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Electrochemical Detection and Spectrophotometry of Dopamine using Commercial Screen-Printed Electrodes

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ABSTRACT. Lab-on-chip is miniaturized devices integrated into a chip which can run one or several analyses which are usually done in laboratory settings, such as biochemical detection. Dopamine is an important neurotransmitter which regulates hormones, control of movement, emotion, attention, and motivation. Excess, lack, and dysregulation of dopamine could cause numbers of diseases and disorders. The technique used to measure and evaluate dopamine usually are expensive to run, require longer time to run, require some technical qualification to run, require expensive equipments, and some are invasive to do. These are the reasons why a lab-on-chip system is needed to make the detection of dopamine concentration faster, easier, and more portable. This paper studied the accuracy of using electrochemical detection to measure the concentration of liquid specimens of dopamine compared to uv/vis spectrophotometry. Electrochemical detection method named cyclic voltammetry was chosen for this study. The hypothesis for this study is that both peak current (i_p) and absorbance positively correlate to concentration, therefore both could be used with minimal error margin. For this study, the peak current (i_p) and absorbance of different concentrations of liquid specimen of dopamine are measured, and its regression were observed. It was shown that the concentration of liquid specimens of dopamine is linear to both anodic peak current (i_{pa}) and absorbance. Due to the high R^2 values of 0.9883, electrochemical detection could be used and implemented to detect dopamine concentration for application of lab-on-chip, as it is more portable and requires less volume of sample compared to spectrophotometry.

Keywords: Dopamine, Cyclic Voltammetry, Spectrophotometry, Electrochemical detection, Lab-on-chip

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1. INTRODUCTION

Dopamine is a neuromodulator and neurotransmitter which is both excitatory and inhibitory depending on the type of receptor it binds to[1]. Dopamine is a naturally occurring catecholamine formed by decarboxylation of dihydroxyphenylalanine and a precursor of norepinephrine and epinephrine[2]. Dopamine binds to alpha-1 and beta-1 adrenergic receptors[2]. Dopaminergic neurons in the substantia nigra which project to the striatum are important for the control of movement, while mesolimbic and mesocortical tracts are important in regulating affect, emotion, attention, and motivation[1]. Dopaminergic tracts in the peripheral nervous system (tuberoinfundibular pathway) regulate secretion of hormones[1]. Excess, lack, and/or dysregulation of dopamine could cause numbers of diseases and disorders such as Parkinson's disease[3], Huntington's disease[4], fibromyalgia[5], schizophrenia[6], attention deficit hyperactivity disorder[7], Tourette syndrome[8], addiction[9], depression[10], obsessive compulsive disorder[11], binge eating disorder[12], bipolar disorder[13], restless leg syndrome[14], Alzheimer's disease[15], and tardive dyskinesia[16]. Other than in the central and peripheral nervous system, dopamine could also be detected in blood plasma[17-18], sweat[18], urine[18-19], and saliva[18,20].

Lab-on-chip is a miniaturized device integrated into a chip which can run one or several analyses which are usually done in laboratory settings. Lab-on-chip systems usually consist of a microchip, an instrument for control and detection, a computer with control and data analysis software, and assays and reagents[21]. Development in biosensors has played an important role in the medical field and is often used for disease identification, prevention, rehabilitation, patients' health surveillance and human health management[22]. The benefit of lab-on-chip systems is not only in reduction in reagent consumption which lowers the cost of analyses, but also for integration and automation[21].

There are different methods to measure and evaluate dopamine, both invasive and non-invasive. Imaging techniques such as single photon emission tomography (SPECT) and Positron Emission Tomography (PET)

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measure dopamine release in the brain over a certain time range[23]. Intracerebral dialysis measures dopamine concentration in the brain[24-25]. Microphysiometer could be used to detect dopaminergic activity in the brain[26]. High Performance Liquid Chromatography (HPLC)[27], capillary electrophoresis[28], Magnetic Resonance Spectroscopic Imaging[29], radioimmunoassay[30], and ELISA[31] could be used to measure the concentration of dopamine. While the techniques mentioned are good to measure and evaluate dopamine, most of those are expensive to run, require longer time to run, require some technical qualification to run, require expensive equipments, and some are invasive to do. These are the reasons why a lab-on-chip system is needed to make the detection of dopamine concentration faster, easier, and more portable. This paper studied the accuracy of using electrochemical detection to measure the concentration of liquid specimens of dopamine compared to uv/vis spectrophotometry. Electrochemical detection method named cyclic voltammetry was chosen for this study. The hypothesis for this study is that both peak current (i_p) and absorbance positively correlate to concentration, therefore both could be used with minimal error margin. This study is going to be used in on-going research on lab-on-chip to measure the concentration of liquid specimens of dopamine.

2. MATERIALS AND METHODS

2.1 Materials, chemicals, and equipments

Dopamine hydrochloride was purchased from Sigma-Aldrich (Darmstaadt, Germany). Phosphate buffer was purchased from Merck (Darmstaadt, Germany). Electrodes used were commercial screen-printed Ag/AgCl disposable flexible electrodes, which consisted of a working electrode with the material of carbon (C), a counter electrode with the material of carbon (C), and a reference electrode with the material of silver/silver chloride (Ag/AgCl). Electrochemical detection was carried out with a single channel potentiostat EmStat4S manufactured by PalmSens (Houten, Netherlands). The UV-Vis Spectrophotometric analysis was carried out with Genesys 150 manufactured by Thermo Fisher Scientific (Massachusetts, United States).

2.2. Preparation of sample

Dopamine solution was prepared by dissolving dopamine hydrochloride (Sigma-Aldrich, Darmstaadt, Germany) in Sorensen's phosphate buffer (Merck, Darmstaadt, Germany) with pH of 7.0. 39.0 ml of 0.2 M NaH2PO4 mixed with 61.0 ml of 0.2 M Na2HPO4 to create 0.1 M Sorensen's phosphate buffer with pH of 7.0. Dopamine hydrochloride was measured at 0.001 g, 0.0019 g, 0.0038g, and 0.0076g to create a concentration of 0.5 mM, 1 mM, 2 mM, and 5 mM after being mixed with 10 ml of 0.1 M Sorensen's Phosphate buffer each. These concentrations were prepared as a standard curve for detection.

2.3. Device setup

2.3.1. Potentiostat

EmStat4S (PalmSens, Houten, Netherlands) was used to carry out electrochemical detection. Sensor connector cable was used to connect screen-printed electrodes to potentiostat, while USB cable was used to connect potentiostat to PC. PSTrace 5 software (version 5.9.1808) was used to read the result of electrochemical detection. The mode chosen for the electrochemical detection was cyclic voltammetry (CV). The current range selected was 1µA to 1 mA. The settings for cyclic voltammetry were t equilibration of 0 second, E begin of 0 V, E vertex 1 of 0 V, E vertex 2 of 0.5 V, E step of 0.05 V, scan rate of 0.05V/s, and number of scans of 5.

2.3.2. UV-Vis Spectrophotometer

Genesys 150 (Thermo Fisher Scientific, Massachusetts, United States) was used to carry out spectrophotometry to detect wavelength used for dopamine and its absorbance. Scan method was picked to find out the most optimal wavelength for dopamine absorbance. Y-Axis was set to ABS, wavelength range was set to 200 nm - 400 nm, interval was set to 1.0 nm, speed was set to fast. Fixed method was picked to find out the absorbance of different concentrations of dopamine in the most optimal wavelength that was picked from the previous experiment. Equation that was used for this spectrophotometry was set to ABS(λ1)xF1 ,the unit was set to mM, λ1 was set to 290 nm, and F1 was set to 1.

2.4 Measurement

2.4.1 Measurement of current for different Dopamine concentrations using electrochemical detection

Electrochemical detection was carried out by EmStat4s (PalmSens, Houten, Netherlands) on Cyclic Voltammetry mode (CV) to measure the current response to a linearly cycled potential sweep between 0 V to 0.5 V with the scan rate of 0.05V/s. The concentration of dopamine that was tested were 0 mM, 0.5 mM, 1 mM, 2 mM, and 5 mM. The electrodes used were screen printed Ag/AgCl electrodes.

2.4.2 Measurement of wavelength using UV-Vis spectrophotometry

The liquid specimen of dopamine was used to find the most optimal wavelength. Spectrophotometry was carried out using Genesys 150 (Thermo Fisher Scientific, Massachusetts, United States). Liquid specimens of 2.5ml each were placed in quartz cuvettes and blank (0 mM) was scanned at first before other different concentrations of dopamine (0.5 mM, 1 mM, 2 mM, and 5mM) were scanned at wavelength of 200 nm to 400 nm.

2.4.3 Measurement of absorbance for different Dopamine concentration using UV-Vis spectrophotometry

The liquid specimen of dopamine was used to find the absorbance of dopamine in different concentrations. Spectrophotometry was carried out using Genesys 150 (Thermo Fisher Scientific, Massachusetts, United States). Liquid specimens of 2.5ml each were placed in quartz

cuvettes and blank (0 mM) was scanned at first before other different concentrations of dopamine (0.5 mM, 1 mM, 2 mM, and 5mM) were scanned at wavelength 290 nm that was picked from the previous experiment.

3. Results and Discussions

3.1. Electrochemical characterization

Screen-printed Ag/AgCl chloride electrodes were used during this experiment and a cyclic voltammetry (CV) method was chosen to measure the current response to a linearly cycled potential sweep of dopamine solution at different concentrations. The screen printed electrodes used a three-electrodes system, which consisted of a working electrode with the material of carbon (C), a counter electrode with the material of carbon (C), and a reference electrode with the material of silver/silver chloride (Ag/AgCl).

Cyclic voltammetry measured the current response of linearly cycled potential sweep between 0 V to 0.5 V with the scan rate of 0.05V/s of different dopamine solution at 0 mM, 0.5 mM, 1 mM, 2 mM, and 5 mM. Fig. 1 shows the result of cyclic voltammetry of 1mM dopamine solution against the blank.

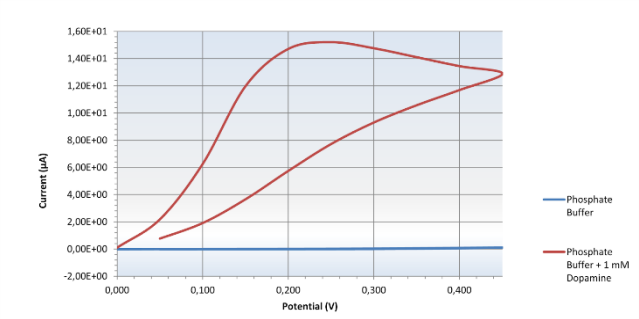

Fig. 1. Voltammogram of the blank (Sorensen's phosphate buffer) against liquid specimen of dopamine of the concentration of 0.1 mM.

Based on electrochemical analysis using cyclic voltammetry as shown as Fig. 1, it was shown the anodic peak current (i_{pa}) of liquid specimen of dopamine with 1 mM of concentration (E) against the Sorensen's phosphate buffer differs with the anodic peak current (i_{pa}) of 15.218942 µA for 1mM of dopamine at the anodic peak potential (E_{pa}) of 0.250194 V and the anodic peak current (i_{pa}) of 0.110947 µA for Sorensen's phosphate buffer at the anodic peak potential (E_{pa}) of 0.45035 V. Fig. 1 showed that in phosphate buffer the current was in steady state during both in oxidative and reductive scan, while in liquid specimen of dopamine with concentration of 1 mM, redox reaction happened which was shown with distinguishable anodic peak current (i_{pa}) which can be observed by the increasing current until it reached its peak at 15.218942 µA during the sweep forward toward more positive and oxidative potential but also in the decreasing current during the sweep backward to more negative and reductive potential. This observation showed the transfer of electrons during the redox reaction from reducing agents to oxidizing agents. According to the paper by Kissinger, P. T., & Heineman, W. R. (1983) [32] this is due to changes in concentration during electrolysis to solution adjacent to electrodes, where the potential excitation signal exert control at the electrode surface in a reversible system that can be described by considering Nernst equation. This can also be explained by concentration distance profile (C-x profiles) which shows how solution concentration (C) varies as a function of distance (x) from the electrode surface. According to Kissinger, P. T., & Heineman, W. R. (1983) [32] the current is proportional to the slope of the C-x profile at the electrode surface, which explained at 0 mM the slope of C would always be 0 and at any point, the current is negligible.

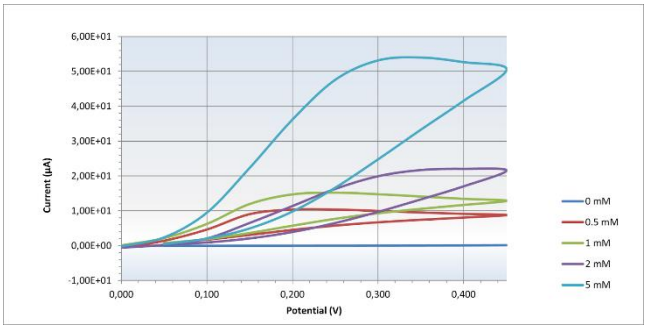

Fig. 2. Voltammogram of liquid specimen of dopamine on concentration of 0 mM, 0.5 mM, 1 mM, 2 mM, and 5 mM.

Based on electrochemical analysis using cyclic voltammetry as shown in Fig. 2, it was shown the difference of the anodic peak current (i_{pa}) of liquid specimens of dopamine in different concentrations. Liquid specimen of dopamine with 0 mM of concentration has anodic peak current (i_{pa}) of 0.110947 µA at the anodic peak potential (E_{pa}) of 0.45035 V. Liquid specimen of dopamine with 0.5 mM of concentration has anodic peak current (i_{pa}) of 10.362033 µA at the anodic peak potential (E_{pa}) of 0.200155 V. Liquid specimen of dopamine with 1 mM of concentration has anodic peak current (i_{pa}) of 15.218942 µA at the anodic peak potential (E_{pa}) of 0.250194 V. Liquid specimen of dopamine with 2 mM of concentration has anodic peak current (i_{pa}) of 22.020494 µA at the anodic peak potential (E_{pa}) of 0.400311 V. Liquid specimen of dopamine with 5 mM of concentration has anodic peak current (i_{pa}) of 53.961484 µA at the anodic peak potential (E_{pa}) of 0.350272 V. From Fig. 2, it can be observed that the concentration of liquid specimens of dopamine positively correlates with the anodic peak current (i_{pa}), as the increase in concentration of dopamine in solution linearly increases the anodic peak current (i_{pa}). Kissinger, P. T., & Heineman, W. R. (1983) [32] explained that the peak current for a reversible system could be described by the Randles-Sevcik equation for the forward sweep of the first cycle, where peak current (i_p) proportional to electron stoichiometry (n), electrode area (A), diffusion coefficient (D), concentration (C), and scan rate (v). This concludes that given the same electron stoichiometry (n), electrode area (A), diffusion coefficient (D), and scan rate(v), the difference in peak current (i_p) could be determined by the difference in concentration and vice versa. Fig 3. illustrates the relationship between peak current,

which in this case is anodic peak current (i_{pa}), to the concentration of liquid specimens of dopamine (C).

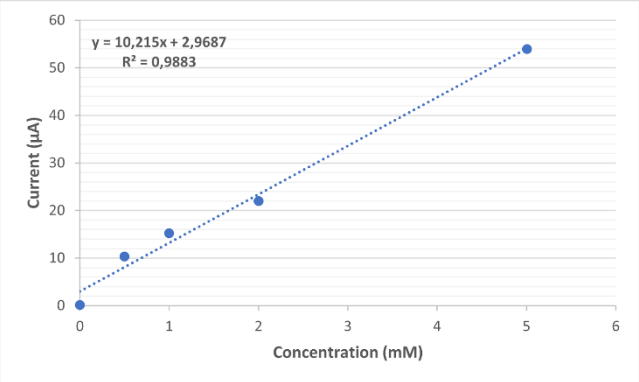

Fig. 3. Plot of concentration of liquid specimens of dopamine to anodic peak current (i_{pa})

Fig. 3. shows that the anodic peak current (i_{pa}) of liquid specimens of dopamine is linearly dependent on its concentration. Fig. 3. shows that the regression plot of anodic peak current of dopamine solution, expressed as I (µA) = 10.215 * concentration of dopamine (mM) + 2.9687 with the slope of 10.215, gradient of +10.215, y-intercept of 2.9687, and a quality of fit (R^2) of 0.9883.

Based of the regression analysis of the plot in Fig. 3., limit of detection (LOD) and limit of quantification (LOQ)[33] could be calculated as

$$LOD = 3 * s \quad (1),$$

and

$$LOQ = 10 * s \quad (2)$$

where σ is the standard deviation of anodic peak current to the blank and s is the slope of the calibration curve. σ has the value of 1.575211615 and s has the value of 10.21536307. Based on the equation (1) and (2), the value of limit of detection (LOD) and limit of quantification (LOQ) are 0.462600772 and 1.542002574.

3.2. Spectrophotometry

UV/Vis Spectrophotometer was used to find the optimal wavelength for liquid specimens of dopamine of differing concentrations (0.5 mM, 1 mM, 2 mM, and 5mM) at a wavelength range of 200 nm to 400 nm. Fig 4. showed that the most optimal wavelength for dopamine absorbance is at 290 nm.

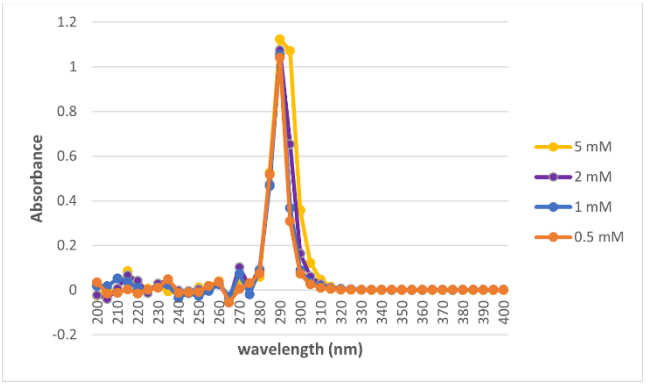

Fig 4. Dopamine absorbance at a wavelength range of 200 nm to 400 nm.

Based on the result that was obtained by this experiment, 290 nm was picked for the most optimal wavelength as it showed the strongest dopamine absorbance of different concentrations of liquid specimens of dopamine at 0.5 mM, 1 mM, 2 mM, and 5mM. The absorbance of a liquid specimen of dopamine with the concentration of 0.5 mM at the wavelength of 290 nm is 1.042. The absorbance of a liquid specimen of dopamine with the concentration of 1 mM at the wavelength of 290 nm is 1.055. The absorbance of a liquid specimen of dopamine with the concentration of 2 mM at the wavelength of 290 nm is 1.075. The absorbance of a liquid specimen of dopamine with the concentration of 5 mM at the wavelength of 290 nm is 1.124. From Fig. 4, it can be observed that the concentration of liquid specimens of dopamine positively correlates with its absorbance, as the increase in concentration of dopamine in solution linearly increases the absorbance of dopamine. Absorbance spectrophotometry is used as a quantitative tool to measure the concentration of a colored substance (chromophore) in a transparent solvent[34]. According to a paper by Swinehart, D. F. (1962) [35] in the Beer-Lambert law, the powers and other functions of distances and concentrations are also a function of the wavelength of the radiation. According to Lambert's law, the fraction of radiant power absorbed when it passes through an infinitesimal thickness of the absorbing medium is proportional to the infinitesimal thickness and it's proportional to absorptivity for the pure medium (at wavelength λ). If an absorbing solute is added at concentration c moles/liter, where c << 1 as is usually the case and absorbance of the solvent independent of c, g(c) as function of c will be used. According to Beer's law, the fractional loss of power due to absorption of increase in the concentration is proportional.

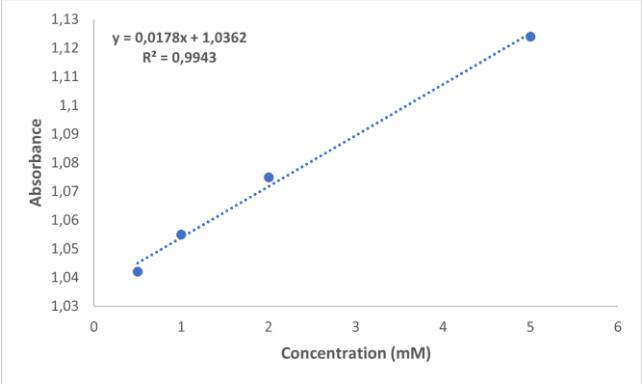

Fig. 5. Plot of concentration of liquid specimens of dopamine to its absorbance

Fig. 5. shows that the absorbance of liquid specimens of dopamine is linearly dependent on its concentration. Fig. 5. shows that the regression plot of absorbance of dopamine solution, expressed as Absorbance = 0.0178 * concentration of dopamine (mM) + 1.0362 with the slope of 0.0178, gradient of +0.0178, y-intercept of 1.0362, and a quality of fit (R^2) of 0.9943.

Based of the regression analysis of the plot in Fig. 5., limit of detection (LOD) and limit of quantification (LOQ)[33] could be calculated where σ is the standard deviation of absorbance to the blank and s is the slope of the calibration curve. σ has the value of 0.002629589 and s has the value of 0.017805128. Based on the equation (1) and (2), the value of limit of detection (LOD) and limit of quantification (LOQ) are 0.443061575 and 1.476871915.

3.3 Comparison of electrochemical characterization and UV-Vis Spectrophotometry

Based on the experiment that was carried out on both electrochemical characterization using cyclic voltammetry (CV) and the uv-vis spectrophotometry, peak current (i_p) and absorbance positively correlate with concentration. Both peak current (i_p) and absorbance of liquid specimens of dopamine are linearly dependent on its concentration.

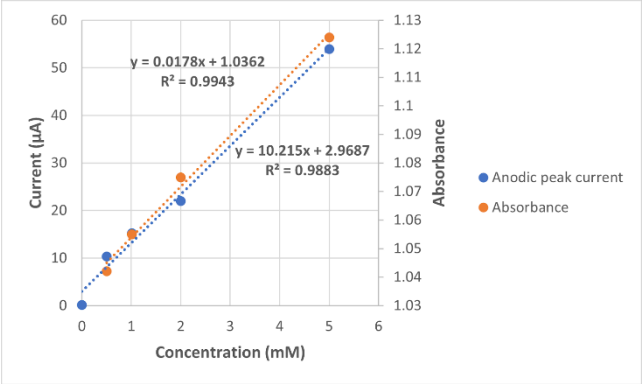

Fig. 6. Plot of concentration of liquid specimens of dopamine to its anodic peak current (i_{pa}) and absorbance

Based on electrochemical detection using cyclic voltammetry (CV), regression plot of anodic peak current of dopamine solution, expressed as I (μA) = 10.215 * concentration of dopamine (mM) + 2.9687. Based on spectrophotometry, the regression plot of absorbance of dopamine solution, expressed as Absorbance = 0.0178 * concentration of dopamine (mM) + 1.0362. Both methods had high R^2 values which are 0.9883 for electrochemical detection and 0.9943 for spectrophotometry. Based on these results, concentration of liquid specimens of dopamine has positive correlation to both its anodic peak current (i_{pa}) and absorbance.

Electrochemical detection using cyclic voltammetry (CV) could be used to determine the concentration of liquid specimens of dopamine for its correlation to its peak current (i_p) in lab-on-chip setup. Electrochemical detection has its own advantages over spectrophotometry due to its being more portable. Electrochemical detection also requires less volume of sample than spectrophotometry.

While this paper studied the linearity of liquid specimens of dopamine concentration and anodic peak current (i_{pa}) during electrochemical detection at the pH of 7.0 and scan rate of 0.05V/s, more experiments and data are needed to study the linearity of liquid specimens of dopamine concentration and anodic peak current (i_{pa}) in different range of pH and different range of scan rate. More experiments and data need to be conducted to study the linearity of dopamine concentration to both its anodic and cathodic peak current. The future application of this paper is for lab-on-chip, to determine the concentration of liquid specimens of dopamine based on its peak current (i_p).

4. Conclusion

This paper studied the correlation of concentration of liquid specimens of dopamine to both its anodic peak current (i_{pa}) and absorbance. It was shown that the concentration of liquid specimens of dopamine is linear to both anodic peak current (i_{pa}) and absorbance. Due to the high R^2 values of 0.9883, electrochemical detection could be used and implemented to detect dopamine concentration for application of lab-on-chip, as it is more portable and requires less volume of sample compared to spectrophotometry.

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