



Original scientific paper

Theoretical and electrochemical analysis of L-serine modified graphite paste electrode for dopamine sensing applications in real samples

Revanappa Santhosh Kumar¹, Gururaj Kudur Jayaprakash^{2,3,✉},
Siddalinganahalli Manjappa¹, Mohan Kumar⁴ and Avvaru Praveen Kumar⁵

¹Department of Chemistry, University B.D.T. College of Engineering, Visvesvaraya Technological University, Davangere - 577004, Karnataka, India

²Laboratory of Quantum Electrochemistry, School of Advanced Chemical Sciences, Shoolini University, Bajhol, Himachal Pradesh, 173229, India

³Department of Chemistry, Nitte Meenakshi Institute of Technology, Bangalore, Karnataka, 560064, India

⁴Department of Chemistry, PES Institute of Technology and Management, Sagar Road, Guddada Arakere, Kotegangoor, 577204, Shivamogga, India

⁵Department of Applied Chemistry, School of Applied Natural Science, Adama Science and Technology University, P O Box 1888, Adama, Ethiopia

Corresponding author: ✉ rajguru97@gmail.com; Tel.: +91-953-876-2343

Received: May 27, 2022; Accepted: June 8, 2022; Published: July 4, 2022

Abstract

In this study, the carbon paste electrode (CPE) was modified by grinding L-serine in a pestle and mortar. L-serine (L-s) was shown to be an effective electrocatalyst at the modified CPE (MCPE) interface for detecting dopamine (DA). L-sMCPE showed excellent activity to detect DA in commercial injection samples with a recovery range of 98.9 to 100.5 %. Theoretical studies were used to understand the electrocatalysis of L-serine at the atomic level using frontier molecular orbitals (FMO) and analytical Fukui assay. According to theoretical findings, the amine group of L-serine works as an extra oxidation site (reason for enhanced reduction peak DA) and the carboxylic acid group acts as an additional reduction site (reason for enhanced oxidation peak DA) at the L-sMCPE interface.

Keywords

Amino acid; redox reaction; quantum chemical modelling; voltammetry; sensor; dopamine

Introduction

Dopamine (DA) is a monoamine neurotransmitter that plays a variety of physiological activities in humans and animals. It is a basic organic molecule from the catecholamine family. The detection of DA in the human body is crucial. DA is also involved in the control of heart rate and blood pressure [1,2]. DA is involved in a person's movement, mood, and conduct [3]. An inadequate DA level

in the human body can lead to serious health issues such as restless leg syndrome, Huntington's disease, schizophrenia, senile dementia, and Parkinson's disease [4]. DA level in urine samples of humans is utilized as a biomarker to study renal and cardiovascular illnesses. Therefore, proper maintenance of the DA level in the human body is necessary. Because of the relevance of DA, the creation of novel dopamine detecting sensors is highly valued for therapeutic applications [5,6].

For DA detection, a variety of methods have been developed such as capillary electrophoresis [7], fluorescence-based sensing [8,9], colorimetry [10], and fluorescence [11,12]. On the other hand, their protocols are complex, costly, time-consuming, and frequently need specialist equipment. Electrochemical methods, however, provide several benefits, including quick and highly sensitive reactions, the convenience of usage, and low cost. Because of the electroactive nature of DA, its determination using electrochemical techniques is a key scientific issue. Over the last few decades, the sensitivity of DA determination has increased significantly.

Carbon paste electrodes (CPEs) offer few beneficial properties, including repeatability, stability, and surface renewability, which make them one of the most appealing working electrodes [13,14]. Due to their low cost relative to other materials, CPEs are becoming more widely used in fields such as pharmaceutical, biological, and environmental investigations. Physical or chemical treatments can improve electrochemical characteristics of CPE such as adsorption capacity, selectivity, and sensitivity [15]. To create a novel sensor with appropriate electrochemical characteristics, a CPE matrix must be modified. Earlier, a lot of research has been published on carbon-based electrodes for sensing applications [16-24].

On the atomic scale, the quantum chemistry approach, such as density functional theory (DFT) can be utilized to quantify the electron transfer (ET) of electrode catalysts. As a result, electro-analytical data can be supported and explained using basic principles and DFT. In catalytical research, a combination of pre-ET (frontier molecular orbital theory (FMO)) and post-ET (Fukui functions) would be more useful [13,14,25,26].

In this study, we have modified the CPE by grinding L-serine in a pestle and mortar. The L-serine molecule redox reactive sites and mediating mechanism were predicted using conceptual DFT-based quantum chemical modelling. The nucleophilic and electrophilic regions of L-serine are identified using the frontier molecular orbitals (FMO), highest occupied molecular orbital (HOMO), and lowest unoccupied molecular orbital (LUMO) densities. The results of the donor-acceptor interactions were further evaluated utilizing analytical Fukui functions to corroborate the findings.

Experimental

Chemicals and reagents

The analytical grade chemicals were used without further purifications. The sodium dihydrogen orthophosphate monohydrate, silicone oil, dopamine, L-serine, disodium hydrogen orthophosphate, and $K_4Fe(CN)_6$ were purchased from Sigma-Aldrich Himedia. Graphite powder was purchased from Loba chemicals.

Preparation of bare carbon paste electrode (BCPE)

The bare graphite paste was made by extensively hand mixing the carbon (graphite) powder and the binder (silicon oil), in an agate mortar with a pestle in a 75:25 (w/w) proportion for 25 minutes until the paste was uniform and homogeneous. Then, the graphite paste was filled into a 3 mm hole Teflon tube. The electrode surface was wiped smoothly on the butter paper for a clean, consistent, and even surface [13-15].

Preparation of L-serine modified carbon paste electrode (L-sMCPE)

L-sMCPE was prepared by hand mixing/grinding 2 to 10 mg of L-serine with carbon paste in an agate mortar. Then, the graphite paste containing L-serine was filled into a 3 mm hole Teflon tube and smoothen on the butter paper.

Electrochemical cell

The potentiostat model CHI-660c was used in the tests (CH Instrument-660 electrochemical workstation). Three-electrode cell was applied, where working electrodes were bare CPE (BCPE) and L-serine modified CPE (L-sMCPE), the reference electrode was saturated calomel electrode (SCE), and the counter electrode was a platinum rod.

Computational methods

To build model geometries, we used the Sinapsis program [27] and density functional theory (DFT) [Auxiliary density perturbation theory] as implemented in the deMon2k [28-30] software, together with PBE [31,32] correlation functions and the TZVP [33] basis set. The FMO [highest occupied molecular orbital (HOMO) and lowest unoccupied molecular orbital (LUMO)] and analytical Fukui functions were visually shown using Sinapsis [27].

Results and discussion

Cyclic voltammetric response of dopamine at L-serine modified carbon paste electrode

Figure 1 depicts cyclic voltammograms (CVs) for 10 μ M DA in 0.1M phosphate buffer solution (PBS) of pH 7.4 at BCPE (red line) and L-sMCPE with different quantities of L-serine, at a scan rate of 100 mV s^{-1} . At the BCPE, redox peak currents are low with higher separation of peak potentials (ΔE_p) when compared to L-serine MCPE.

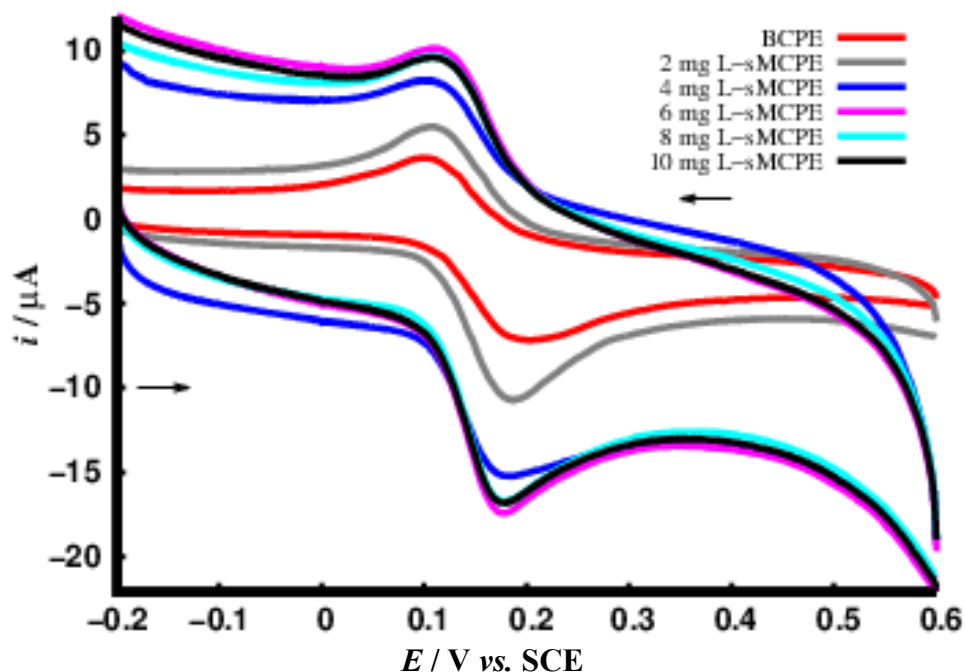


Figure 1. CVs of 10 μ M DA in 0.1 M PBS, pH 7.4 at BCPE (red line) and MCPE with different quantities of L-serine (2-10 mg)

In Table 1, ΔE_p and i_{pa} values for DA are compared for BCPE and MCPE with different quantities of L-serine. From Figure 1 and Table 1, it can be seen that MCPE with 6 mg of L-serine has displayed

the highest redox current value and lower ΔE_p . Therefore we have considered 6 mg L-sMCPE for further analysis.

Table 1. ΔE_p and i_{pa} values of BCPE and MCPE with different quantities of L-sMCPE (data taken from Fig. 1)

El. No.	Electrode	ΔE_p / mV	i_{pa} / μA
1	BCPE	98	7.157
2	2 mg L-sMCPE	70	10.84
3	4 mg L-sMCPE	67	15.24
4	6 mg L-sMCPE	62	17.46
5	8 mg L-sMCPE	61	16.83
6	10 mg L-sMCPE	61	16.87

Computational studies of L-serine

When L-serine is bound by physisorption to the surface of graphite electrode, the electrocatalytic activities of L-sMCPE towards DA are boosted. For mathematical modelling purposes, a monomer of L-serine is considered. To determine which atoms of L-serine are involved in the redox electron transfer processes, the frontier molecular orbitals were estimated and utilized the Fukui concept to predict the redox electron transfer sites.

L-serine HOMO is present in the amine group (Figure 2a), while the LUMO is in the carboxylic acid group (Figure 2b). Therefore, according to FMO findings, the amine group in L-serine is engaged in oxidation, whereas the carboxylic acid group is engaged in reduction.

The Fukui function is frequently used in electrochemistry to understand redox reaction pathways [13,14,25,26]. Simulations based on the Fukui function can be utilized in chemical and electrochemical applications to locate electron transfer sites [13,14]. The Fukui function [34] can be defined using Equation (1):

$$f^{\pm}(\mathbf{r}) \equiv \lim_{\Delta N \rightarrow 0^{\pm}} \left(\frac{\sigma N + \Delta N(\mathbf{r}) - \sigma N(\mathbf{r})}{\Delta N} \right) \quad (1)$$

Here $\rho(\mathbf{r})$ is the electron density, N denotes the number of electrons in the system, and the + and - signs denote electron addition and removal, respectively.

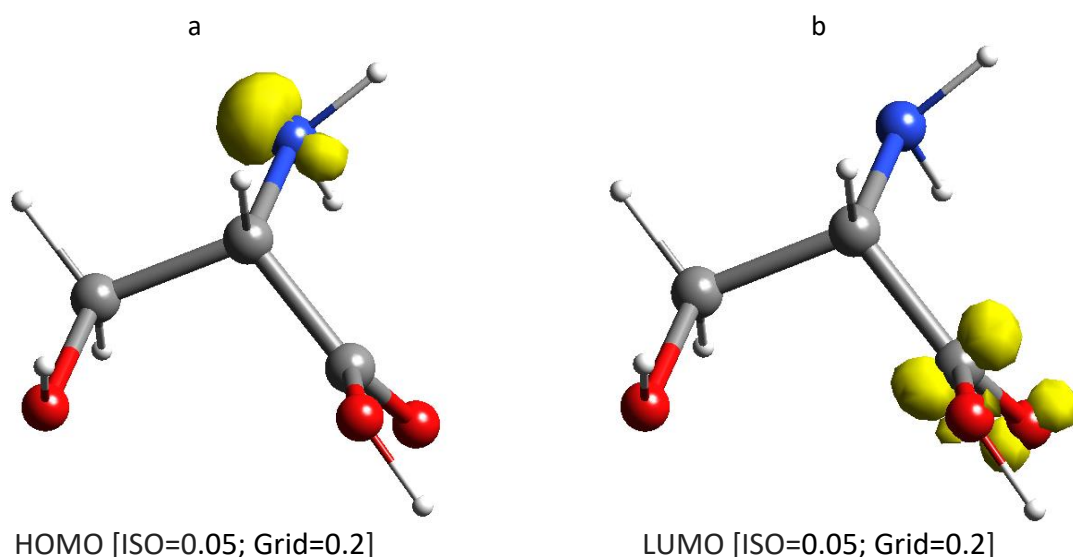


Figure 2. Average reactive orbital space of frontier molecular orbital of L-serine

The analytical Fukui findings for L-serine are displayed in Figure 3. Figure 3a displays $f(r)$ and $f^+(r)$ (Figure 3b) plots of the L-serine surface, respectively. The amine group of L-serine functions as an oxidation site and the carboxylic group of L-serine functions as a reduction site.

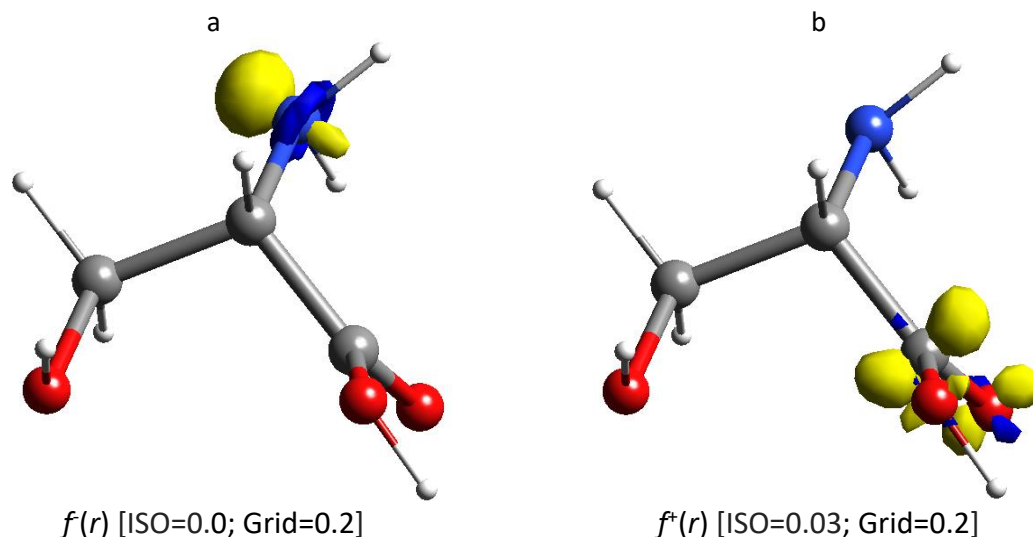


Figure 3. Analytical Fukui isosurface results [H = white, C = grey, N = blue, and O = red]

FMO analysis provides information on reactive redox sites without accounting for electronic relaxation. Analytical Fukui's findings, however, provide details on the places that would suffer the most redox reaction changes while accounting for relaxation effects. Hence, FMO and Fukui researches should be correlated to more precisely forecast redox reactivity locations. In the current studies, both FMO and Fukui, studies are in agreement with each other. As a result, we get more consistent results that amine groups are oxidation centers and carboxylic acid groups are reduction centers.

Effect of DA concentration

Using the CV approach, the influence of DA concentration was investigated at the surface L-sMCPE electrochemical sensor in 0.1 M PBS, pH 7.4. The rise in anodic peak current with increasing DA concentration (10 to 70 μM) is shown in Figure 4. A linearity was observed between anodic peak current (i_{pa}) and DA concentration, with a corresponding linear regression equation: $i_{pa} = 0.448896C_{DA} + 5.1907$, with $r^2 = 0.99532$.

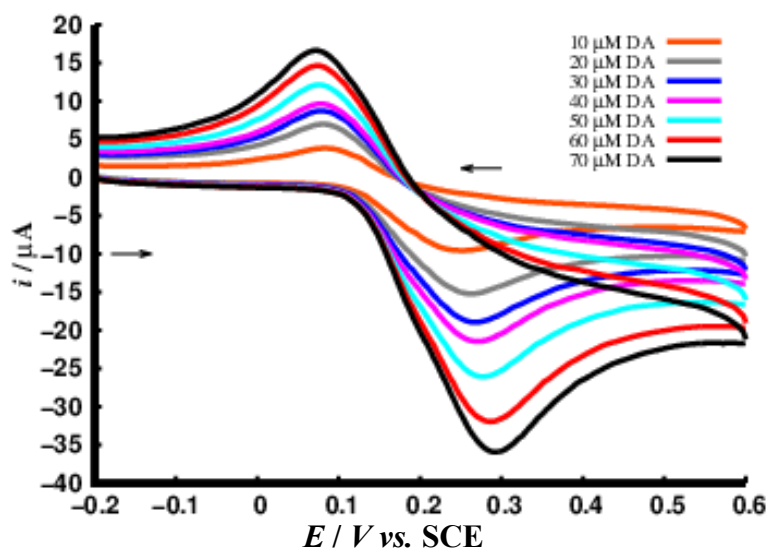


Figure 4. CVs of different DA concentrations (10 -70 μM) at L-sMCPE in 0.1M PBS, pH 7.4

Effect of scan rate

The impact of changing the scan rate (150 to 350 mV s^{-1}) on the oxidation peak current of DA in 0.1 M PBS as the supporting electrolyte is displayed in Figure 5. It can be seen that over the range of 150 to 350 mV s^{-1} , the oxidation peak current rises linearly with the scan rate.

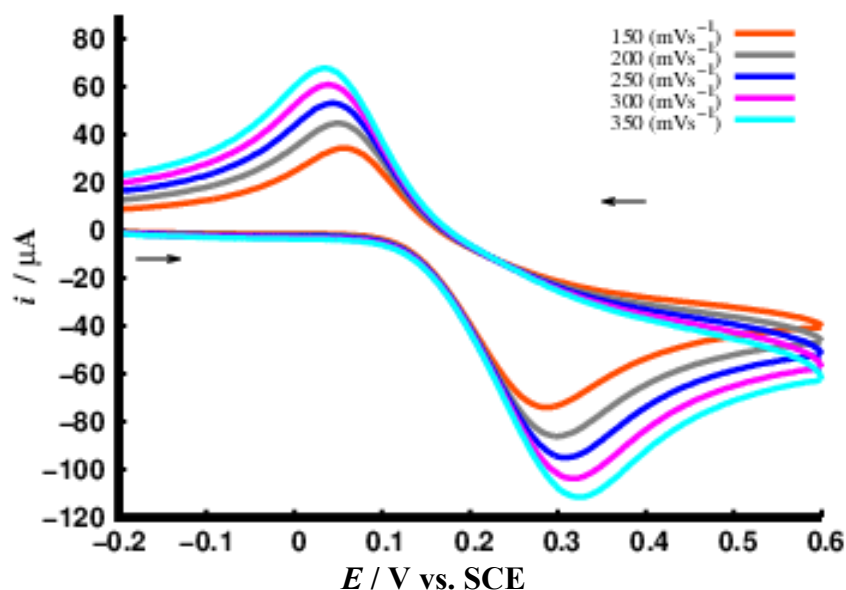


Figure 5. CVs of 10 μM DA at L-sMCPE in 0.1M PBS, pH 7.4 at different scan rates

The graph of anodic peak current vs. scan rate shown in Figure 6 reveals a linear relation with a correlation coefficient of 0.9974. This suggests that DA oxidation at L-sMCPE is adsorption controlled process.

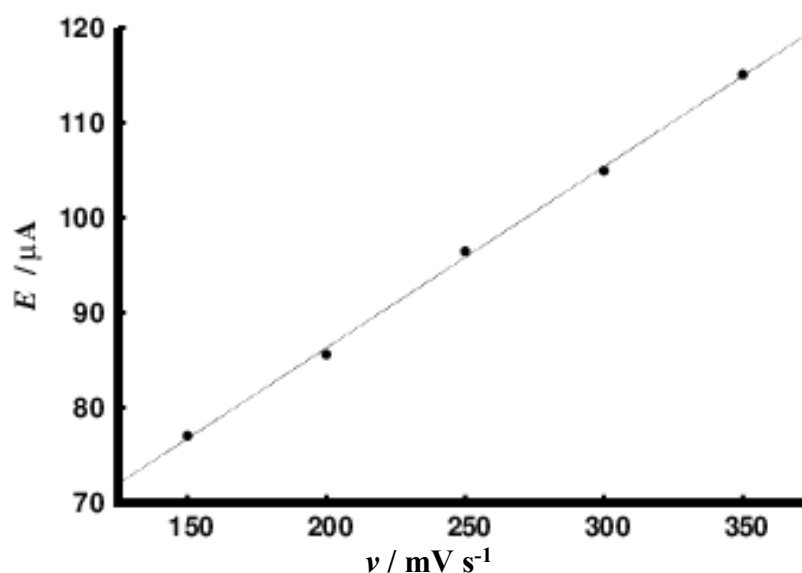


Figure 6. Anodic peak current vs. scan rate (data from Fig. 5)

Determination of DA in real samples

The analysis of DA in the commercial injection sample was carried out at L-sMCPE in order to evaluate the reliability of the proposed approach by using the standard addition method. The results summarized in Table 2 reveal that the found values are close to the labeled content with a recovery range of 98.9 to 100.5 %. Therefore L-serine mediated ET can detect DA in injection samples effectively.

Table 2. Determination of DA in injection samples

Number	$C_{DA} / \mu\text{M}$		Recovery, %
	Spiked	Found	
1	10	10.05	100.5
2	20	19.78	98.90
3	30	29.98	99.93

Conclusion

In the current work, the CPE was modified by grinding L-serine (eco-friendly modifier) in a pestle and mortar. L-serine showed excellent electrocatalytic at the L-sMCPE interface for sensing DA in real injection samples with a recovery range of 98.9 to 100.5 %. The catalytical activity of L-serine was theoretically examined using FMO and analytical Fukui analysis. Theoretical observation proved that the amine group of L-serine acts like an additional oxidation site (reason for enhanced reduction peak of DA) and a carboxylic acid group acts as an additional reduction site (reason for enhanced oxidation peak of DA) of L-serine at the L-sMCPE interface. In the current study, both FMO and Fukui studies are in agreement with each other. Therefore predicted electron transfer sites are precise amine groups of L-serine that have more probability of loose electrons and carboxylic acid groups to gain electrons. Therefore, FMO and Fukui function can be helpful for explaining the improved performance of the L-sMCPE at the molecular level.

Acknowledgements: All authors are very thankful to the editor for giving constructive suggestions to improve the quality of the article.

References

- [1] Y. Wang, Y. Zhang, C. Hou, M. Liu, *Microchimica Acta* **183** (2016) 1145-1152. <https://doi.org/10.1007/s00604-016-1742-6>
- [2] H. X. Zhao, H. Mu, Y.H. Bai, H. Yu, Y.M. Hu, *Journal of Pharmaceutical Analysis* **1** (2011) 208-212. <https://doi.org/10.1016/j.jpha.2011.04.003>
- [3] A. Hammami, R. Sahli, N. Raouafi, *Microchimica Acta* **183** (2016) 1137-1144. <https://doi.org/10.1007/s00604-015-1739-6>
- [4] Z. Guo, M. L. Seol, M. S. Kim, J. H. Ahn, Y. K. Choi, J. H. Liu, X. J. Huang, *Analyst* **138** (2013) 2683-2690. <https://doi.org/10.1039/C3AN36669C>
- [5] M. Wang, L. Bai, L. Zhang, G. Sun, X. Zhang, S. Dong, *Analyst* **141** (2016) 2447-2453. <https://doi.org/10.1039/C6AN00016A>
- [6] J. X. Liu, S. N. Ding, *Journal of Electroanalytical Chemistry* **781** (2016) 395-400. <https://doi.org/10.1016/j.jelechem.2016.08.027>
- [7] Y. Li, H. Song, L. Zhang, P. Zuo, B. C. Ye, J. Yao, W. Chen, *Biosensors and Bioelectronics* **78** (2016) 308-314. <https://doi.org/10.1016/j.bios.2015.11.063>
- [8] E. Alipour, M. R. Majidi, A. Saadatirad, S. Mahdi Golabi, A. M. Alizadeh, *Electrochimica Acta*. **91** (2013) 36-42. <https://doi.org/10.1016/j.electacta.2012.12.079>
- [9] V. Carrera, E. Sabater, E. Vilanova, M. A. Sogorb, *Journal of Chromatography B* **847** (2007) 88-94. <https://doi.org/10.1016/j.jchromb.2006.09.032>
- [10] B. Kong, A. Zhu, Y. Luo, Y. Tian, Y. Yu, G. Shi, *Angewandte Chemie International Edition* **50** (2011) 1837-1840. <https://doi.org/10.1002/anie.201007071>
- [11] A. Yildirim, M. Bayindir, *Analytical Chemistry* **86** (2014) 5508-5512. <https://doi.org/10.1021/ac500771q>
- [12] H.Y. Wang, Y. Sun, B. Tang, *Talanta* **57** (2002) 899-907. [https://doi.org/10.1016/S0039-9140\(02\)00123-6](https://doi.org/10.1016/S0039-9140(02)00123-6)

- [13] G. K. Jayaprakash, B. E. K. Swamy, N. Casillas, R. Flores-Moreno, *Electrochimica Acta* **258** (2017) 1025-1034. <https://doi.org/10.1016/j.electacta.2017.11.154>
- [14] G. K. Jayaprakash, B. E. K. Swamy, S. Rajendrachari, S. C. Sharma, R. Flores-Moreno, *Journal of Molecular Liquids* **334** (2021) 116348. <https://doi.org/10.1016/j.molliq.2021.116348>
- [15] R. Shashanka, G. K. Jayaprakash, B. G. Prakashaiah, M. Kumar, B. E. Kumara Swamy, *Materials Research Innovations* **26(4)** (2021) 229-239. <https://doi.org/10.1080/14328917.2021.1945795>
- [16] G. Tigari, J. G. Manjunatha, *Journal of Analysis and Testing* **3(4)** (2019) 331-340. <https://doi.org/10.1007/s41664-019-00116-w>
- [17] N. Hareesha, J. G. Manjunatha, *Journal of Science: Advanced Materials and Devices* **5(4)** (2020) 502-511. <https://doi.org/10.1016/j.jsamd.2020.08.005>
- [18] N. Hareesha, J. G. Manjunatha, C. Raril, G. Tigari, *ChemistrySelect* **4(15)** (2019) 4559-4567. <https://doi.org/10.1002/slct.201900794>
- [19] N. Hareesha, J. G. Manjunatha, *Materials Research Innovations* **24(6)** (2020) 349-362. <https://doi.org/10.1080/14328917.2019.1684657>
- [20] J. G. Manjunatha, *Chemical Data Collections* **25** (2020) 100331. <https://doi.org/10.1016/j.cdc.2019.100331>
- [21] S. Rajendrachari, B. E. K. Swamy, S. Reddy, D. Chaira, *Analytical & Bioanalytical Electrochemistry* **5(4)** (2013) 455-466. http://abechem.ir/index.php?option=com_content&view=article&id=9&Itemid=8
- [22] E. Turunc, I. Gumus, H. Arslan, *Materials Chemistry and Physics* **243** (2020) 122597. <https://doi.org/10.1016/j.matchemphys.2019.122597>
- [23] R. Shasanka, B. E. K. Swamy, *Physical Chemistry Research* **8(1)** (2020) 1-18. <https://dx.doi.org/10.22036/pcr.2019.205211.1688>
- [24] R. Shashanka, B. E. Kumara Swamy, *SN Applied Sciences* **2** (2020) 956. <https://doi.org/10.1007/s42452-020-2785-1>
- [25] G. K. Jayaprakash, *Chemical Physics Letters* **789** (2022) 139295. <https://doi.org/10.1016/j.cplett.2021.139295>
- [26] G. K. Jayaprakash, R. Flores-Moreno, *New Journal of Chemistry* **42(23)** (2018) 18913-18918. <https://doi.org/10.1039/C8NJ03679A>
- [27] *Sinapsis developers*, <http://sinapsis.sourceforge.net> (accessed July 20, 2020)
- [28] *deMon*, A software package for density functional theory (DFT) calculations, http://demon-software.com/public_html/index.html (accessed and downloaded February 13, 2019)
- [29] G. Geudtner, P. Calaminici, J. Carmona-Espíndola, J. M. del Campo, V. D. Domínguez-Soria, R. F. Moreno, G. U. Gamboa, A. Goursot, A. M. Köster, J. U. Reveles, T. Mineva, *WIREs Computational Molecular Science* **2(4)** (2012) 548-555. <https://doi.org/10.1002/wcms.98>
- [30] R. Flores-Moreno, J. Melin, J. V. Ortiz, G. Merino, *The Journal of Chemical Physics* **129(22)** (2008) 224105. <https://doi.org/10.1063/1.3036926>
- [31] J. P. Perdew, K. Burke, M. Ernzerhof, *Physical Review Letters* **77** (1996) 3865. <https://doi.org/10.1103/PhysRevLett.77.3865>
- [32] J. P. Perdew, K. Burke, M. Ernzerhof, *Physical Review Letters* **80** (1998) 891. <https://doi.org/10.1103/PhysRevLett.80.891>
- [33] N. Godbout, D. R. Salahub, J. Andzelm, E. Wimmer, *Canadian Journal of Chemistry* **70** (1992) 560-571. <https://doi.org/10.1139/v92-079>
- [34] R. G. Parr, W. Yang, *Journal of the American Chemical Society* **106(14)** (1984) 4049-4050. <https://doi.org/10.1021/ja00326a036>

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