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Electrochemical determination of melatonin using disposable self-adhesive inked paper electrode

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ABSTRACT

Melatonin is a hormone that affects sleep-wake cycles and plays a role in the understanding of neuronal disorders and has excellent potential for therapeutical applications in infectious diseases, becoming an important target of chemical analysis. In this context, we report the development of an electrochemical device comprising a self-adhesive electrode based on a graphite-automotive varnish (Gr-AV) mixture as a conductive material to produce a printable ink applied over a paper adhesive easily transferred to a polyethylene terephthalate substrate. The Gr-AV electrode presented a high electrochemically active surface area which showed to be suitable for melatonin oxidation. The association of the device alongside a square-wave voltammetry method offered a linear behavior in the concentration range from 10.0 to 100.0 μmol L^{-1}, a limit of detection of 0.49 μmol L^{-1}, as well as presenting exciting recovery and relative standard deviation over samples analysis. The results showed the valid application of the device for the determination of melatonin in biological samples, pharmaceutical formulations, and its potential for point-of-care analysis.

1. Introduction

Melatonin (5-methoxy-*N*-acetyltryptamine) is an indole-derived substance found in many living organisms, playing a pivotal role as a hormonein vertebrates. It is mostly produced in the pineal gland and is intimately related to circadian rhythm, which regulates physiological processes, including oxidative stress, cardiac rhythm, and homeostasis in mitochondria. In summary, melatonin has a substantial impact on endogenous cycles known as the "internal clock." Moreover, it shows to be a multifunctional molecule, presenting antitumor, immunoregulatory, anti-inflammatory, and antioxidant properties [1,2].

Synthetic melatonin is found as the main ingredient of many supplements being designated against short-term sleep disorders. Melatonin supplementation has gained popularity even with weak evidence of its benefits [3–6]. However, some pieces of evidence indicate that exogenic melatonin can be useful as supporting medication in other neural disorders, such as epilepsy, Parkinson's, and Alzheimer's diseases [7,8]. Recently, clinical evidence suggests that melatonin can play a protective role against lung injury in viral infections, including SARS-CoV-2 and influenza, by the inhibition of inflammatory pathways, being a potential adjuvant drug applied in the treatment of these diseases [9,10]. Additionally, as an endocrine substance, melatonin can be found in a variety of body fluids and tissues, including saliva, urine, and blood, presenting oscillating concentrations according to circadian cycle [11]. For this reason, monitoring melatonin levels is required in medicine to comprehend its signaling mechanisms and how it affects the endocrine system. Many analytical methodologies have been described for melatonin quantification, which stands out chromatographic [12–15], optical [16–20], and electrochemical techniques [21–24].

Electroanalytical methodologies are known for their great sensitivity, short-time analysis, the possibility of miniaturization, and versatility for the development of sensory platforms, which allows the integration of functional materials, resulting in a large variety of sensors based on polymers [22–25], nanoparticles [26], carbon-based materials [27–29], hybrid arrangements [30] and biomolecules [31]. However, despite their proven efficiency, such materials associations

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can increase the analysis costs, especially with the emerging global demand for non-exclusive health solutions, particularly for underdeveloped nations.

In this way, the alternative solution arises in the search for portable and disposable electrochemical devices based on low-cost materials suitable for large-scale production and point-of-care testing. The development of such devices requires a minimal number of components, which can include a substrate, preferable flexible and biodegradable, for receiving a printable electrode material. Thereby, the paper has been widely used in electrochemical devices due to characteristics such as chemical inertness, biocompatibility and biodegradability, relatively low cost, and affordability of a variety of types, such as adhesive paper, which in this report becomes a field application alternative as there is no need for a set place for analysis [32,33]. Thus, poly(ethylene terephthalate) (PET) stood out among the possibilities for a substrate due to advantages such as chemical and biological inertness, good flexibility, mechanical resistance, and safe handling. In addition to its use as a substrate, its use also has sustainability attractiveness. With considerable high degradation periods, the proposed use as substrate presents recycling options and reusing the material [34,35].

Therefore, these devices development and characteristics can be achieved using conductive inks based on graphite incorporated into polymers or dispersed in a proper solvent, sequentially stamped over a paper substrate. Graphite-based conductive inks for electrode manufacturing have been extensively reported in the literature, thanks to their high electrical conductivity and chemical inertia [35–37]. Recently, it is being reported the association of a graphite/automotive varnish ink (Gr-AV) disposed on self-adhesive paper, which has resulted in a highly versatile adhesive electrode for application in electrochemical sensing of dopamine serotonin as well as in enzyme-based biosensing of glucose [33].

Here, we present a methodology for melatonin quantification based on a self-adhesive inked paper (Gr-AV) electrode set using square wave voltammetry (SWV) and a brief study of the electrochemical behavior melatonin oxidation on the electrode surface. The resulting sensor was applied for melatonin analysis in serum, urine, and commercial pharmaceutical formulations.

2. Experimental

2.1. Reagents and solutions

All reagents used in this work were of analytical grade and purchased from Sigma-Aldrich and/or Fluka, being used directly as received without further treatment. Graphite powder was obtained from Fischer Chemical (USA), and the automotive varnish acquired from Sherwin-Williams (Brazil), Lazzudur 2K Auto Brilho was used as the ink polymer-based vehicle. The human serum from male AB clotted whole blood (USA origin, sterile-filtered) was obtained from Sigma-Aldrich. Commercial samples of melatonin in capsules were purchased from local drugstores in Araras - Brazil. The electrochemical characterization of the device and melatonin detection was performed using 0.5 mol L^{-1} McIlvaine buffer solution. All aqueous solutions were prepared using ultrapure water processed through a Millipore Milli-Q system (resistivity ≥18.2 MΩ·cm).

2.2. Apparatus

All electrochemical measurements were performed with an Autolab PGSTAT204 (Eco Chemie) potentiostat/galvanostat (with FRA32M module) managed by NOVA 2.1.3 software. An 827 pH-meter (Metrohm) was used for pH measurements. The morphological characterization of the Gr-AV electrode was performed by Scanning Electron Microscopy (SEM) field emission gun (FEG) using a scanning electron microscope FEI Magellan 400L.

2.3. Preparation of paper-based Gr-AV electrodes

Preparation of the conductive ink was carried out following a procedure previously reported [33], where 7.2 g of graphite powder was added to 18 g of the automotive varnish, representing an amount equivalent to 40% of the final ink mass. The resulting suspension was mixed for 3 cycles of 3500 rpm for 90 s in a dual asymmetric centrifuge SpeedMixer™ Dac 150.1 FVZ-K (FlackTec Inc) and the ink was solidified at room temperature. Afterward, the graphite ink was applied onto the adhesive paper sheet and cut using a cutting printer (Silhouette, Cameo 3). After 40 min of the drying process, the excess material was removed and discarded. The resulting device comprised a centered working electrode (Ø = 2.06 mm diameter according to pre-printing design), a surrounding counter electrode, and a reference electrode, according to Fig. 1, which shows the fabrication process and the design of the resulting electrode set.

2.4. Preparation of samples

To evaluate potential interference caused by major substances in biological samples, synthetic urine was prepared according to the previous report [38]. The urine sample was prepared using a 100 mL volumetric flask dissolving the following amounts of compounds in deionized water: 0.29 g of NaCl, 0.16 g of KCl, 0.11 g of $CaCl_2{\cdot}2H_2O$, 0.22 g of sodium sulfate, 0.14 g of KH_2PO_4, 0.1 g of NH_4Cl, 0.11 g of creatinine and 2.5 g of urea. Human serum samples were diluted in a 1:2 ratio (human serum: McIlvaine buffer solution) as performed by Wang and collaborators [39]. The content in commercial melatonin capsules, with labeled 3.0 mg the active principle, was dissolved and diluted adequately in supporting electrolytes.

2.5. Analytical procedure

Oxidation behavior of melatonin was investigated by square-wave voltammetry considering the effect of the pH of the electrolyte support solution (from pH 3.0 to pH 8.0), as well as the optimization of the following experimental parameters in SWV: frequency (*f*), amplitude (*a*) and step (*s*). Once the analysis conditions were set up, the analytical curve was built to acquire analytical parameters for SWV, including linear concentration range, the limit of detection, and quantification. As a final step, the proposed voltammetric method was applied for melatonin quantifications in the synthetic sample of urine, a human serum sample, as well as in melatonin capsules.

3. Results and discussion

3.1. Morphological characterization of the Gr-AV electrode

Fig. 2 shows SEM images for the Gr-AV electrode in three different magnifications (Fig. 2a, 2b, and 2c), showing a rough and heterogeneous deposition pattern of the conductive ink over the working electrode area delimited by the printing process, with a slightly distorted circumference and diameter (Ø = 1.68 mm) with a small deviation of pre-printing design (Fig. 2a). It is possible to observe the overlapping graphite sheets and the pores scattered over the entire surface, as well as the coating of the automotive varnish on the material (Fig. 2b and 2c), which suggests the presence of a high surface area for conduction and suitable for the electrochemical process.

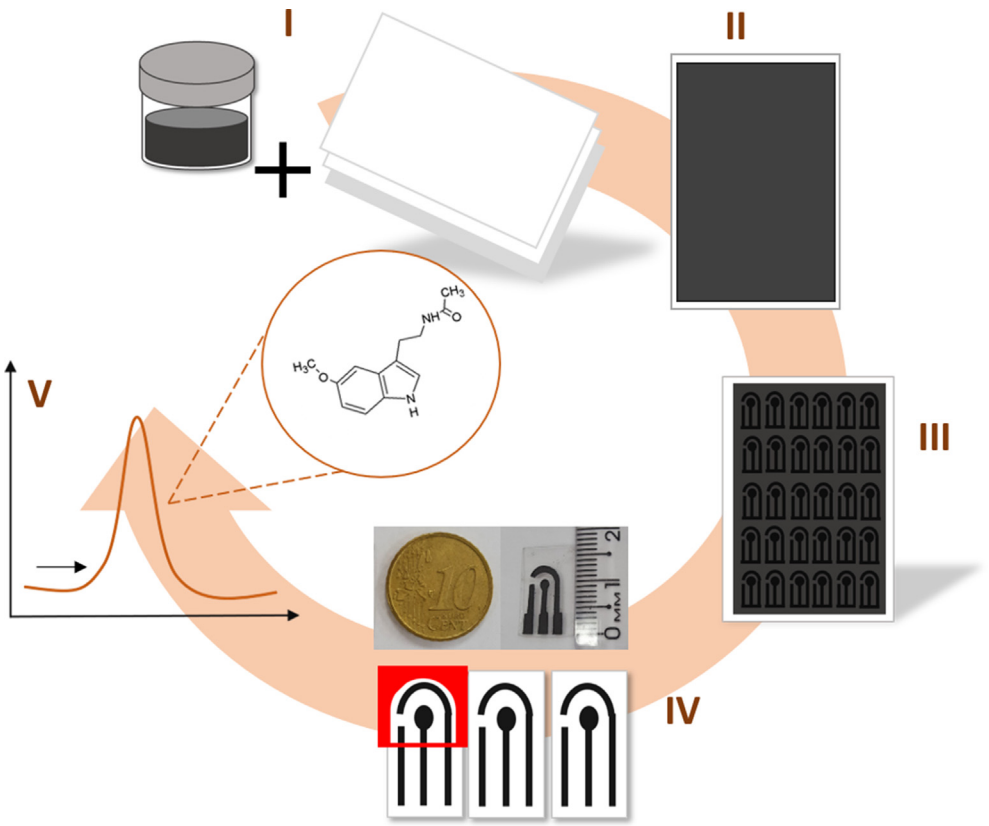

Fig. 1. Preparation of the proposed sensor. (I) Conductive is prepared. (II) The conductive ink is spread on the self-adhesive paper and drying time is optimized. (III) Electrode printing. (IV) Electrode clipping and bonding over PET substrate with drop delimiter. The device is then ready for (V) electrochemical analyses.

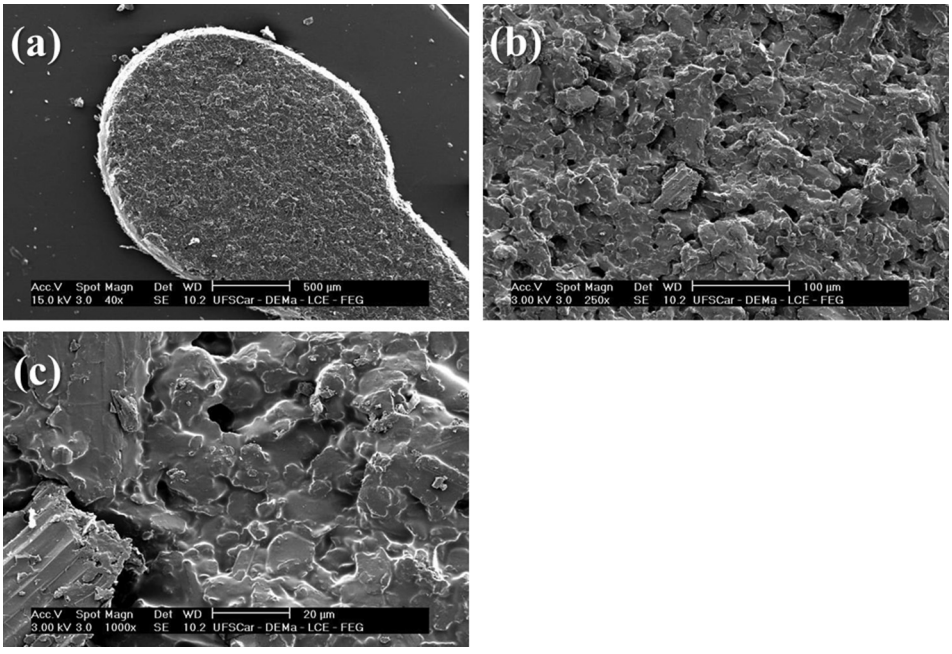

Fig. 2. SEM images obtained for Gr-AV electrode surface using magnifications of (a) 40x, (b) 250x e (c) 1000x.

3.2. Electrochemical characterization of Gr-AV electrode

Fig. 3a shows the cyclic voltammogram for Gr-AV electrode at the presence of $[Fe(CN)_6]^{3-/4-}$ at 50 mV s^{-1}, presenting oxidation peak at 230 mV (63 μA) and reduction peak at − 260 mV (-60 μA), with a peak-to-peak separation of 490 mV and a current ratio of 1.06, therefore, indicating a quasi-reversible behavior. This peak-to-peak separation is close to similar works in literature [33,36,40–42] and it is attributed to the high electron transfer resistance of lab-made inks. However, such behavior does not interfer with the disposable device performance or signal resolution for the proposed application. The voltammogram shape indicates a mixed kinetic and diffusion control

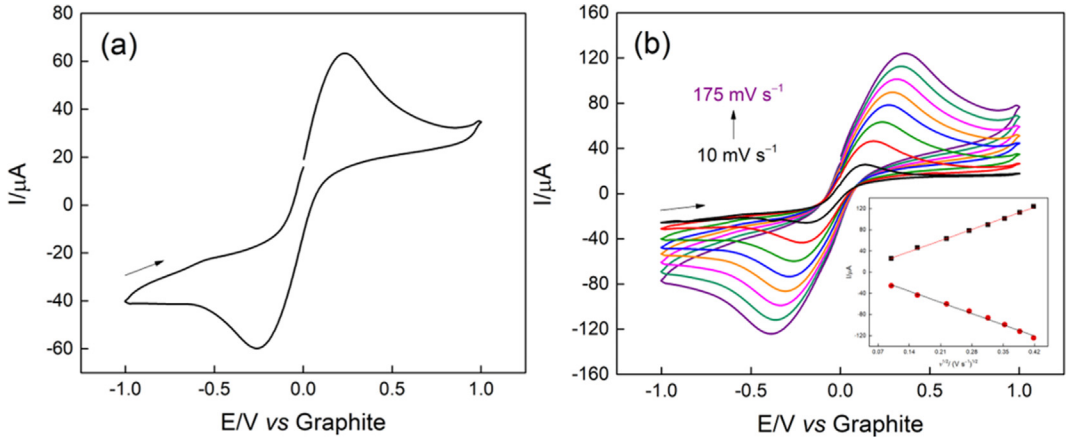

Fig. 3. (a) Cyclic voltammogram obtained by Gr-AV electrode in presence of an equimolar solution of $[Fe(CN)_6]^{3-/4-}$ 1.0 × 10^{-3} mol L^{-1} in KCl 0.1 mol L^{-1} electrolyte solution; ν = 10 mV s^{-1} (b) Cyclic voltammograms obtained by Gr-AV electrode in presence of 1.0 × 10^{-3} mol L^{-1} equimolar solution of $[Fe(CN)_6]^{3-/4-}$ in KCl 0.1 mol L^{-1} electrolyte solution, with varying scan rates, from 10 to 175 mV s^{-1}. Inset: I_p *vs* $\upsilon^{1/2}$ plot.

in a semi-infinite electrode surface. This effect is credited to combining the fibrous electrode surface and the unexpressive enlargement of the diffusion layer at slow scan rates. As the scan rate increases (Fig. 3b), a predominant diffusion-controlled behavior is observed with a continuous increase of peak-to-peak separation. Additionally, the electroactive area of the Gr-AV electrode was estimated by the Randles-Sevcik equation:

$$I_p = \pm(2.69 \times 10^5) n^{3/2} A D^{1/2} C \nu^{1/2}$$

where I_p is the peak current (A), n the number of electrons transferred, A the electroactive area (cm^2), D the diffusion coefficient of $[Fe(CN)_6]^{3-/4-}$ in the 0.1 mol L^{-1} KCl solution (7.63 × 10^{-6} and 6.32 × 10^{-6} cm^2 s^{-1} for the respective reduced and oxidated forms of the probe), C the probe concentration (mol cm^{-3}) and ν the potential scan rate (V s^{-1}). The estimation resulted in an electroactive area of 0.404 cm^2, which is about 12 times larger than the geometrical area (0.033 cm^2).

3.3. Electrochemical behavior of melatonin on Gr-AV electrode

The electrochemical behavior of melatonin was evaluated by cyclic voltammetry along with the potential range from 0.0 to 1.0 V in a 0.5 mol L^{-1} McIlvaine buffer solution with pH 7.0. From Fig. 4a is possible to observe the presence of an oxidation wave with a low-resolution peak at 0.570 V, with a magnitude of 0.17 μA. As no cathodic peak is observed, the process is classified as irreversible in this potential range.

The acquisition of kinetic parameters for the charge transfer process associated with melatonin oxidation on Gr-AV electrode was carried out by cyclic voltammetry with varying scan rates. Correlating the obtained data and the Laviron theory for irreversible processes, which shows a linear dependence between peak potential and the natural logarithm of the scan rate (showed in Fig. 4b), according to the following equation

$E_p = E^0 - \left(\frac{RT}{\alpha nF}\right) ln\left(\frac{RTk_s}{\alpha nF}\right) + \left(\frac{RT}{\alpha nF}\right)$ ln υwhere a is the charge-transfer coefficient, k_s is the heterogeneous electron-transfer rate constant, T is the temperature of the analysis (298.15 K), F is the Faraday constant (96,485 C mol^{-1}), R the ideal gas constant (8.315 J K^{-1} mol^{-1}), n is the number of electrons transferred in the melatonin oxidation process (n = 1 [36]), and E^0 is the standard potential, obtained by the intersect of E_p *vs* I_p plot (544 mV). As a result, the α value was obtained by dividing the correlation for irreversible oxidations [43]:

$$|E_p - E_{1/2}| = 1.857 \frac{RT}{\alpha F}$$

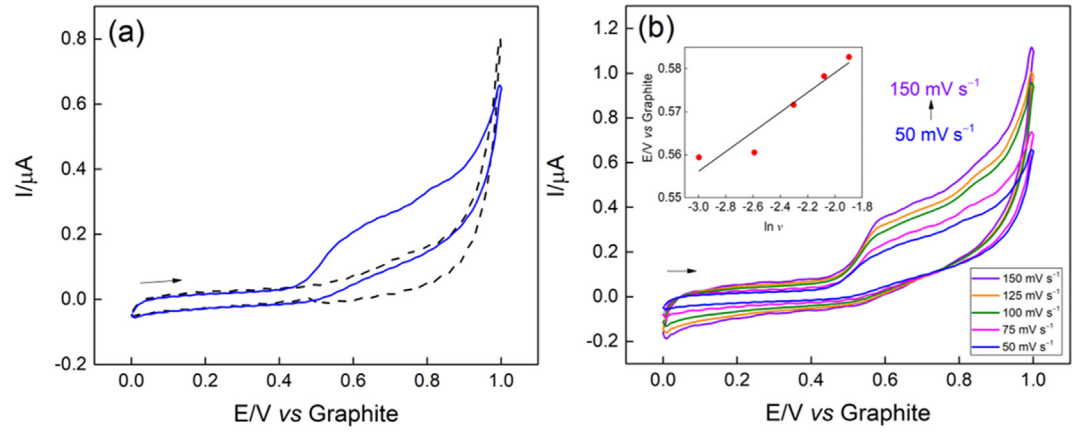

Fig. 4. (a) Cyclic voltammograms obtained by Gr-AV electrode in presence of 50 μmol L^{-1} melatonin, in 0.5 mol L^{-1} McIlvaine buffer solution (pH 7.0); ν = 50 mV s^{-1}. (b) Cyclic voltammograms obtained by Gr-AV electrode in presence of 50 μmol L^{-1} melatonin, in 0.5 mol L^{-1} McIlvaine buffer solution (pH 7.0); with varying scan rates, from 50 to 150 mV s^{-1}.

and corresponds to 0.60 with is an acceptable value for this system morphology. Therefore, the k^0 could be calculated, resulting in 0.085 s^{-1}, suggesting a somewhat sluggish or more complex reaction, not being limited to simple electron transfer. The response mechanism of melatonin can be seen in Fig. 5. It shows how the substance reaction occurs through irreversible oxidation, possibly due to a two-electrons and one-proton transfer, resulting in the formation of a radical cation. This behavior can be identified in the literature in Camargo [36], Tavakkoli [44], and Levent [45] and their collaborators, and is supported by the obtained data. The linear equation correlating the E_p shift with the scan rate is E_p (V) = 0.624 + 0.023 ln(ν) (V s^{-1}).

3.4. Optimization of analytical parameters on SWV

Fig. 6 shows a set of square-wave voltammograms for melatonin oxidation under different pH values of McIlvaine buffer solution at 0.5 mol L^{-1} over the pH range of 3.0 to 8.0. The voltammograms indicate a tendency of peak potential to shift to lower values as the pH increases, presenting a slight oscillation at pH 6. The magnitude of oxidation current, in turn, intensifies as the pH increases and reaches a maximum value at pH 7. At pH 8, the current decreases significantly. For this reason, aiming at a higher sensitivity of the sensor, the ideal value for the pH of the supporting electrolyte was 7.0, which was selected for further studies. Next, the analytical parameters that affected the current response in SWV were evaluated to obtain the maximum current magnitude as follows: potential amplitude (a), frequency (f), and potential step (s). The optimized values obtained for these parameters were f = 100 Hz, a = 20 mV, s = 6.0 mV,

3.5. Voltammetric determination of melatonin

The determination of melatonin was conducted by SWV through successive additions of analite using the Gr-AV sensor in 0.5 mol L^{-1} McIlvaine buffer solution (pH 7.0). According to Fig. 7, the peak current recorded for melatonin oxidation increases linearly as the increment of concentration of the electrochemical cell. The resulting analytical curve (inset of Fig. 7) has shown the dependence between peak current and melatonin concentration over a linear range from 10.0 to 100.0 μmol L^{-1}, generating the following equation: I_p (μA) = (1.86 ± 0.3) × 10^{-7} + (129 ± 7) × 10^{-4} [melatonin] (mol L^{-1}), presenting a coefficient of determination, R^2 = 0.995. The limit of detection (LOD) was found to be 0.47 μmol L^{-1} estimated from the relationship 3 × (σ/m), where σ is the standard deviation of ten measurements (n = 3) performed for the blank solution and m is the sensitivity of analytical curve (angular coefficient).

Gr-AV electrode was applied to melatonin determination in commercial capsules and biological fluid (synthetic urine and human serum). The serum and urine samples were doped using known melatonin concentrations (10, 20, 40, 80, and 100 μmol L^{-1} for urine; and 10 and 20 μmol L^{-1} for serum). The results for commercial melatonin capsules were compared with the labeled value (3.0 mg). The voltammograms of all these data are provided in the supplementary material (Fig. S1-3), where it can be observed that, in complex matrices, few unknown peaks are present but with no signal interfering effect. These can be attributed to several salts used in the synthetic urine and melatonin capsule formulation. As shown in Table 1, the recovery percentages (n = 3) obtained for the synthetic samples were in the range of 87.6 to 110%, indicating that the proposed sensor was able to quantify the melatonin without significant interference of the sample matrix. Additionally, the analysis of commercial capsules presented low values of relative standard deviation (RSD) from the labeled amount of melatonin, as can be seen in the final section of Table 1.

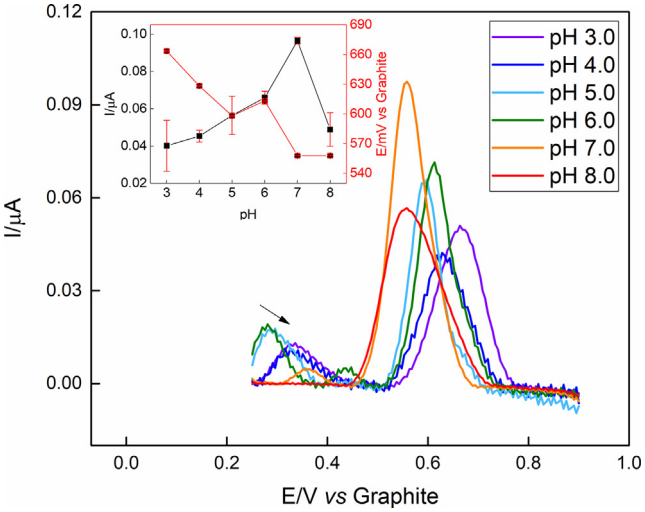

Fig. 6. Square wave voltammograms obtained by Gr-AV in presence of 10 μmol L^{-1} melatonin, in McIlvaine buffer solution with different pH, ranging from 3.0 to 8.0; s = 5.0 mV; a = 20 mV; f = 25 Hz. Inset: I_p and E_p *vs* pH plot.

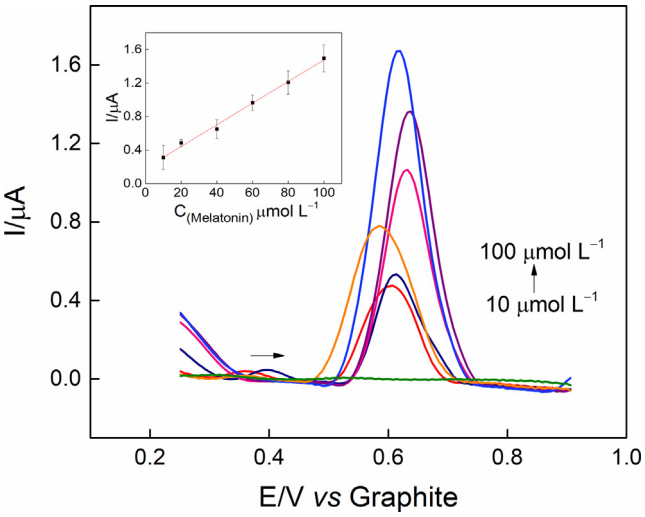

Fig. 7. Square-wave voltammograms obtained by Gr-AV in presence of increasing concentrations of melatonin (10.0 to 100 μmol L^{-1}), in 0.5 mol L^{-1} McIlvaine buffer solution (pH 7.0); s = 6.0 mV; a = 20 mV; f = 100 Hz. The inset presents the calibration curve.

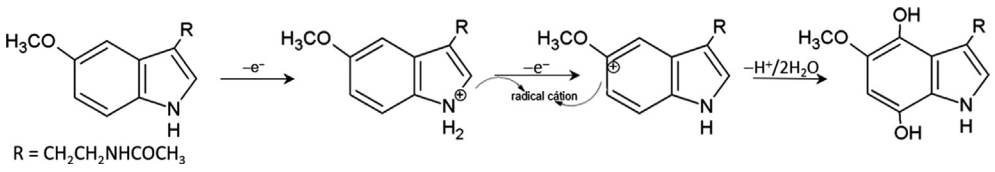

Fig. 5. Oxidation mechanism of melatonin.

Table 1
Results obtained using the proposed SWV method using Gr-AV electrode in the determination of melatonin in synthetic urine, synthetic serum, and commercial samples.

Synthetic urinefv			
Sample	Added (μmol L^{-1})	Recovered (mol L^{-1})*	Recovery (%)**
A	10.0	9.74 ± 0.01	97.4
B	20.0	21.96 ± 0.07	110
C	40.0	35.01 ± 0.02	87.5
D	80.0	73.57 ± 0.08	91.9
E	100	95.14 ± 0.08	95.1
AB blood serum			
Sample	Added (μmol L^{-1})	Recovered (μmol L^{-1})*	Recovery (%)**
A	10.0	8.98 ± 0.08	89.8
B	20.0	18.1 ± 0.1	90.4
Commercial melatonin capsules			
Sample	Labeled (mg)	Found (mg)*	RSD (%)***
A	3.00	2.96 ± 0.02	−1.24
B	3.00	3.19 ± 0.01	6.48
C	3.00	3.14 ± 0.05	4.64

* Average of 3 measured concentrations.
** Recovery percentage (proposed method) = [Found] / [Added] × 100.
*** RSD = [(Proposed method – Labeled concentration) / (Labeled concentration)] × 100.

Table 2
Comparison of electrodes proposed for melatonin determination.

Sensors	Linear range (μmol L^{-1})	LOD (μmol L^{-1})	Literature
GPT/WPE*	0.8 to 100	0.033	[36]
Poly-MM/poly-OAP modified SPCs**	0.5 to 60.0	0.066	[22]
CNTs and graphene-based CSPE***	5.0 to 300	1.1	[46]
ZnFe2O4/CPE****	6.5 to 145	3.0	[44]
Gr-Av	10 to 100	0.47	This work

* Waterproof paper electrodes.
** Modified screen-printed sensor with poly-(melamine)/poly-(o-aminophenol) composite.
*** Modified screen-printed electrode with carbon nanotubes or graphene.
**** Modified carbon paste electrode with zinc ferrite nanoparticles.

The comparison of the Gr-AV electrode with other similar systems found in the literature for the determination of melatonin is present in Table 2. It is possible to observe that the performance of the Gr-AV electrode, presented through this work, can be considered analytically appreciable, with a linear range and LOD acceptable for the proposed application, when compared with other works in the literature. Another important aspect to highlight is that the Gr-Av device is of considerably diminished size compared to others, which was not necessary to further surface modification for the working electrode.

4. Conclusions

This study demonstrated the applicability of a disposable device based on a self-adhesive inked electrode in melatonin quantification based on analyte oxidation. The manufacturing process of the device showed to be straightforward with a relatively low cost. Since the conductive material was based on a graphite-automotive varnish (Gr-AV) dispersion, the proposed device can be eligible for large-scale production. The application of the electrode alongside the SWV technique resulted in appreciable analytical features, including LOD of 0.47 μmol L^{-1}, a linear concentration range from 10.0 to 100.0 μmol L^{-1}, as well as a good recovery in samples with complex matrices. The SWV method using the Gr-AV electrode has shown to be suitable for melatonin determination in biological samples and commercial pharmaceutical formulations alternative to conventional approaches, especially in the point-of-care analysis.

CRediT authorship contribution statement

Rafaela C. Freitas: Data curation, Investigation, Methodology, Writing - original draft. **Luiz O. Orzari:** Data curation, Investigation, Methodology, Conceptualization, Writing - original draft, Supervision. **Luís M.C. Ferreira:** Investigation, Conceptualization, Writing - original draft. **Thiago R.L.C. Paixão:** Conceptualization, Investigation, Methodology, Supervision. **Wendell K.T. Coltro:** Conceptualization, Investigation, Methodology, Supervision. **Fernando C. Vicentini:** Conceptualization, Investigation, Methodology. **Bruno C. Janegitz:** Conceptualization, Funding acquisition, Investigation, Methodology, Supervision.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jelechem.2021.115550.

References

[1] A. Goheer, K. Holzhauer, J. Martinez, T. Woolf, J.W. Coughlin, L. Martin, D.i. Zhao, H. Lehmann, J.M. Clark, W.L. Bennett, What influences the “when” of eating and sleeping?a qualitative interview study, Appetite 156 (2021) 104980, https://doi.org/10.1016/j.appet.2020.104980.
[2] Selmaoui, B., Touitou, Y., Association between mobile phone radiation exposure and the secretion of melatonin and cortisol, two markers of the circadian system: a review. Bioelectromagnetics 2020.
[3] N. Buscemi, B. Vandermeer, N. Hooton, R. Pandya, L. Tjosvold, L. Hartling, S. Vohra, T.P. Klassen, G. Baker, Efficacy and safety of exogenous melatonin for secondary sleep disorders and sleep disorders accompanying sleep restriction: meta-analysis, BMJ 332 (7538) (2006) 385–393.
[4] N. Buscemi, B. Vandermeer, R. Pandya, N. Hooton, L. Tjosvold, L. Hartling, G. Baker, S. Vohra, T. Klassen, Melatonin for Treatment of Sleep Disorders, 108, Agency for Healthcare Research and Quality, 2004, pp. 1–7.
[5] T. Li, S. Jiang, M. Han, Z. Yang, J. Lv, C. Deng, R.J. Reiter, Y. Yang, Exogenous melatonin as a treatment for secondary sleep disorders: a systematic review and meta-analysis, Front. Neuroendocrinol. 52 (2019) 22–28.
[6] R.L. Riha, The use and misuse of exogenous melatonin in the treatment of sleep disorders, Curr. Opin. Pulm. Med. 24 (6) (2018) 543–548.
[7] S.R. Pandi-Perumal, V. Srinivasan, D.W. Spence, D.P. Cardinali, Role of the Melatonin System in the Control of Sleep. 2007, 21 (12), 995–1018.
[8] V. Srinivasan, D.P. Cardinali, U.S. Srinivasan, C. Kaur, G.M. Brown, D.W. Spence, Rüdiger Hardeland, S.R. Pandi-Perumal, Therapeutic potential of melatonin and its analogs in Parkinson’s disease: focus on sleep and neuroprotection, Therap. Adv. Neurol. Dis. 4 (5) (2011) 297–317.
[9] G. Anderson, R.J. Reiter, Melatonin: roles in influenza, Covid-19, and other viral infections, Rev. Med. Virol. 30 (3) (2020). e2109.
[10] R. Zhang, X. Wang, L. Ni, X. Di, B. Ma, S. Niu, C. Liu, R.J. Reiter, COVID-19: melatonin as a potential adjuvant treatment, Life Sci. 250 (2020) 117583.
[11] S. Benloucif, H.J. Burgess, E.B. Klerman, A.J. Lewy, B. Middleton, P.J. Murphy, B. L. Parry, V.L. Revell, Measuring melatonin in humans, J. Clin. Sleep Med. 4 (1) (2008) 66–69.

[12] A. Ishizaki, A. Uemura, H. Kataoka, A sensitive method to determine melatonin in saliva by automated online in-tube solid-phase microextraction coupled with stable isotope-dilution liquid chromatography-tandem mass spectrometry, Anal. Methods 9 (21) (2017) 3134–3140.
[13] C. Domenech-Coca, R. Marine-Casado, A. Caimari, L. Arola, J.M. Del Bas, C. Blade, M.I. Rodriguez-Naranjo, Dual liquid-liquid extraction followed by LC-MS/MS method for the simultaneous quantification of melatonin, cortisol, triiodothyronine, thyroxine and testosterone levels in serum: applications to a photoperiod study in rats, J. Chromatogr. B Analyt. Technol. Biomed. Life Sci. 1108 (2019) 11–16.
[14] S. Karakawa, R. Nishimoto, M. Harada, N. Arashida, A. Nakayama, Simultaneous analysis of tryptophan and its metabolites in human plasma using liquid chromatography-electrospray ionization tandem mass spectrometry, Chromatography 40 (3) (2019) 127–133.
[15] Ö. Yetgin Çetin, H. Karadeniz, A. Karakaş, S. Yenisoy-Karakaş, Determination of melatonin hormone and neurotransmitters in cerebrospinal fluid: method validation and uncertainty calculations, J. Anal. Chem. 73 (6) (2018) 613–625.
[16] A.S. Moody, P.C. Baghernejad, K.R. Webb, B. Sharma, Surface enhanced spatially offset raman spectroscopy detection of neurochemicals through the skull, Anal. Chem. 89 (11) (2017) 5688–5692.
[17] W. Huang, Y. Deng, Y. He, Visual colorimetric sensor array for discrimination of antioxidants in serum using MnO2 nanosheets triggered multicolor chromogenic system, Biosens. Bioelectron. 91 (2017) 89–94.
[18] B. Liu, Y. Chen, M. Zhang, Z. Chen, X. Zuo, Colorimetric discriminatory array for detection and discrimination of antioxidants based on HAuCl4/3,3',5,5'-tetramethylbenzidine, Analyst 145 (15) (2020) 5221–5225.
[19] U. Puc, A. Abina, A. Jeglič, A. Zidanšek, I. Kašalynas, R. Venckevičius, G. Valušis, Spectroscopic analysis of melatonin in the Terahertz frequency range, Sensors (Basel) 18 (12) (2018) 4098.
[20] D.S.M. Ribeiro, R.C. Castro, J.X. Soares, J.L.M. Santos, Photocatalytic activity of AgInS2 quantum dots upon visible light irradiation for melatonin determination through its reactive oxygen species scavenging effect, Microchem. J. (2020) 155.
[21] N. Soltani, N. Tavakkoli, F. Shahdost-Fard, H. Salavati, F. Abdoli, A carbon paste electrode modified with Al2O3-supported palladium nanoparticles for simultaneous voltammetric determination of melatonin, dopamine, and acetaminophen, Mikrochim. Acta 186 (8) (2019) 540.
[22] N. Kumar, R.N. Goyal, Simultaneous determination of melatonin and 5-hydroxytrptophan at the disposable poly-(melamine)/poly-(o-aminophenol) composite modified screen printed sensor, J. Electroanal. Chem. (2020) 874.
[23] E. Castagnola, K. Woeppel, A. Golabchi, M. McGuier, N. Chodapaneedi, J. Metro, I. M. Taylor, X.T. Cui, Electrochemical detection of exogenously administered melatonin in the brain, Analyst 145 (7) (2020) 2612–2620.
[24] S.P. Selvam, M. Hansa, K. Yun, Simultaneous differential pulse voltammetric detection of uric acid and melatonin based on a self-assembled Au nanoparticle–MoS2 nanoflake sensing platform. Sensors Actuators B: Chem. 2020, 307.
[25] D. Zembrzuska, J. Kalecki, M. Cieplak, W. Lisowski, P. Borowicz, K. Noworyta, P.S. Sharma, Electrochemically initiated co-polymerization of monomers of different oxidation potentials for molecular imprinting of electroactive analyte. Sensors Actuators B: Chem. 2019, 298.
[26] P.R. Martins, L.M.C. Ferreira, K. Araki, L. Angnes, Influence of cobalt content on nanostructured alpha-phase-nickel hydroxide modified electrodes for electrocatalytic oxidation of isoniazid, Sens. Actuators, B 192 (2014) 601–606.
[27] J. Smajdor, R. Piech, M. Pięk, B. Paczosa-Bator, Carbon black as a glassy carbon electrode modifier for high sensitive melatonin determination, J. Electroanal. Chem. 799 (2017) 278–284.
[28] Z. Yang, M. Li, H. Li, H. Li, C. Li, B. Yang, Polycrystalline boron-doped diamond-based electrochemical biosensor for simultaneous detection of dopamine and melatonin, Anal. Chim. Acta 1135 (2020) 73–82.
[29] N. Alpar, P.T. Pınar, Y. Yardım, Z. Şentürk, Voltammetric method for the simultaneous determination of melatonin and pyridoxine in dietary supplements using a cathodically pretreated boron-doped diamond electrode, Electroanalysis 29 (7) (2017) 1691–1699.
[30] D. Duan, Y. Ding, L. Li, G. Ma, Rapid quantitative detection of melatonin by electrochemical sensor based on carbon nanofibers embedded with FeCo alloy nanoparticles, J. Electroanal. Chem. (2020) 873.
[31] L.C. Brazaca, C.B. Bramorski, J. Cancino-Bernardi, S. Da Silveira Cruz-Machado, R. P. Markus, B.C. Janegitz, V. Zucolotto, An antibody-based platform for melatonin quantification, Colloids Surf., B 171 (2018) 94–100.
[32] D. Sharp, R.J.M.T. Burkitt, Carbon materials for analytical electrochemistry: printed carbon materials and composites. 2015, 30 (sup7), B155-B162.
[33] L.O. Orzari, R. Cristina de Freitas, A. de Araujo, I. Andreotti, A. Gatti, B.C. Janegitz, A novel disposable self-adhesive inked paper device for electrochemical sensing of dopamine and serotonin neurotransmitters and biosensing of glucose, Biosens. Bioelectron. 138 (2019) 111310.
[34] I.A. de Araujo Andreotti, L.O. Orzari, J.R. Camargo, R.C. Faria, L.H. Marcolino-Junior, M.F. Bergamini, A. Gatti, B.C. Janegitz, Disposable and flexible electrochemical sensor made by recyclable material and low cost conductive ink. 2019, 840, 109–116.
[35] L.A. Pradela-Filho, I.A.A. Andreotti, J.H.S. Carvalho, D.A.G. Araújo, L.O. Orzari, A. Gatti, R.M. Takeuchi, A.L. Santos, B.C. Janegitz, Glass varnish-based carbon conductive ink: A new way to produce disposable electrochemical sensors. Sensors Actuators B: Chem. 2020, 305.
[36] J.R. Camargo, I.A.A. Andreotti, C. Kalinke, J.M. Henrique, J.A. Bonacin, B.C. Janegitz, Waterproof paper as a new substrate to construct a disposable sensor for the electrochemical determination of paracetamol and melatonin, Talanta 208 (2020) 120458, https://doi.org/10.1016/j.talanta.2019.120458.
[37] C. Kalinke, N.V. Neumsteir, P. Roberto de Oliveira, B.C. Janegitz, J.A. Bonacin, Sensing of L-methionine in biological samples through fully 3D-printed electrodes, Anal. Chim. Acta 1142 (2021) 135–142.
[38] G.C. Mauruto de Oliveira, E.P. de Palma, M.H. Kunita, R. Antigo Medeiros, R. de Matos, K.R. Francisco, B.C. Janegitz, Tapioca biofilm containing nitrogen-doped titanium dioxide nanoparticles for electrochemical detection of 17-β estradiol, Electroanalysis 29 (11) (2017) 2638–2645.
[39] Y. Wang, J. Xie, L. Tao, H. Tian, S. Wang, H.J.S. Ding, A.B. Chemical, Simultaneous electrochemical determination of epirubicin and methotrexate in human blood using a disposable electrode modified with nano-Au/MWNTs-ZnO composites. 2014, 204, 360–367.
[40] I.A. de Araujo Andreotti, L.O. Orzari, J.R. Camargo, R.C. Faria, L.H. Marcolino-Junior, M.F. Bergamini, A. Gatti, B.C. Janegitz, Disposable and flexible electrochemical sensor made by recyclable material and low cost conductive ink, J. Electroanal. Chem. 840 (2019) 109–116.
[41] J.R. Camargo, L.O. Orzari, D.A.G. Araújo, P.R. de Oliveira, C. Kalinke, D.P. Rocha, A. Luiz dos Santos, R.M. Takeuchi, R.A.A. Munoz, J.A. Bonacin, B.C. Janegitz, Development of conductive inks for electrochemical sensors and biosensors, Microchem. J. 164 (2021) 105998.
[42] D.A.G. Araújo, J.R. Camargo, L.A. Pradela-Filho, A.P. Lima, R.A.A. Muñoz, R.M. Takeuchi, B.C. Janegitz, A.L. Santos, A lab-made screen-printed electrode as a platform to study the effect of the size and functionalization of carbon nanotubes on the voltammetric determination of caffeic acid, Microchem. J. 158 (2020) 105297.
[43] R.G. Compton, C.E. Banks, Understanding Voltammetry, World Scientific, 2018.
[44] N. Tavakkoli, N. Soltani, F. Shahdost-Fard, M. Ramezani, H. Salavati, M.R.J.M.A. Jalali, Simultaneous voltammetric sensing of acetaminophen, epinephrine and melatonin using a carbon paste electrode modified with zinc ferrite nanoparticles. 2018, 185 (10), 479.
[45] A. Levent, Electrochemical determination of melatonin hormone using a boron-doped diamond electrode, Diam. Relat. Mater. 21 (2012) 114–119.
[46] F.J.V. Gomez, A. Martín, M.F. Silva, A. Escarpa, Screen-printed electrodes modified with carbon nanotubes or graphene for simultaneous determination of melatonin and serotonin, Microchim. Acta 182 (11-12) (2015) 1925–1931.