metal ions (K^+, Na^+ and Fe^{2+}; 1 mM) and amlodipine concentration was varied in presence of metal ions. The results show that the $NiMoO_4$/CHIT modified electrode has good selective in presence of metal ions and biological analytes.

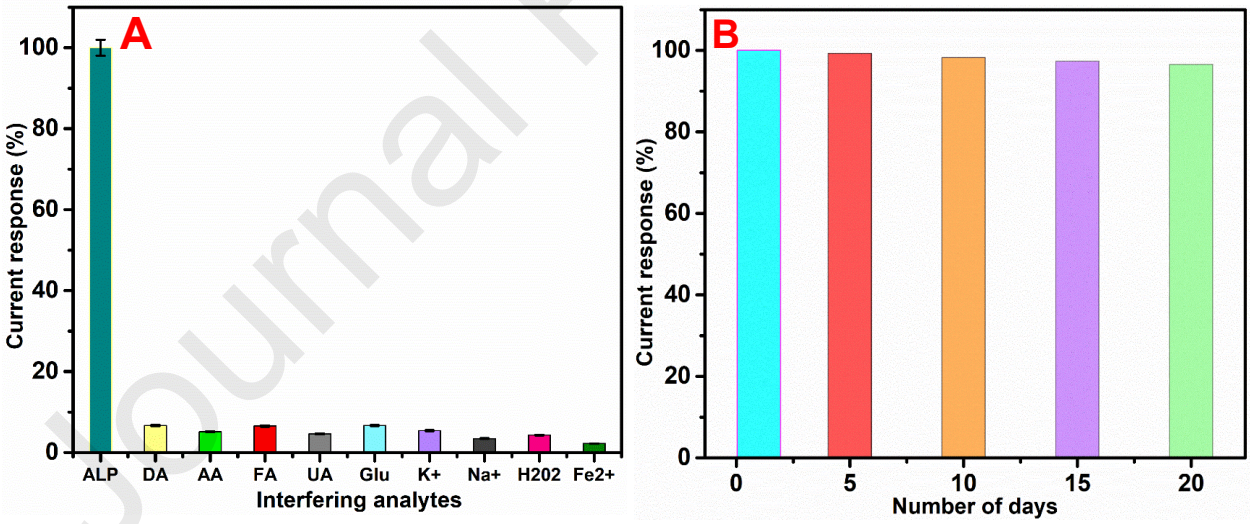


Figure 7. (A) DPVs recorded for amlodipine oxidation in the presence of different interfering compounds (DA-dopamine, AA-ascorbic acid, FA-folic acid, UA-uric acid, Glu-glucose, K^+,

Na^+, Fe^{2+} and H_2O_2) at $NiMoO_4$/CHIT/GCE. (B) Stability analysis of $NiMoO_4$/CHIT/GCE (n=3).

3.7. Reproducibility, repeatability and stability analysis of $NiMoO_4$/CHIT/GCE

The stability of $NiMoO_4$/CHIT/GCE was also examined. The DPV experiments were also carried out using the modified electrode once a day under the same operation conditions. In order to ascertain the stability of the proposed electrochemical sensor, the anodic peak current intensity was investigated by DPV for over a period of 20 days at $NiMoO_4$/CHIT/GCE (figure 7B). The sensor can be kept at room temperature. After 20 days of storage, the obtained peak current response for the modified electrode decreases only by 4.57% from its initial current response. Therefore, the $NiMoO_4$/CHIT modified sensor retains superior stability as well as excellent applicable electrode material towards the electrochemical oxidation of amlodipine drug.

The reproducibility experiment was analyzed by DPV for four independent $NiMoO_4$/CHIT modified GCE in 0.05 M phosphate buffer containing 100 μM of amlodipine drug and its consistent result is shown in figure 8A along with the current response for the oxidation of amlodipine drug is represented as calibration diagram is displayed. The obtained results clearly explained that the developed sensor exhibits outstanding reproducibility with relative standard deviation (RSD) of 3.15%. Besides that, the repeatability test was investigated for identical $NiMoO_4$/CHIT nanocomposite modified electrode containing 100 μM of amlodipine drug concentration in PB (pH 7.0) at a scan rate of 50 mV/s, we observed nearly equivalent current response (figure 8B) with less deviation of less than 3.6% for repeated fifteen runs at single $NiMoO_4$/CHIT modified GCE with RSD of 3.28%. From these studies, it successfully reveals that the good electrochemical sensor possesses predominant performance towards the detection of amlodipine drug.

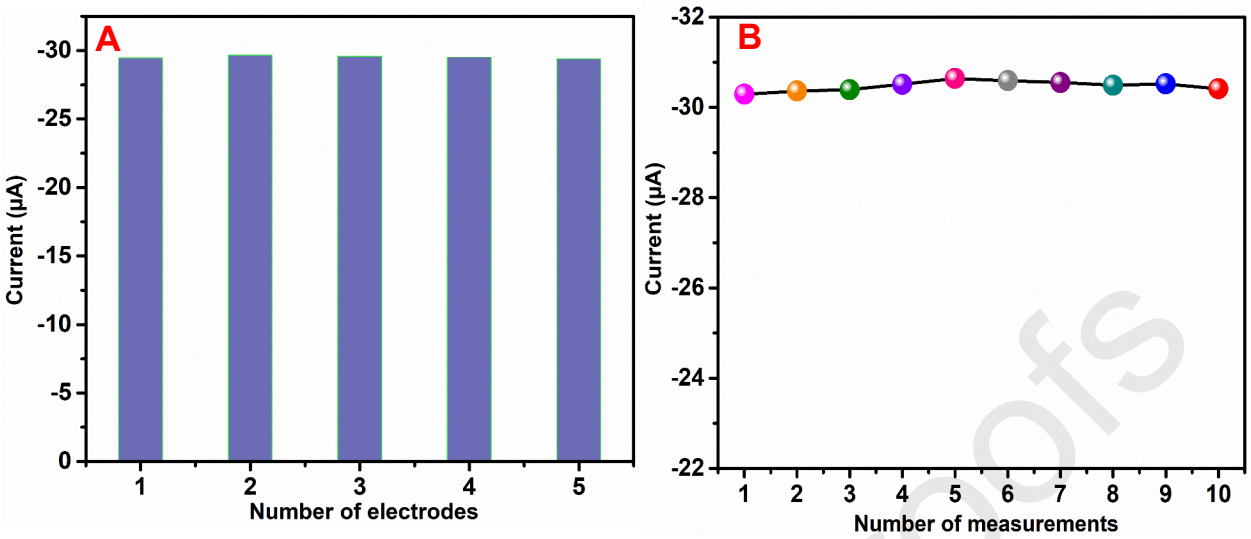


Figure 8. (A) Reproducibility analysis of $NiMoO_4$/CHIT/GCEs (n=3) and (B) repeatability analysis of $NiMoO_4$@CHIT/GCE.

3.8. Real sample analysis

Practical applicability of the modified electrode was demonstrated in pharmaceutical product and biological samples. Amlodipine tablet samples were collected from a pharmaceutical company and diluted in phosphate buffer pH 7.0. Then, the resulting samples are analyzed by DPV and then known amounts of amlodipine were spiked to prepare stock real sample solution. Afterwards, aliquots (each 5, 25 and 50 μM) of lab sample and spiked drug samples were injected into the supporting electrolyte. The electrode delivered prompt and stable sensor responses toward each addition of real samples. The amount of amlodipine added, found and recovery are calculated and given in Table 2. They are in the agreeable analytical range, indicating the suitably of the method in analyzing amlodipine in drug samples. The same sets of experiments were carried out using human serum samples in parallel, and the obtained results are given in Table 2. The biological samples were collected from Chang Gung Memorial Hospital.

Table 2. Determination of amlodipine in real sample analysis in biological and pharmaceutical samples

Samples	Added (µM)	Found (µM)	Recovery (%)	RSD (%) (n=3)
Urine	5	4.76	95.2	3.16
	25	23.61	94.44	2.68
	50	47.11	94.22	3.49
amlodipine	5	4.68	93.6	3.28
tablet	25	24.19	96.76	3.62
	50	48.37	96.74	2.94

4. Conclusion

In this research, we have synthesized more potential nanosheets like nickel molybdate by simple sonochemical method. A simple, novel and low-cost electrochemical sensor for the rapid determination of amlodipine using $NiMoO_4$/CHIT nanocomposite was developed. The morphological and surface properties of as-synthesized $NiMoO_4$/CHIT nanocomposite samples were characterized by XRD pattern, SEM, TEM, EDX and mapping analysis. Furthermore, the $NiMoO_4$/CHIT/GCE was scrutinized for the electrochemical sensing of amlodipine. Fascinatingly, the developed sensor retains higher electrocatalytic activity with low LOD, LOQ, wide linear range, excellent selectivity, reproducibility and repeatability. Upon considering the above-obtained results, the as-synthesized nanocomposite could be utilized for futurity electrochemical applications including biosensor and practical pharmaceutical analysis.

Acknowledgement

The authors gratefully acknowledge the financial support of the Ministry of Science and Technology, Taiwan through contract nos. MOST108-2221-E-182-030 and MOST 107-2113-M-027-005-MY3. The financial support from the Chang Gung Memorial Hospital through contract no. CMRPD5H0032 to B.S. Lou is also acknowledged.

Conflict of interest

The authors declare that they have no conflicts of interest to this research work.

Reference

[1] N.F. Atta, A. Galal, Y.M. Ahmed, H. Ekram, Design strategy and preparation of a conductive layered electrochemical sensor for simultaneous determination of ascorbic acid, dobutamine, acetaminophen and amlodipine, Sensors and Actuators B: Chemical, (2019) 126648.

[2] E. Djaalab, M. Samar, S. Zougar, R. Kherrat, Electrochemical Biosensor for the Determination of Amlodipine Besylate Based on Gelatin–Polyaniline Iron Oxide Biocomposite Film, Catalysts, 8 (2018) 233.

[3] M. Govindasamy, V. Mani, S.-M. Chen, T. Maiyalagan, S. Selvaraj, T.-W. Chen, S.-Y. Lee, W.-H. Chang, Highly sensitive determination of non-steroidal anti-inflammatory drug nimesulide using electrochemically reduced graphene oxide nanoribbons, RSC Advances, 7 (2017) 33043-33051.

[4] W.B. Machini, D.N. David-Parra, M.F. Teixeira, Electrochemical investigation of the voltammetric determination of hydrochlorothiazide using a nickel hydroxide modified nickel electrode, Materials Science and Engineering: C, 57 (2015) 344-348.

[5] H. Hrichi, L. Monser, N. Adhoum, A novel electrochemical sensor based on electropolymerized molecularly imprinted poly (aniline-co-anthranilic acid) for sensitive detection of amlodipine, Journal of Electroanalytical Chemistry, 805 (2017) 133-145.

[6] M. Govindasamy, S.-M. Chen, V. Mani, R. Devasenathipathy, R. Umamaheswari, K.J. Santhanaraj, A. Sathiyan, Molybdenum disulfide nanosheets coated multiwalled carbon nanotubes composite for highly sensitive determination of chloramphenicol in food samples milk, honey and powdered milk, Journal of colloid and interface science, 485 (2017) 129-136.

[7] M. Govindasamy, S.-F. Wang, B. Subramanian, R.J. Ramalingam, H. Al-lohedan, A. Sathiyan, A novel electrochemical sensor for determination of DNA damage biomarker (8-hydroxy-2'-deoxyguanosine) in urine using sonochemically derived graphene oxide sheets covered zinc oxide flower modified electrode, Ultrasonics Sonochemistry, (2019) 104622.

[8] L. Zhang, P. Song, H. Long, M. Meng, Y. Yin, R. Xi, Magnetism based electrochemical immunosensor for chiral separation of amlodipine, Sensors and Actuators B: Chemical, 248 (2017) 682-689.

[9] M. Arvand, H.A. Samie, Electrospun CeO 2–Au nanofibers/graphene oxide 3D nanonetwork structure for the electrocatalytic detection of amlodipine, Ionics, 24 (2018) 1813-1826.

[10] U. Rajaji, M. Govindasamy, S.-M. Chen, T.-W. Chen, X. Liu, S. Chinnapaiyan, Microwave-assisted synthesis of Bi2WO6 flowers decorated graphene nanoribbon composite for electrocatalytic sensing of hazardous dihydroxybenzene isomers, Composites Part B: Engineering, 152 (2018) 220-230.

[11] U. Rajaji, K. Murugan, S.-M. Chen, M. Govindasamy, T.-W. Chen, P.H. Lin, Graphene oxide encapsulated 3D porous chalcopyrite (CuFeS2) nanocomposite as an emerging electrocatalyst for agro-hazardous (methyl paraoxon) detection in vegetables, Composites Part B: Engineering, 160 (2019) 268-276.

[12] K. Pandya, M. Satia, T. Gandhi, I. Modi, R. Modi, B. Chakravarthy, Detection and determination of total amlodipine by high-performance thin-layer chromatography: a useful technique for pharmacokinetic studies, Journal of Chromatography B: Biomedical Sciences and Applications, 667 (1995) 315-320.

[13] S. Tatar, S. Atmaca, Determination of amlodipine in human plasma by high-performance liquid chromatography with fluorescence detection, Journal of Chromatography B: Biomedical Sciences and Applications, 758 (2001) 305-310.

[14] B. Streel, C. Laine, C. Zimmer, R. Sibenaler, A. Ceccato, Enantiomeric determination of amlodipine in human plasma by liquid chromatography coupled to tandem mass spectrometry, Journal of biochemical and biophysical methods, 54 (2002) 357-368.

[15] B.A. Moussa, A.A. El-Zaher, M.A. Mahrouse, M.S. Ahmed, Simultaneous determination of amlodipine besylate and atorvastatin calcium in binary mixture by spectrofluorimetry and HPLC coupled with fluorescence detection, Analytical chemistry insights, 8 (2013) ACI. S12921.

[16] S. Yaqoob, S. Rahim, A.M. Bhayo, M.R. Shah, A. Hameed, M.I. Malik, A Novel and Efficient Colorimetric Assay for Quantitative Determination of Amlodipine in Environmental, Biological and Pharmaceutical Samples, ChemistrySelect, 4 (2019) 10046-10053.

[17] V. Mani, M. Govindasamy, S.-M. Chen, T.-W. Chen, A.S. Kumar, S.-T. Huang, Core-shell heterostructured multiwalled carbon nanotubes@ reduced graphene oxide nanoribbons/chitosan, a robust nanobiocomposite for enzymatic biosensing of hydrogen peroxide and nitrite, Scientific reports, 7 (2017) 11910.

[18] V. Mani, M. Govindasamy, S.-M. Chen, R. Karthik, S.-T. Huang, Determination of dopamine using a glassy carbon electrode modified with a graphene and carbon nanotube hybrid decorated with molybdenum disulfide flowers, Microchimica Acta, 183 (2016) 2267-2275.

[19] S.-M. Chen, R. Umamaheswari, G. Mani, T.-W. Chen, M.A. Ali, A.-H. Fahad, M. Elshikh, M.A. Farah, Hierarchically structured CuFe 2 O 4 ND@ RGO composite for the detection of oxidative stress biomarker in biological fluids, Inorganic Chemistry Frontiers, 5 (2018) 944-950.

[20] T.-W. Chen, U. Rajaji, S.-M. Chen, M. Govindasamy, S.S.P. Selvin, S. Manavalan, R. Arumugam, Sonochemical synthesis of graphene oxide sheets supported Cu2S nanodots for high sensitive electrochemical determination of caffeic acid in red wine and soft drinks, Composites Part B: Engineering, 158 (2019) 419-427.

[21] M. Govindasamy, S. Shanthi, E. Elaiyappillai, S.-F. Wang, P.M. Johnson, H. Ikeda, Y. Hayakawa, S. Ponnusamy, C. Muthamizhchelvan, Fabrication of hierarchical NiCo2S4@ CoS2 nanostructures on highly conductive flexible carbon cloth substrate as a hybrid

electrode material for supercapacitors with enhanced electrochemical performance, Electrochimica Acta, 293 (2019) 328-337.

[22] S.K. Ray, D. Dhakal, S.W. Lee, Rapid degradation of naproxen by AgBr-α-NiMoO4 composite photocatalyst in visible light: mechanism and pathways, Chemical Engineering Journal, 347 (2018) 836-848.

[23] J.-S. Park, J.S. Cho, Y.C. Kang, Scalable synthesis of NiMoO4 microspheres with numerous empty nanovoids as an advanced anode material for Li-ion batteries, Journal of Power Sources, 379 (2018) 278-287.

[24] T. Dong, M. Li, P. Wang, P. Yang, Synthesis of hierarchical tube-like yolk-shell Co3O4@ NiMoO4 for enhanced supercapacitor performance, International Journal of Hydrogen Energy, 43 (2018) 14569-14577.

[25] K. Xu, Q. Tang, W. Zhao, X. Yu, Y. Yang, T. Yu, C. Yuan, In situ growth of Co3O4@ NiMoO4 composite arrays on alumina substrate with improved triethylamine sensing performance, Sensors and Actuators B: Chemical, (2019) 127154.

[26] X. Du, J. Fu, X. Zhang, NiCo2O4@ NiMoO4 Supported on Nickel Foam for Electrocatalytic Water Splitting, ChemCatChem, 10 (2018) 5533-5540.

[27] S. Chen, Z. Zhang, W. Zeng, J. Chen, L. Deng, Construction of NiCo2S4@ NiMoO4 Core-Shell Nanosheet Arrays with Superior Electrochemical Performance for Asymmetric Supercapacitors, ChemElectroChem, 6 (2019) 590-597.

[28] X. Guo, H. Dong, T. Xia, T. Wang, H. Jia, L. Zhu, Highly Efficient Degradation toward Tylosin in the Aqueous Solution by Carbon Spheres/g-C3N4 Composites under Simulated Sunlight Irradiation, ACS Sustainable Chemistry & Engineering, 6 (2018) 12776-12786.

[29] Q. Bkour, O.G. Marin-Flores, M.G. Norton, S. Ha, A highly active and stable bimetallic Ni-Mo2C catalyst for a partial oxidation of jet fuel, Applied Catalysis B: Environmental, 245 (2019) 613-622.

[30] M. Govindasamy, V. Mani, S.-M. Chen, T.-W. Chen, A.K. Sundramoorthy, Methyl parathion detection in vegetables and fruits using silver@ graphene nanoribbons nanocomposite modified screen printed electrode, Scientific reports, 7 (2017) 46471.

[31] M. Govindasamy, B. Subramanian, S.-F. Wang, S. Chinnapaiyan, R.J. Ramalingam, H. Al-lohedan, Ultrasound-Assisted Synthesis of Tungsten Trioxide Entrapped with Graphene Nanosheets for Developing Nanomolar Electrochemical (Hormone) Sensor and Enhanced Sensitivity of the Catalytic Performance, Ultrasonics Sonochemistry, (2019).

[32] M. Govindasamy, S.-F. Wang, R. Jothiramalingam, S.N. Ibrahim, H.A. Al-lohedan, A screen-printed electrode modified with tungsten disulfide nanosheets for nanomolar detection of the arsenic drug roxarsone, Microchimica Acta, 186 (2019) 420.

[33] M. Govindasamy, S.-F. Wang, S. Kumaravel, R.J. Ramalingam, H.A. Al-lohedan, Facile synthesis of copper sulfide decorated reduced graphene oxide nanocomposite for high sensitive detection of toxic antibiotic in milk, Ultrasonics sonochemistry, 52 (2019) 382-390.

[34] F. Xiao, F. Zhao, Y. Zhang, G. Guo, B. Zeng, Ultrasonic electrodeposition of gold− platinum alloy nanoparticles on ionic liquid− chitosan composite film and their application in fabricating nonenzyme hydrogen peroxide sensors, The Journal of Physical Chemistry C, 113 (2008) 849-855.

[35] A. Bouvree, J.-F. Feller, M. Castro, Y. Grohens, M. Rinaudo, Conductive polymer nano-biocomposites (CPC): chitosan-carbon nanoparticle a good candidate to design polar vapour sensors, Sensors and Actuators B: Chemical, 138 (2009) 138-147.

[36] M. Govindasamy, S.-F. Wang, W.C. Pan, B. Subramanian, R.J. Ramalingam, H. Al-lohedan, Facile sonochemical synthesis of perovskite-type SrTiO3 nanocubes with reduced graphene oxide nanocatalyst for an enhanced electrochemical detection of α-amino acid (tryptophan), Ultrasonics sonochemistry, 56 (2019) 193-199.

[37] M. Potara, A.-M. Gabudean, S. Astilean, Solution-phase, dual LSPR-SERS plasmonic sensors of high sensitivity and stability based on chitosan-coated anisotropic silver nanoparticles, Journal of Materials Chemistry, 21 (2011) 3625-3633.

[38] S. Voznesenskiy, A. Sergeev, A.Y. Mironenko, S.Y. Bratskaya, Y.N. Kulchin, Integrated-optical sensors based on chitosan waveguide films for relative humidity measurements, Sensors and Actuators B: Chemical, 188 (2013) 482-487.

[39] M. Mathew, S. Sureshkumar, N. Sandhyarani, Synthesis and characterization of gold–chitosan nanocomposite and application of resultant nanocomposite in sensors, Colloids and Surfaces B: Biointerfaces, 93 (2012) 143-147.

[40] X.-L. Luo, J.-J. Xu, J.-L. Wang, H.-Y. Chen, Electrochemically deposited nanocomposite of chitosan and carbon nanotubes for biosensor application, Chemical Communications, (2005) 2169-2171.

[41] V. Mani, M. Govindasamy, S.-M. Chen, B. Subramani, A. Sathiyan, J.P. Merlin, Determination of folic acid using graphene/molybdenum disulfide nanosheets/gold nanoparticles ternary composite, Int. J. Electrochem. Sci., 12 (2017) e267.

[42] V. Mani, S. Shanthi, T.-K. Peng, H.-Y. Lin, H. Ikeda, Y. Hayakawa, S. Ponnusamy, C. Muthamizhchelvan, S.-T. Huang, Real-time quantification of hydrogen peroxide production in living cells using NiCo2S4@ CoS2 heterostructure, Sensors and Actuators B: Chemical, 287 (2019) 124-130.

[43] G. Kianpour, M. Salavati-Niasari, H. Emadi, Sonochemical synthesis and characterization of NiMoO4 nanorods, Ultrasonics sonochemistry, 20 (2013) 418-424.

[44] Q. Zhang, Y. Deng, Z. Hu, Y. Liu, M. Yao, P. Liu, Seaurchin-like hierarchical NiCo 2 O 4@ NiMoO 4 core–shell nanomaterials for high performance supercapacitors, Physical Chemistry Chemical Physics, 16 (2014) 23451-23460.

[45] Y. Chen, B. Liu, Q. Liu, J. Wang, J. Liu, H. Zhang, S. Hu, X. Jing, Flexible all-solid-state asymmetric supercapacitor assembled using coaxial NiMoO4 nanowire arrays with chemically integrated conductive coating, Electrochimica Acta, 178 (2015) 429-438.

[46] A.R.M. Sikkander, C. Vedhi, P. Manisankar, Electrochemical determination of calcium channel blocker drugs using multiwall carbon nanotube-modified glassy carbon electrode, International Journal of Industrial Chemistry, 3 (2012) 29.

[47] A. Mohammadi, A.B. Moghaddam, K. Eilkhanizadeh, E. Alikhani, S. Mozaffari, T. Yavari, Electro-oxidation and simultaneous determination of amlodipine and atorvastatin in commercial tablets using carbon nanotube modified electrode, Micro & Nano Letters, 8 (2013) 413-417.

[48] Z. Stoiljković, M. Avramov Ivić, S.D. Petrović, D. Mijin, S. Stevanović, U. Lačnjevac, A. Marinković, Voltammetric and square-wave anodic stripping determination of amlodipine besylate on gold electrode, Int. J. Electrochem. Sci, 7 (2012) 2288-2303.

[49] L.u. Švorc, K. Cinková, J. Sochr, M. Vojs, P. Michniak, M. Marton, Sensitive electrochemical determination of amlodipine in pharmaceutical tablets and human urine using a boron-doped diamond electrode, Journal of Electroanalytical Chemistry, 728 (2014) 86-93.

[50] R.N. Goyal, S. Bishnoi, Voltammetric determination of amlodipine besylate in human urine and pharmaceuticals, Bioelectrochemistry, 79 (2010) 234-240.

[51] G. Altiokka, D. Dogrukol-Ak, M. Tunçel, H.Y. Aboul-Enein, Determination of Amlodipine in Pharmaceutical Formulations by Differential-Pulse Voltammetry with a Glassy Carbon Electrode, Archiv der Pharmazie: An International Journal Pharmaceutical and Medicinal Chemistry, 335 (2002) 104-108.

[52] H. Beitollahi, F. Ebadinejad, F. Shojaie, M. Torkzadeh-Mahani, A magnetic core–shell Fe 3 O 4@ SiO 2/MWCNT nanocomposite modified carbon paste electrode for amplified electrochemical sensing of amlodipine and hydrochlorothiazide, Analytical Methods, 8 (2016) 6185-6193.

Research highlights

- A facile and green sonochemical synthesis of $NiMoO_4$/CHIT nanocomposite
- The nanocomposite was characterized by SEM, TEM, EDX, XRD and CV
- The obtained $NiMoO_4$/CHIT NC applied to the electrochemical detection of calcium channel blocker drug (amlodipine)
- The modified sensor has explored high sensitivity and nanomolar detection limit towards amlodipine drug