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Voltammetric Detection of Uric Acid at Screen Printed Electrode: A Review

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Abstract. Uric acid is a compound produced from purine metabolism. The excess amount of these compounds could causes diseases in the body. Effective and practical methods are needed for early detection of uric acid. Technically, uric acid could be detected using enzymes (enzymatic) and without enzymes (non-enzymatic) approach. Several methods have already reported for uric acid detection in biological samples, including fluorimetry, colorimetry, liquid chromatography, flow injection analysis, chemiluninescence, and electrochemical detection. Among electrochemical detection methods, voltammetry is one of the most prospective for uric acid detection. This review covers the approach of uric acid detection including enzymatic and nonenzymatic approach, several voltammetric technique for uric acid detection, and screen printed and modified electrode as platform for uric acid detection. Analytical performance such as linear range, sensitivity, selectivity and reproducibility of uric acid detection using various voltammetric method and at different platform were also highlighted.

Introduction

Uric acid (IUPAC name: *7,9-Dihydro-1-H-purine-2,6,8 (3H)-trione*) is the end product of purin metabolism which excreted through urine. It is a weak acid and dissolved in water (Arvand *et al.* 2017). The acceptable concentrations of uric acid in adult man and woman serum range from 3.5–7.2 mg/dL (210–430 μM) and 2.6–6.0 mg/dL (150–360 μM), respectively (Xue *et al.* 2018). Excess amount of uric acid relates with several diseases such as Lesch-Nyhan syndrome (Dinesh *et al.* 2017), pneumonia, gout (Muthukumaran *et al.* 2019), hyperuricemia (Piermarini *et al.* 2013), cardiovascular and *multiple sclerosis* (Stozhko *et al.* 2018). Several factors that influence uric acid concentrations are food, drugs, obesity, race (especially African-American race), endothelial dysfunction, hypertension, atherosclerosis, kidney disorders, oxidative stress and other genetic disorders (Siemińska *et al.* 2020). Excess uric acid is dangerous in the body. Therefore, it is necessary to monitor uric acid to prevent diseases.

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Several analytical methods have been used to detect uric acid level, namely liquid chromatography (Kand *et al.* 2011), injection flow analysis (Yang and Zhang 2010), capillary electrophoresis(Mu and Valiente 2010), fluorimetry (Pang 2019), colorimetry (Wu *et al.* 2015), *chemiluminescence* (Vakh *et al.* 2017) and electrochemical analysis (Verma *et al.* 2019). Electrochemical analysis methods are the prospective method because of their good sensitivity, high selectivity, and low cost (Madhuchandra and Swamy 2020). One of the widely used electrochemical techniques is voltammetry. The voltammetric technique is based on measuring the oxidation or reduction current of the analyte at the electrode surface when a potential is applied. The amount of analyte concentration will be proportional to the resulting current response (Sinha *et al.* 2018). Voltammetric technique was reported for its advantage in uric acid detection compare to chromatography, electrophoresis, fluorimetry, chemiluminescence, and colorimetry such as simple analysis (without complicated preparation step), small amount of reagent needed, and fast detection with comparable sensitivity and limit of detection to other method.

Voltammetry is capable to analyze small amounts of analyte and provides information on the analyte electrochemical characteristics. Voltammetry is divided into several types, namely cyclic voltammetry (CV), differential pulse voltammetry (DPV), square wave voltammetry (SWV), and linear sweep voltammetry (LSV) (Lu *et al.* 2018). Measurements in voltammetry involve three types of electrodes, namely working electrode, reference electrode and auxiliary electrode. The electrode material must exhibit good electron transfer properties. One of the most widely developed was carbon-based materials, such as boron-doped diamond electrode (BDD), carbon paste electrode (CPE), glass carbon electrode (GCE), graphene electrode (GE), and screen printed electrode (SPE) (Carvalho *et al.* 2020). In this study, we focus on the use of screen printed electrode (SPE) for the voltammetric detection of uric acid. SPE-based sensors are very economical because they facilitate the design process of the working electrode pattern, reference electrode pattern and auxiliary electrode pattern on the same substrate. SPE has been widely used for the detection of environmental pollutants, biomolecules, biomarkers, neurotransmitters and other chemical compounds (Ahammad *et al.* 2018). This technology is designed with aspects of portability, low cost and allows for mass production (Antuña-jim and Hern 2020).

There have been many reports of voltammetric detection of uric acid at SPE and other modified electrode. A comprehensive review on these work are needed to provide information and references regarding the successful detection of uric acid using various voltammetric techniques. This review is expected to provide information related to the general approach of uric acid detection, voltammetry technique for uric acid detection, and modified electrode as the platform for uric acid detection.

Analytical Approach of Uric Acid Detection

The analytical approach for detecting uric acid is divided into two types, enzymatic and non-enzymatic approach. Enzymatic method usually used uricase enzyme. This enzyme act as a catalyst in the decomposition reaction of uric acid into carbon dioxide, hydrogen peroxide, and allantoin (Figure 1) (Idrees *et al.* 2019). The uric acid detection method using uricase is divided into two types, namely direct and indirect (Chaudhari *et al.* 2012). The direct method is carried out by measuring the uric acid ratio before and after the enzymatic reaction such as using spectrometry. Indirect quantification method is conducted by measuring hydrogen peroxide produced in enzymatic reaction either using colorimetry, fluorescence, and electrochemistry.

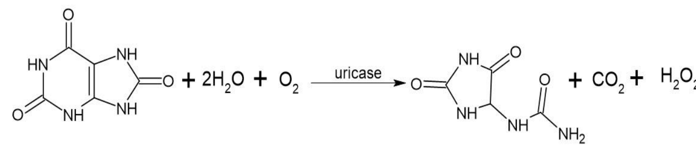

Figure 1 Enzymatic reaction of uric acid oxidation

Hydrogen peroxide quantification using colorimetry was performed in the presence of a chromogenic reagents which form colored complex and detected using UV-Vis spectrophotometer (Lu *et al.* 2017). In addition to colorimetry, fluorometry also could be applied for the detection. High energy fluorescent material is required in this method to produce light emission(Kong 2017). The process of fluorometric-enzymatic analysis of uric acid is based on changes in the intrinsic fluorescence of the uricase enzyme at 287 and 330 nm. This method do not need to combine the enzymatic process with a second reaction involving a fluorophore (Galba *et al.* 2001).

Electrochemical analysis methods could be used to detect uric acid by quantifying the formation of hydrogen peroxide or quantifying the decrease in the amount of oxygen consumption. Quantification of the decreased amount of oxygen consumption showed unsatisfactory results due to the narrow linear range (0.1 – 0.5 μM) (Liang *et al.* 2013). The measurement of hydrogen peroxide formation has attracted much attention. Various designs of biosensors were developed to minimize the effect of signal falsification by other compounds due to the high oxidation potential of hydrogen peroxide (i.e > 0.4 V). Selection of the right transducer matrix in the biosensor could increase electron transfer activity, facilitate enzyme immobilization and maintain enzyme stability. Therefore, it is very important to develop a matrix-based biosensor for uric acid detection in order to increase precision, accuracy and reduce interference (Verma *et al.* 2019). Several studies involving enzymes for the detection of uric acid could be seen in (Table 1).

Non-enzymatic approach in uric acid detection could be studied by colorimetry, injection flow analysis, high performance liquid chromatography (HPLC), capillary electrophoresis, fluorescent, chemiluminescence and electrochemistry. Several studies related to non-enzymatic approach for uric acid detection could be seen in (Table 2). Non-enzymatic colorimetric methods often utilized nanomaterials, for example silver nanoparticles (AgNPs). The oxidation process of AgNPs is inhibited by the presence of uric acid, resulting a change in color (Li *et al.* 2020). This method has easy visual observation without expensive instruments, as well as fast and good sensitivity (Fang *et al.* 2016), however this method is influenced by changes in temperature, less stable and need expensive reagent (Fang *et al.* 2016).

HPLC could provide superior performance in uric acid detection. However sample pretreatment are usually needed prior to analysis (Li and Franke 2009). In addition, simultaneously determination of uric acid using this method is quite difficult, especially for compounds that have similar chemical structures due to the overlap of the resulting chromatogram peaks (George *et al.* 2006).

Fluorescent method is fast, simple, and non-destructive, however several fluorescent probes are toxic and insoluble in water (Qi *et al.* 2020). Chemiluminescence (CL) involves chemical reactions between samples with various reagents and releases energy in the form of light emission. The wavelength resulting from the emission of light could occur in the UV-Vis to infrared region. This method could be used for organic and inorganic chemical analysis and has good sensitivity, wide dynamic range, fast process, and low limit of detection (Zhao *et al.* 2008). However, this method has several weakness such as less selective and light emission was resistant to the temperature, solvent, pH, ionic strength, and mixing time of reagents (Baeyens *et al.* 1998).

The capillary electrophoresis (CE) method uses electrical energy to separate charged compounds. Capillary electrophoresis combined with electrochemiluminescence (Tao *et al.* 2012), electrochemical detection (Zhou and Cong 2016), and ultraviolet detection (Zinellu *et al.* 2004) could be used for uric acid detection. This method is most widely used because of its fast analysis, high sensitivity and selectivity, fast response, simple, and low cost (Jalalvand 2020).

Voltammetric Detection of Uric Acid

Electrochemical methods particularly voltammetry has been widely developed for uric acid detection. Type of voltammetry such as differential pulse voltammetry (DPV), square wave voltammetry (SWV), cyclic voltammetry (CV), linear sweep voltammetry (LSV), and stripping voltammetry were applied for uric acid detection at many kinds of electrode including screen printed electrode (SPE). Voltammetric detection of uric acid at SPE could be performed both as single compound or simultaneous with other compound (Table 3). Several supporting electrolyte with different pH also reported for uric acid detection at different electrodes. The schematic diagram for uric acid oxidation at the electrodes in voltametric technique is showed in Figure 2.

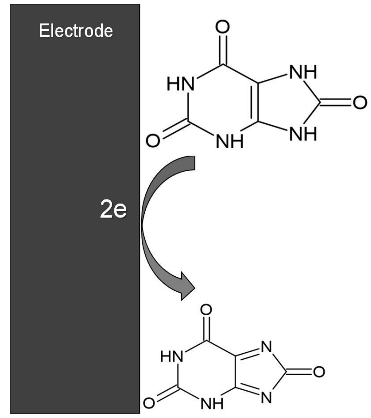

Figure 2. Voltammetric measurement of uric acid ozidation at the electrode.

Differential pulse voltammetry (DPV) is able to eliminate residual current and has been widely employed for quantitative analysis (Vilas-boas *et al.* 2018). The parameter optimization is carried out based on the potential amplitude and scan rate (Faria *et al.* 2012). This technique has been used for various analyses, one of which is uric acid. Rezaei *et al.* (2018) reported the modified ZnO/Gr/SPE electrode with the DPV technique can detect uric acid in urine samples. Measurements were made in 0.1 M PBS (pH 7) at various concentrations of uric acid.

The results show that the peak current of uric acid oxidation increases linearly in the concentration range of 1-100 µM with a linearity coefficient of 0.9982 and a detection limit of 0.43 µM. Metto *et al.* (2019) described the modified DMF/SPCE electrodes with the DPV technique can detect uric acid in serum. Measurements were made with a scan rate of 10 mV/s and a pulse amplitude of 240 mV. The results show that the peak of the DMF/SPCE voltammogram is more symmetrical than the non-modified SPE. The peak current response of DPV shows two linear segments with LOD and LOQ of 0.19 µM and 0.633 µM, respectively.

SPCE fabricated at polyvinyl chloride (PVC) substrate was used to detect uric acid (Wahyuni *et al.* 2021). Measurements were made using the DPV technique at a potential range of +0.2 to 0.7 V, scan rate 25 mVs^{-1}, pulse potential 25 mV, potential step 5 mV, and pulse time 0.1 s. The linearity coefficient (R^2) obtained from the concentration range of 10-80 µM was 0.997, with a LOD 1.94 µM, LOQ 6.46 M, sensitivity of 5 nA M^{-1} and reproducibility (% RSD = 3.06 %). The modified PEDOT:PSS/SPCE electrode with the DPV technique reported by Wahyuni et al (2021) used to detect uric acid in urine samples with good analytical performance. The measurement results showed R^2 value of 0.9985 with a LOD 1.62 µM, LOQ of 5.39 µM, sensitivity of 0.024 µA/µM and precision (%RSD= 2.40 %).

Table 1. Enzymatic approach for the uric acid detection

Matrix	Methods	Sample	Concentration range	LOD	Ref.
Uricase/Th-MOF	*Colorimetry*	Urine, Serum	4 – 70 μM	1.15 μM	Badoei-dalfard *et al.* 2019
Uricase/BSA-stabilized Au nanocluster	*Colorimetry*	Urine	2 – 200 μM	0.36 μM	Zhao *et al.* 2012
Heme-Ficin complexes	*Colorimetry*	Urine, serum	1 – 120 μM	0.25 μM	Pan *et al.* 2018
Uricase/MIL-53 (Fe)	*Colorimetry*	Urine, Serum	4.5 – 60 μM	1.3 μM	Lu *et al.* 2015
Uricase/Trimer-DZ	*Colorimetry*	Serum	2.5 - 40 μM	0.66 μM	Karami *et al.* 2020
Uricase/Au-rGO/ITO	*Electrochemical (DPV)*	Serum	50 – 800 μM	7.32 ±0.21 μM	Verma *et al.* 2019
Uricase/Pt NPs/PANI/MEA	*Electrochemical (MEAB)*	Serum	100 - 1200 μM	4 μM	Gao *et al.* 2019
Uricase/Ppy-Pt	*Electrochemiluminescence*	Seafood	0.0162 – 8.3 μM	75 pM	Chu *et al.* 2012
Uricase/μPAD	*Chemiluninescence*		2600–49000 μM	1900 μM	Yu *et al.* 2011
Uricase/ Prussian blue/SPE	*Electrochemical (Chronoamperometry)*	Serum	30–300 μM	10 μM	Piermarini *et al.* 2013
Uricase/c-MWCNT/PBNPs/Au	*Electrochemical (Amperometric)*	Serum	0.005–0.8 mM	5 μM	Rawal *et al.* 2012
Uricase/Chi-Gr Cry/PB/SPCE	*Electrochemical (Amperometric)*	Serum	2.5–400 μM	0.25 μM	Jirakunakorn *et al.* 2020
Uricase/GO	*Electrochemical (Amperometric)*	Serum	20–490 μM	3.45 μM	Omar *et al.* 2016
Silica(MCM-41)-Nafion/GCE	*Electrochemical (Amperometric)*	Serum	2– 12 μM	0.33 μM	Mundaca-uribe *et al.* 2014
Uricase/c-MWCNT/GEL/PVF/GCE	*Electrochemical (Amperometric)*	Serum	0.2 – 710 μM	2.3×10^{-2} μM	Erden *et al.* 2014
Uricase/HRP-Cds quantum dots	*Fluorescence*	Urine	125–1000 μM	125 μM	Ellina *et al.* 2014

Notes: Th-MOF: The thorium-metal organic framework; **BSA-stabilized Au nanocluster**: Bovine serum albumin-stabilized Au nanocluster; **MIL-53 Fe**: Metal organic framework Fe; **Trimer-DZ**: Trimeric CatG4 DNAzyme; **Au-rGO/ITO**: Gold nanoparticles-reduced graphene oxide/Indium tin-oxide; **Pt NPs/PANI/MEA**: Pt nanoparticles polyaniline microneedle electrode array; **Ppy-Pt**: Polypyrrole-Pt; **μPAD**: microfluidic paper-based analytical device; **c-MWCNT/PBNPs/Au:** multiwalled carbon nanotube/ Prussian blue nanoparticles/ Au electrode; **Chi-Gr/ Cry/PB/SPCE:** Chitosan-graphene/ Cryogel/ Prussian blue/ Screen printed electrode; **GO:** Graphene oxide; **Silica(MCM-41)-Nafion/GCE**: mesoporous silica with hexagonal symmetry (MCM-41)-nafion/Glassy carbon electrode; **c-MWCNT/GEL/PVF/GCE:** carboxylated multiwalled carbon nanotubes/gelatin/ poly(vinylferrocene)/modified glassy carbon electrode; **HRP-Cds quantum dots:** horseradish peroxidase-Cds quantum dots

Table 2 Non-enzymatic approach for uric acid detection

Methods	Sample	Concentration range	LOD	Ref.
Colorimetric	plasma, urine	0.1–1 μM	0.065 μM	Amjadi *et al.* 2020
Flow injection	plasma	0.5–4 mg/L	0.12 mg/L	Boroumand *et al.* 2016
Chemiluminesense	Plasma,	0.05 – 1.5 μM	0.017 μM	Hallaj *et al.* 2020
HPLC	Human nails	1–10000 ng	2 pg	Xi-ling Li *et al.* 2015
Cappilary electrophoresis	plasma, urine	10 – 500 μM	3.3 μM	Pormsila *et al.* 2009
Fluorescent	Blood serum	0.1 – 50 μM	0.028 μM	Qi *et al.* 2020
Electrochemical analysis	serum, urine	0 – 1 μM	2.07 x 10^{-2} μM	Han *et al.* 2019

DPV could also be used for the simultaneous detection of uric acid, dopamine and ascorbic acid. Ping *et al*. (2012) reported the SPGrNE modified electrode with DPV technique can be used for the simultaneous detection of uric acid, dopamine and ascorbic acid. The presence of anodic peaks corresponded to the oxidation of uric acid, dopamine and ascorbic acid, at 300 mV, 150 mV and -50 mV, respectively. The limit of detection (LOD) for these compounds were 0.20 μM, 0.12 μM and 0.95 μM respectively. Simultaneous detection of uric acid, dopamine and ascorbic acid by DPV technique exhibited good peak separation and peak currents which increased proportionally with increasing analyte concentration (Kunpatee *et al.* 2020).

Square Wave Voltammetry (SWV), this technique applied modulating potential with a square potential function (Mirceski *et al.* 2013). SWV could be used for analyzing reversible and irreversibel reactions, as well as reactions involving catalysts and electron transfer(Chen 2013). Muthukumaran *et al*. (2019) described the the modified NiS/Ppy/SPE electrode with the SWV technique can detect individually or simultaneously uric acid and theophylline. Individual measurements showed that SWV was able to detect uric acid at concentrations (1×10^{-9} – 400×10^{-6} M) with a detection limit of 16×10^{-11} M. Simultaneous measurement of uric acid with theophylline using this technique showed an increase in the oxidation current at concentrations of 10×10^{-9} – 900×10^{-6} M and 20×10^{-9} – 1×10^{-3} M with a detection limit of 1×10^{-9} M and 5×10^{-9} M for uric acid and theophylline. The linearity coefficients of the two analytes were obtained at 0.983 and 0.996. SWV is also able to study the effect of changes in pH on uric acid analysis. The peak oxidation potential shifted to a less positive potential when the pH increased from 2.5 to 4. This might be due to the deprotonation of the molecules (Fernandes *et al.* 2014). SWV is very sensitive for the analysis of organic molecules with low non-faradic currents. Its detection limit could be three times lower than conventional voltammetric methods (Medeiros *et al.* 2008).

Cyclic voltammetry (CV), the potential was set between the initial, final, then back to initial potential. Current measurements are carried out during the trigonal potential application. The initial potential (V1) was set at the point when there is no redox reaction at the electrode surface. Then the potential is changed to V2. Once the set potential is reached, the potential is scan back to V1. This technique could be used to investigate the electrochemical behavior of an analyte. In addition, it could also be used to measure samples in real time on a sub-second time scale and measure changes in sample concentrations in the nanomolar to micromolar range (Robinson *et al.* 2003).

CV is good for determining oxidation and reduction potential of an analyte, but is less sensitive for quantitative analysis. Individual determination of uric acid, ascorbic acid and dopamine at modified AgNW/rGO electrodes using CV technique showed clear and sharp anodic peaks corresponding to the oxidation of each analyte. The anodic peak current increases as the scan rate increases. The plot between the anodic peak current and the square of the scan rate shows a good linear relationship (R^2 = 0.9888 (UA), R^2 = 0.9930 (AA), R^2 = 0.9949 (DA) (Li *et al.* 2015). Azeredo (2020) revealed the modified Ni/Zn $(OH)_2$ electrode could be used for the analysis of uric acid in saliva. The results showed a good linear current response at pH 7.4 (0.1 mol L^{-1} PBS). CV could study the effect of scan rate on the measurement of uric acid and dopamine using the modified rGO-SP-FTO electrode. The current response to oxidation at 200 μM uric acid and 50 μM dopamine increased with increasing scan rate (5–300 mVs^{-1}). The correlation between peak oxidation and scan rate shows a linear relationship with determination coefficient of 0.99046 and 0.99508 for uric acid and dopamine, respectively (Ahammad *et al.* 2018).

Linear Sweep Voltammetry (LSV), is commonly used to study the thermodynamic and kinetic behavior of insertion compounds. This method is sensitive to structural variations in the insertion compound (Montella *et al.* 2021). Stozhko *et al*. (2018) described the LSV could be used for uric acid analysis in urine and milk samples. Uric acid measurements were carried out with a modified 2.5% NF/Au(5nm)/SPCE electrode in pH 5, scanning rate of 50 mV/s, and a potential range of 0.1-0.8 or 0.1-0.9 V. The oxidation potential of uric acid was obtained at 0.69 V. Concentration plots with anodic peaks generated the regression equation $y = 0.0294x + 0.0359$ (R2 = 0.9966) with a detection limit of 5 μM. Another application of LSV, which is used to study the adsorption time (t_{ADS}) and adsorption potential (E_{ADS}) for the purpose of increasing the selectivity of the sensor. Nagles *et al.* (2017) determined t_{ADS} and E_{ADS} on uric acid and dopamine in the presence of ascorbic acid. The measurements were carried out with a modified cis-SWCNT-IL/SPCE electrode. The optimum measurement conditions were pH 2.4, t_{ADS}=100 s, E_{ADS}= -0.10 V. The anodic peak current of uric acid was constant with an increase in potential between -0.1 V to 0.1 V, while the anodic peak of dopamine decreased with an increase in potential. The detection limits for the determination of uric acid and dopamine are 0.17 μM and 0.16 μM, respectively.

AgNW/rGO/SPE modified electrode with LSV technique reported by Li *et al* (2015) could detect uric acid, ascorbic acid, and dopamine simultaneously. Oxidation of three analyte were observed at potential of 338 mV (uric acid), 6 mV (ascorbic acid) and 204 mV (dopamine) vs. Ag/AgCl. The detection limits for the three analytes were 0.30 μM, 0.81 μM, 0.26 μM, respectively.

Adsorptive Stripping voltammetry is one of the voltammetry techniques reported by Kewket *et al.* (2020) as a technique that can analyze the adsorption characteristics of environmental contaminants. In principle, the first step is to accumulate the desired species onto the surface of the electrode. The magnitude of the concentration of the species will be equal to the response to oxidation or reduction. Fanjul-bolado *et al.* (2015) revealed the modified MWCNT/SPE electrode with ASV technique could be used for the analysis of uric acid in urine samples. Measurements were carried out at an adsorption time of 5 minutes with a scan rate of 50 mV/s. Repeating a series of measurements 5 times resulted in an RSD = 4.8%. The relationship plot of concentration (1 x 10^{-6} to 1 x 10^{-4} M) with peak current shows good linearity with coefficient R^2 = 0.996.

The difference between all type of voltammetric technics was evaluated based on the voltammogram, information from voltammogram, and from application of each technique. CV and DPV techniques are commonly used because they have high current sensitivity and good peak resolution to observe analyte interactions in electrochemical cells. DPV technique could be used to measure samples in low concentrations since this technique could provide low detection limit. Uric acid analysis using the DPV technique showed the lowest detection limit compare to other techniques. Apart from the difference in voltammetric technique, the type of electrode and modified material, scan rate, potential window, sample matrix and pH of electrolyte solution also affects the measurement of uric acid. In general, the LOD of voltametric technique in uric acid detection are lower than the threshold value of uric acid in human biological fluid such as blood serum (Table 3).

Screen printed electrode and modified electrode as the platform for uric acid detection.

Electrochemical measurement at a screen-printed electrodes (SPE) have attracted a lot of attention because it provides good analytical performance for environmental, food, biomarkers, metabolites, and pharmaceuticals monitoring. SPE has many advantages besides simple and easy, this electrode could also minimize analysis time, amount of reagents and sample volume (Mohamed 2016). Screen-printed electrodes (SPE) could be modified for the introduction of various analytes. The modification proses could also be done by depositing several substances such as metal nanoparticles, conductive films, enzymes, and polymers on the surface of the electrodes to increase its sensitivity and selectivity. This modification was carried out through changing printing ink composition and combining it with new materials such as polymers, enzymes, ligands, complexing agents, and other nanostructured materials.

Moleculary imprinted polymer (MIP) is a material that is made by inserting printed molecules into a polymer network with the aim of increasing selectivity to certain analytes, improving chemical and physical stability, and potential for reusability (Khosrokhavar *et al.* 2020). MIP could be printed in the presence of functional monomers, initiators in media and crosslinking agents (Abbas 2015). Increased conductivity and surface area is feasible by combining MIP and nanoparticle components. MIP based on reduced graphene oxide (rGO) could be used for simultaneous analysis of uric acid and tyrosinase with detection limits of 0.0032 μM and 0.046 μM. The sensitivity of the voltammetric response came from the synergistic electrocatalytic effect of the poly *2-amino-5-mercapto-1,3,4-thiadiazole* (AMT)-based MIP and rGO nanosheet. The presence of hydrogen bonds and interactions between the poly –AMT conjugated backbone and the target molecule could increase the binding efficiency. On the other hand, the presence of rGO nanosheets could increase the conductivity due to the large surface area (Zheng *et al.* 2018). The graphite-based electrode coated with a sol gel that has been anodized with a molecular imprinted polymer (poly-melamine-co-chloranyl) could detect uric acid selectively at 15.56-177.42 μgmL^{-1} in aqueous media, 4.78-106.96 μgmL^{-1} in blood serum and 7.81 -148.42 μgmL^{-1} in urine. The measurement provided the detection limit in the range of 3.71-4.10 μgmL^{-1} (Patel *et al.* 2009).

Chemical ligands are feasible for SPE modification. For example, the tris(2,2'-bipyridyl)Ru(II) ligand in a polytyramine (Pty) film complex could detect uric acid, dopamine and ascorbic acid simultaneously with good separation peaks and detection limits of 0.58, 0.08 and 0.031μM, respectively (Khudaish *et al.* 2014). Another electrode material that is commonly used for modification of screen-printed electrodes is graphene (Antiochia and Gorton 2014), graphene oxide (GO) (Thunkhamrak *et al.* 2020), reduced graphene oxide (rGO) (J. Wu and Lee 2020), carbon nanofiber (CNF) (Erdem, Eksin, and Congur 2015), carbon nanotube (CNT) (Upan *et al.* 2015), single-walled carbon nanotube (SWCNT) (Viet *et al.* 2019), and multi-walled carbon nanotube (MWCNT) (Yousefi *et al.* 2018). The integration of nanomaterials in the electrochemical field is in great demand because these nanomaterials have good conductivity and large surface area, thus facilitating the electron transfer process when measuring the instrument (Eissa *et al.* 2019).

Table 3 Voltammetry for uric acid detection

Electrode modified	Analyte	Detection method	LOD (μM)	Ref.
SPGNE	UA	DPV	0.2	Ping *et al.* 2012
	AA		0.95	
	DA		0.12	
PVC/SPCE	UA	DPV	1.94	Wahyuni *et al.* 2021
PEDOT: PSS/SPCE	UA	DPV	1.62	Wahyuni *et al.* 2021
		CV	1.61	
GQDS/IL-SPCE	UA	DPV	0.03	Kunpatee *et al.* 2020
	AA		6.64	
	DA		0.06	
GO/FeO₄ @SiO₂ nanocomposite	UA	DPV	0.57	H. Beitollahi *et al.* 2017
	DA		0.089	
ND/SPE	UA	DPV	0.89	Baccarin *et al.* 2019
	DA		0.57	
DMF/SPCE	UA	DPV	0.19	Metto *et al.* 2019
CNTs-G-pMet-SPCE	UA	DPV	0.034	Y. Si *et al.* 2020
	DA		0.0029	
rGO/AgNWs/AgNPs/SPCE	UA	DPV	0.58	Q. Zhao *et al.* 2020
	DA		0.16	
	EST		0.58	
3DG/CNT/SPE	UA	DPV	0.6	Farahani and Sereshti 2019
	AA		2.5	
	DA		0.4	
PAA-MWCNTs/SPCE	UA	DPV	0.458	Huang *et al.*2010
	AA		49.8	
	NE		0.131	
ZnO/GR/SPE	UA	DPV	0.43	Rezaei *et al.* 2018
β -CD/rGO/SPE	UA	DPV	0.026	Qin *et al.* 2016
	AA		0.067	
	DA		0.017	
rGO-SPCE	UA	DPV	0.1	Kanyong *et al.* 2016
	AA		50	
	DA		0.4	
β-NiS/Ppy/SPE	UA	SWV	0.005	Muthukumaran *et al.* 2019
	TP		0.001	
Ni/Zn(OH)₂/SPE	UA	CV		Azeredo et al. 2020
rGO-SP-FTO	UA	CV/DPV	0.39	Ahammad *et al.* 2018
	DA		0.07	
AgNW-rGO/SPCE	UA	CV/ LSV	0.3	S. Li *et al.* 2015
	AA		0.81	
	DA		0.26	
2.5%NF/Au(5nm)/CSPE	UA	LSV	0.25	Stozhko N *et al.* 2018
Cis-SWCNT-IL/SPCE	UA	LSV	0.17	Nagles *et al.* 2017
	DA		0.16	
MWCNT/SPCE	UA	ASV	0.86	Fanjul-bolado *et al.* 2015

Note: SPGNE: Screen-printed graphene electrode, **GQDS/IL-SPCE:** Graphene quantum dots and ionic liquid modified screen-printed carbon electrode, **GO/FeO₄ @SiO₂ nanocomposite:**Graphene oxide Fe_3O_4 nanoparticles at silica, **ND/SPE:** Nanodiamonds modification screen-printed graphite macroelectrodes, **DMF/SPCE:** N,N-dimethylformamide/ screen-printed carbon electrode, **CNTs-G-pMet-SPCE:** Poly (L-methionine) followed by coating of carbon nanotube-graphene complexes and electrodeposited gold nanoparticles on a screen printed carbon electrode surface, **rGO/AgNWs/AgNPs/SPCE:** Reduced graphene oxide/ silver nanowires / silver nanoparticles/ screen printed carbon electrode, **2.5%NF/Au(5nm)/CSPE:**Nafion/gold nanoparticles/ carbon screen-printed electrode, **3DG/CNT/SPE:** Three-dimensional graphene/carbon nanotube/ modified screen printed electrode, **PAA-MWCNTs/SPCE:** Polyacrylic acid-coated multi-wall carbon nanotubes/ screen printed carbon electrode, **ZnO/GR/SPE:** Zinc oxide/ graphene/ screen printed electrode, **β -CD/rGO/SPE**: β-cyclodextrin polymer onto a reduced graphene oxide decorated screen-printed electrode, **rGO-SPCE:** Reduced graphene oxide/screen printed carbon electrode, **β-NiS/Ppy/SPE:** Nanosheets of nickel sulfide (**β** -NiS) and randomly attached polypyrrole (Ppy) nanospheres over a screen-printed electrode**, CisSWCNT-IL/SPCE:** Single walled carbon nanotubes dispersed in chitosan solution (cs) and deposited on a screen-printed carbon electrode, **AgNW-rGO/SPCE:** Silver nanowire/reduced graphene oxide nanocomposites/ screen-printed carbon electrode, **rGO-SP-FTO:** screen printing reduced graphene oxide paste on F-doped tin oxide, **Ni/Zn/SPE:** Nickel double

Screen printed graphene electrodes (SPGNE) have been widely used in the field of electrochemical sensors. A study reported the electrochemical properties of these electrodes are using cyclic voltammetry (CV). The result showed a good potential peak with separation (ΔE) which means faster electron transfer. The electron transfer kinetics could be attributed to the high conductivity of graphene. Another advantage of graphene-based electrodes is that they have a wide potential window and low background current. The SPGNE electrode could detect uric acid with a concentration range of 0.8-2500 µM and a detection limit of 0.20 µM (Ping *et al.* 2012). Graphene oxide (MC-GO-Fe_3O_4) based electrode has good electron conductivity and catalytic activity. Methylcellulose as polymer could increase Fe_3O_4 immobilization area and maintain GO conductivity. MC-GO-Fe_3O_4 electrode could be used to measure uric acid in urine with a detection limit of 0.17 µM (Sohouli *et al.* 2020). The rGO based electrode has more hydrophobic properties than GO because it has lost its oxygen atom (deoxygenation). The rGO has the ability to transfer electrons faster in redox reactions, for example the Ag-rGO electrode. The electrode produced four times higher anodic current than the unmodified electrode. Ag-rGO electrodes could analyze the oxidation of uric acid and dopamine at 0.27 V and 0.15 V vs Ag/AgCl by DPV technique. The detection limits of uric acid and dopamine measurements with these electrodes are 1 µM respectively (Prasad *et al.* 2020).

Carbon nanotube (CNT) modified electrodes have been widely developed due to their good mechanical, electrical, structural and electrochemical properties, high porosity, and large area. An example of a CNT-based electrode is the modified carbon nanotube paste electrode (MCNPE) which showed an increase in selectivity, a large decrease in anodic potential and a shift in the potential peak towards negative direction. This electrode is capable to detect uric acid, carbidopa, and folic acid using SWV and shows anodic peaks at potentials of 290, 100 and 630 mV (Rastakhiz *et al.* 2012).

Single-walled carbon nanotube (SWCNT) electrodes have attracted a lot of attention due to their high conductivity, fast electron transfer and antifouling properties. An example of a modified electrode of SWCNT, namely cs-SWCNT/SPCE could detect uric acid and dopamine with good separation peaks. The detection limit of the study was 0.17 µmol L^{-1} for uric acid and 0.16 µmol L^{-1} for dopamine (Nagles *et al.* 2017). The modified multi walled carbon nanotube (MWCNT) electrode has several advantages, including specific area, hollow structure, and high porosity (Motaharian *et al.* 2019). An example of a MWCNT-based electrode is MWCNT/SPCE. The electrode could analyze uric acid quantitatively at a potential of 0.18V (Fanjul-bolado *et al.* 2015).

Several SPEs and modified SPEs that have successfully detected uric acid could be seen in Table 3. The detection limit shows the lowest number that could still be detected by an instrument. Through these data, the candidate material that has better analytical performance is graphene quantum dots (GQD) because it shows the lowest detection limit. GQD has a thickness of 10 nm, contains carboxyl, hydroxyl, carbonyl and epoxide functional groups that play a role in chemical interactions (Valcárcel 2015). This material is stable and has low toxicity (Tan *et al.* 2015). Its complicated preparation is an obstacle in its application. The difference in value is influenced by several factors such as electrode material, electrode surface area, nature of the compound, pH, temperature, reaction time, potential, and type of solvent. Therefore, the optimum conditions for each measurement need to be investigated so that the measurements made produce good data (Chen *et al.* 2021).

Conclusion

Voltammetric technique including differential pulse voltammetry, square wave voltammetry, cyclic voltammetry, linear sweep voltammetry, and adsorptive stripping voltammetry are widely used for uric acid detection both individually and simultaneously. Those voltammetric detection widely performed at screen-printed electrode (SPE). To increase the performance of SPE in uric acid detection, modification using conductive and selective material such as PEDOT, polypyrrole, graphene, graphene oxide (GO), graphene reduce oxide (rGO), carbon nanotubes (CNTs), single wallet carbon nanotubes (SWCNT), multi wallet carbon nanotubes (MWCNT), gold nanoparticles (AuNPs), silver nanoparticles (AgNPs), and silver nanowire (AgNW) was widely reported.

Conflict of Interest

The authors declare that there is no conflict of interest.

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