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# Redox-active gold nanoparticle-encapsulated poly(amidoamine) dendrimer for electrochemical sensing of 4-aminophenol

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## ARTICLE INFO

## ABSTRACT

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Keywords: PAA dendrimer Gold nanoparticles 4-Aminophenol Ferrocene Nonenzymatic electrochemical sensor Metal nanoparticle-encapsulated with dendrimer networks have gained enormous interest towards fabrication of various electrochemical devices, including electrochemical sensors. In this work, we have designed a redox active electrochemical sensor using ferrocene terminated poly(amidoamine) (PAA) dendrimers encapsulated with gold nanoparticles (AuNPs) for the detection of 4-aminophenol (4-AP). The redox mediator, ferrocene (as ferrocene carboxaldehyde), was covalently attached to an amine terminated third generation of PAA dendrimer through Schiff base condensation to form a stable imine bond. Thereafter, AuNPs were entrapped in the dendritic network to yield a Fc-PAA-AuNPs, which was deposited over a glassy carbon electrode (GCE) to form Fc-PAA-AuNPs/GCE. The cyclic voltammogram of 0.1 M phosphate buffer at the fabricated electrode displayed a set of distinct redox peaks with an oxidation peak at 0.427 V and reduction peak at 0.345 V corresponding to ferrocene/ ferrocenium (Fc/Fc<sup>+</sup>) redox couple. Further, the fabricated electrode has shown prominent electrocatalytic response for the detection of 4-AP based on which an electrochemical sensor towards the determination of 4-AP has been developed. Noticeably, the newly developed electrochemical sensor has shown impressive performance towards detection of 4-AP with a linear range from 30 to  $1064 \,\mu$ M, with a sensitivity of  $87.8 \,\mu$ A mM<sup>-1</sup> cm<sup>-2</sup> and a limit of detection of 7.61 µM. Besides, the developed sensor exhibited good selectivity and excellent stability towards the detection of 4-AP. The superior efficacy of the developed sensor could be due to the covalent immobilization of Fc and effective encapsulation of AuNPs in the hyperbranched Fc terminated PAA dendritic network, which augumented their electronic conductivity as well as operational stability.

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## 1. Introduction

Development of facile, robust and reliable analytical techniques for the selective and sensitive determination of crucial analytes is a compelling requirement in human healthcare and environmental safety [1,2]. One such analyte is 4-aminophenol (4-AP), which is a derivative of phenol with an amine substitution in the para position and it is formed during the degradation of azo dyes, pesticides and paracetamol (widely used analgesic and antipyretic drug) [3–5]. 4-AP has adverse effects on human health causing skin and eye irritation, respiratory problems, teratogenic and nephrotoxicity and affects other life forms as well [6,7]. Thus, the maximum amount of 4-AP in pharmaceutics is restricted to 50 ppm by the European Pharmacopeias and United States [8,9]. Moreover, 4-AP is a commonly used synthetic material in a variety of fields such as plastics, petroleum additives, pharmaceutical ingredients, dyestuffs, rubber, chemical inhibition. As a result, tremendous amounts of 4-AP are inevitably released into the atmosphere and poses a serious threat to the environment [10-13]. Therefore, the detection and

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Applications of various analytical techniques including spectrophotometry [14], colorimetric [15], capillary electrophoresis [16], gas chromatography [17], chemiluminescence [18], liquid chromatography [19] to the detection of 4-AP yielded satisfactory results. However, these techniques are time consuming, expensive, tedious and require skilled operators for sample preparation and operation of sophisticated instrumentation, which restrict them in real time use and onsite determination. On the contrary, electrochemical methods are simple, robust, rapid, portable, robust, involve no sample preparation, which could favor the sensitive and selective determination of 4-AP [10,20,21]. The performance of the electrochemical sensors manifestly relies on the nature of electrode modifying materials, which stipulate the sensitivity, selectivity and stability of the fabricated electrode. Therefore, enormous effort has been devoted towards the fabrication of suitable platforms, which include carbon nanomaterials, metal organic frameworks, polymers, redox mediators, metal oxides, carbides, complexes and nanoparticles [22-25]. Despite all these efforts, these sensors suffer from one or more of the demerits such as narrow linear range, limited sensitivity and long-term stability. These challenges could be addressed with appropriate choice of materials which in turn could afford firm immobilization, proper wiring, improved surface area and high conductivity. Accordingly, we intended to develop an electrochemical sensor for the determination of 4-AP by judicious modifying the electrode in order to circumvent the above-mentioned challenges.

Dendrimers belong to a special type of synthetic polymer materials, which have high surface functionality, well-defined three-dimensional and highly branched architectures [26,27]. In particular, the poly(amidoamine) (PAA) dendrimer is most commonly studied due to its good biocompatibility, high structural flexibility and functionality, excellent mono dispersity, tunable porosity, high physical and chemical stability [28,29]. Hence, PAA dendrimers have found a wide range of applications from simple coating and adhesion to complex membrane chemistry, biomimetic, nanotechnology, electrochemical sensing, biosensing and immunosensing [30-33]. Further, the pores of PAA can accommodate suitable metal nanoparticles to enhance the electrical conductivity of PAA dendrimers. Among various metal nanoparticles, gold nanoparticles (AuNPs) have received extensive attention in electrochemical sensors due to their high electrocatalytic activity, good biocompatibility and unique optical and electronic properties [34-37]. AuNP encapsulated PAA dendrimers have received massive interest among researchers for fabricating novel electrode platforms for various electrochemical applications [38].

Another advantage of PAA dendrimer is their synthetic versatility and affordability in tailor-made architect. PAA dendrimers coated on an electrode surface can be used to immobilise desirable redox mediators or biomolecules to develop novel electrochemical sensors. Redox mediators such as azure-A, toluidine blue, thionine, ferrocene, phenothiazine, viologen have often been used in electrochemical sensing because of their well-resolved redox mediating properties [39-42]. Therefore, a variety of redox mediators and their derivatives are frequently being explored for the immobilization over a PAA network in order to develop redox active platforms for facile electrochemical sensors. There is still a demand for the immobilization of different molecules on PAA dendrimers for improving their performance. Ferrocene (Fc) is an organometallic molecule widely used as a redox mediator for the voltammetric determination of various substrates due to its unique electrochemical properties [43,44]. However, Fc has poor adhesion on the surface of bare electrodes with a low solubility in aqueous medium which limits its inclusive application in voltammetric determination. Many approaches have been used to improve the adhesion of Fc onto an electrode such as composite matrix, mechanical immobilization, self-assembled monolayers and covalent bonding [45,46].

In the present work, we sought to develop a redox-active dendrimer, encapsulated with AuNPs as an electrochemical sensor for 4-AP by harnessing the synthetic versatility of PAA dendrimer. Initially, an amine terminated third generation PAA dendrimer was synthesized, to which ferrocene carboxaldehyde (Fc-CHO) was covalently attached to the terminal amine of PAA and free aldehyde of Fc-CHO to form the Fc terminated PAA dendrimer (Fc-PAA). Further, AuNPs were encapsulated in the Fc-PAA dendritic network to form Fc-PAA-AuNPs. The PAA dendrimers assist towards the covalent immobilization of Fc and also the preparation of AuNPs with reasonable monodispersity and are thus imperative in this setup. The electrochemical sensor was fabricated by immobilising the prepared Fc-PAA-AuNPs on a glassy carbon electrode to yield a Fc-PAA-AuNPs/GCE. The fabricated Fc-PAA-AuNPs/GCE showed promising electrocatalytic behaviour towards the oxidation of 4-AP. In addition, the fabricated electrochemical sensor has shown a broad linear range, high selectivity and good reproducibility.

## 2. Experimental section

## 2.1. Chemicals and reagents

Ferrocene carboxaldehyde (98%), methyl acrylate (99%), ethylene diamine (99.5%), gold(III) chloride trihydrate (99.9%) were procured

from Sigma-Aldrich, India. 4-AP (98%), sodium borohydride, sodium sulfate anhydrous, disodium hydrogen phosphate, sodium dihydrogen phosphate and sulfuric acid were received from Merck, India. All other chemicals and solvents used were of high purity analytical grade. All aqueous solutions were prepared using Milli-Q water obtained from Merck Millipore.

#### 2.2. Instrumentation

The prepared Fc-PAA-AuNPs were characterized using high resolution transmission electron microscopy (HR-TEM; FEI-TECNAI G2 20 Twin) at 200 kV. Energy dispersive X-ray analysis (EDX) was carried out using a Bruker Xflash 6 T130 spectrometer with a liquid nitrogen free detector. Absorption spectra of synthesized Fc-PAA dendrimer and corresponding AuNPs were measured in a Jasco V-670 UV-visible spectrophotometer. The functional groups of PAA and Fc-PAA dendrimers were confirmed by Fourier-transform infrared spectroscopy (FTIR) using a Shimadzu, IR Affinity-1 spectrophotometer. Electrochemical experiments were performed in a three-electrode type electrochemical cell with using a CHI760E electrochemical workstation. Modified/unmodified GCEs were used as a working electrode, a platinum coil as a counter electrode and an aqueous Ag/AgCl (3 M KCl) electrode as a reference electrode. Autolab PGSTAT 204 potentiostat (Metrohm Autolab, Netherlands) was used for performing the electrochemical impedance measurements and the results were processed using Autolab NOVA 2.1.2 software.

#### 2.3. Synthesis of ferrocene terminated PAA dendrimer (Fc-PAA)

Fc terminated PAA dendrimers were synthesized using a simple Schiff base condensation reaction as displayed in Fig. 1A. A PAA dendritic network was synthesized using the procedure previously reported by us [47] and the synthesis scheme is provided in the supplementary information (scheme S1). Thereafter, a toluene solution of Fc carboxaldehyde (96 mmol) was dropwise added into a stirred toluene solution of PAA dendrimer (2.9 mmol). This mixture was refluxed at 70 °C for 24 h, after which the solvent was removed to obtain a residue. The obtained residue was dissolved using ethanol (30 mL) to which NaBH<sub>4</sub> was added and the mixture was refluxed for 6 h to reduce the -C=N- double bond in imine groups [48]. After completion of reaction, ethanol was removed and the resulting residue was washed using 3% (w/v) aqueous NaHCO<sub>3</sub> and extracted using CH<sub>2</sub>Cl<sub>2</sub>. The combined extracts were dried using anhydrous Na<sub>2</sub>SO<sub>4</sub> and then filtered. The filtrate was concentrated under reduced pressure to obtain Fc functionalised PAA dendrimers (Fc-PAAs).

## 2.4. Synthesis of Fc-PAA encapsulated with gold nanoparticles (Fc-PAA-AuNPs)

Fc-PAA encapsulated with gold nanoparticles were synthesized based on the procedure reported earlier [49,50] with minor modification (Fig. 1B). In brief, 5 mL of freshly prepared aqueous HAuCl<sub>4</sub> solution (5.5. mM) was added dropwise to a constantly stirred solution of 5 mL of Fc-PAA dendrimer in ethanol to form a pale-yellow solution, which was further continuously stirred for 30 min. Subsequently, a fresh solution of 0.1 M NaBH<sub>4</sub> in water was injected and the solution immediately changed its color from pale yellow to red, which indicates the reduction of Au(III) to Au(0). The solution was continuously stirred for another 15 min. The Fc-PAA-AuNPs obtained were stored at 5 °C in refrigerator.

## 2.5. Fabrication of Fc-PAA-AuNPs/GCE

Initially, the GCE was carefully polished until free from any physically adsorbed materials to mirror-like surface with 1.00, 0.30 and 0.05  $\mu$ m alumina slurries and sonicated in an EtOH/H<sub>2</sub>O mixture (1:1) and then dried under the stream of N<sub>2</sub>. Different volumes of Fc-PAA-



Fig. 1. Scheme for (A) Synthesis of ferrocene terminated PAA dendrimer and (B) Synthesis of Fc-PAA encapsulated with gold nanoparticles.

AuNPs (in 1 µL increment) have been immobilized by dropcasting on the surface of GCE and the cyclic voltammetric response was recorded. The current response was found to increase up to 5 µL of Fc-PAA-AuNPs. Slightly higher currents were obtained at higher volumes, whereas the CV response was unstable. Hence, 5 µL of Fc-PAA-AuNPs was chosen as the optimum amount for the fabrication of Fc-PAA-AuNPs/GCE. Subsequently, 5 µL of Fc-PAA-AuNPs was dropcasted on the surface of a GCE and dried at room temperature to form Fc-PAA-AuNPs/GCE. Similarly, Fc-PAA/GCE and PAA/GCE were also fabricated for comparison.

## 3. Results and discussion

#### 3.1. Characterization of PAA, Fc-PAA and Fc-PAA-AuNPs dendrimers

The FTIR spectra of synthesized PAA dendrimer (pink) and ferrocene terminated PAA dendrimer (red) are shown in Fig. 2A. The spectrum of PAA dendrimer shows a sharp intense band at 1636 cm<sup>-1</sup> and the value is in agreement with that reported in literatures [51,52] for -C=O stretching band in the PAA network. Thus, this band at 1636 cm<sup>-1</sup> has been assigned to the stretching vibration of -C=O groups in the PAA dendritic network. The strong absorption bands appeared at 1546 and 3282 cm<sup>-1</sup> were in accordance with the bending and stretching vibration of N-H groups, as reported in literature [53] and this indicated the presence of primary amine groups in PAA dendrimer. Further, a new sharp peak appeared at 1243 cm<sup>-1</sup>, which is similar to that observed for C-N stretching vibration in literature [54,55] and also the N-H

stretching band of terminal free amine group  $(-NH_2)$  was found to disappear. These observations ensure the covalent attachment of ferrocene carboxaldehyde to amine terminated PAA dendrimer to form Fc-PAA. Additionally, new sharp bands appeared at 823 and 485 cm<sup>-1</sup> which were found to be similar to that of C-H bending and Fe-C out of the plane bending vibration of Fc rings, reported for a covalently immobilized on silane [43]. These two new bands further affirm that ferrocene has been attached to the PAA dendritic network. Fig. 2B depicts the UV-vis spectra of synthesized PAA dendrimer, Fc-PAA dendrimer and Fc-PAA-AuNPs recorded in ethanol. Typically, the PAA dendrimer, Fc-PAA dendrimer and Fc-PAA-AuNPs exhibited two absorption bands at 217 and 285 nm, similar to that observed for  $\pi \rightarrow \pi^*$ transition (at 250 and 275 nm) in the -C=O group present in dendritic network reported earlier [56]. On the other hand, Fc-PAA and Fc-PAA-AuNPs showed a strong peak around 365 nm. The observed peak is in agreement with literature report on Fc terminated dendrimer [56] and thus ascribed to the charge transfer band in ferrocene unit. This further witnesses the attachment of ferrocene to the dendrimer network. A broad band observed at 535 nm for Fc-PAA-AuNPs, which is in accordance with the surface plasmon resonance (SPR) of AuNPs entrapped in PAA network reported earlier [57]. Hence, this SPR band at 535 nm evidences the encapsulation of AuNPs in the Fc-PAA dendrimer network. Fig. 2C displays the transmission electron micrograph of a gold nanoparticles encapsulated Fc-PAA dendritic network, which clearly shows the formation of spherical shaped AuNPs with particle sizes ranging from 5 to 8 nm. Further, the EDX spectra of the Fc-PAA-AuNPs exhibited peak at 2.15 keV (Fig. 2D) indicating the presence of AuNPs.



Fig. 2. (A) FTIR spectra of PAA (brown) and Fc-PAA (red). (B) UV–Vis spectra of PAA, Fc-PAA and Fc-PAA-AuNPs (blue). (C) Transmission electron micrograph of Fc-PAA-AuNPs. (D) Energy dispersive X-ray (EDX) analysis of Fc-PAA-AuNPs/GCE.



Fig. 3. (A) EIS of 2.5 mM [Fe(CN)<sub>6</sub>]<sup>4-</sup> and 2.5 mM [Fe(CN)<sub>6</sub>]<sup>3-</sup> at various modified electrodes in 0.1 M KCl. Inset: Proposed equivalent circuit (B) Cyclic voltammograms of 0.1 M phosphate buffer (pH 7.0) at a bare GCE (black), PAA/GCE (pink), Fc-PAA/GCE (red) and Fc-PAA-AuNPs/GCE (blue) at a scan rate of 50 mV s<sup>-1</sup>.

## 3.2. Electrochemical behaviour of Fc-PAA-AuNPs/GCE modified electrode

The electrochemical behaviour of the assembled electrode was investigated by electrochemical impedance spectroscopy (EIS) and cyclic voltammetry (CV). EIS gives substantial information regarding the impedimetric changes that occur between the electrode and electrolyte interface during the electrode assembly process. EIS was recorded at an open circuit potential of 0.2 V, over the frequency range of 1 mHz to 100 mHz with an AC amplitude of 0.01 V. Fig. 3A portrays the EIS spectra of 2.5 mM  $[Fe(CN)_6]^{4-}$  and 2.5 mM  $[Fe(CN)_6]^{3-}$  at a bare GCE (black), a PAA/GCE (pink), a Fc-PAA/GCE (red) and a Fc-PAA-AuNPs/GCE (blue) in 0.1 M KCl. An equivalent circuit (inset to Fig. 3A) consisting of a solution resistance  $(R_s)$  in series with the parallel combination of a constant phase element (CPE) and the impedance of the faradaic reaction was used to fit the experimental EIS results. The impedance of the faradaic reaction includes a charge transfer resistance  $(R_{ct})$  in series with Warburg impedance (W). EIS spectra of bare GCE displays an  $R_{ct}$  (corresponding to the diameter of a fitted semicircle) of 559  $\Omega$ , indicative of feeble electron transfer process on the surface of bare electrode. After immobilization of PAA dendrimer on bare GCE, the R<sub>ct</sub> value has reduced to 385  $\Omega$ , indicating that PAA dendrimer improves electron transfer ability [58]. On the other hand, immobilization of Fc-PAA on GCE (Fc-PAA/GCE) significantly reduces the  $R_{ct}$  to 252  $\Omega$  due to the inclusion of Fc on the dendritic network, which improved electron shuttling due to the redox nature of the Fc mediator. Further, encapsulation of AuNPs on the Fc-PAA dendritic network dramatically reduces the  $R_{ct}$  to a lowest value of 145  $\Omega$ , signifying the highly conducting behaviour of the newly developed Fc-PAA-AuNPs/GCE. The increased conductivity of the fabricated sensor could be due to the covalent anchoring of highly redox active Fc as well as the effective encapsulation of AuNPs on the dendritic network, which augmented the electron transfer process.

Fig. 3B illustrates the cyclic voltammograms of 0.1 M phosphate buffer (pH 7.0) at a bare GCE (black), PAA/GCE (pink), Fc-PAA/GCE (red) and Fc-PAA-AuNPs/GCE (blue) at a scan rate of 50 mV s<sup>-1</sup>. As anticipated, the bare and PAA/GCE did not show any redox response due to their non-redox nature within the given potential window. After the covalent attachment of ferrocene on PAA dendrimer (Fc-PAA/GCE), a set of distinct redox peak at 0.416 V (anodic, *E*<sub>pa</sub>) and 0.328 V (cathodic,  $E_{pc}$ ) with the respective formal potential  $(E^{\circ'})$  and peak-to-peak separation ( $\Delta E_p$ ) of 0.372 V and 88 mV was observed. The obtained redox peaks are in accordance with the literature reports on immobilized Fc [45,59], which correspond to the characteristic ferrocene/ferrocenium (Fc/Fc<sup>+</sup>) redox couple. This further confirms that the ferrocene moieties have been successfully attached to the PAA dendritic network. Further, encapsulation of AuNPs in the Fc-PAA dendritic network (Fc-PAA-AuNPs/GCE) has exhibited a similar redox behaviour with an E°'and  $\Delta E_{\rm p}$  of 0.386 V and 82 mV, respectively. Distinct increase in the peak currents of Fc-PAA-AuNPs/GCE could be due to the encapsulation of a large number of AuNPs within the dendritic network, which improved their surface area and conductivity with Fc synergistically. This electrode setup with integration of redox-active ferrocene and highly conductive AuNPs in the dendrimer network could be effectively utilized in electrochemical sensing.

The electroactive surface area of Fc-PAA/GCE and Fc-PAA-AuNPs/ GCE has been estimated using Randles-Sevick Eq. (1).

$$I_{\rm p} = \left(2.69 \times 10^5\right) n^{3/2} A D^{1/2} {\rm C} v^{1/2} \tag{1}$$

where  $I_p$  is the peak current (A), n is the number of electrons involved in the redox reaction, A is the electroactive surface area of the modified electrode (cm<sup>2</sup>), D is the diffusion coefficient (6.2 × 10<sup>-6</sup> cm<sup>2</sup> s<sup>-1</sup> for 1 mM K<sub>4</sub>[Fe(CN)]<sub>6</sub> in 0.1 M KCl) [60], C is the concentration (mol cm<sup>-3</sup>) and v is scan rate (V s<sup>-1</sup>). The surface areas were determined to be 0.077 and 0.095 cm<sup>2</sup> for Fc-PAA/GCE and Fc-PAA-AuNPs/GCE, respectively. It becomes obvious that the incorporation of AuNPs in the electrode setup has considerably enhanced the electroactive surface area.

To probe the effect of scan rate on the redox reaction of Fc at Fc-PAA-AuNPs/GCE, cyclic voltammetry of 0.1 M phosphate buffer (pH 7.0) was performed by increasing the scan rate from 10 to 200 mV s<sup>-1</sup>. The results are shown in Fig. S1. The oxidation and reduction peak currents of Fc-PAA-AuNPs/GCE progressively increased with increase in scan rate. Both the peak currents varied linearly with the square root of scan rate (Fig. S2), denoting a diffusion controlled redox process [42]. Thereafter, cyclic voltammetry of 0.1 M phosphate buffer of increasing pH from 4.0 to 10.0 was conducted to study the effect of pH and the obtained results are shown in Fig. S3. On increasing the pH from 4.0 to 7.0, the oxidation peak current at the Fc-PAA-AuNPs/GCE also increased gradually and on further increasing the pH beyond 7.0, the peak current at Fc-PAA-AuNPs/GCE began to decrease. The maximum current response was achieved at pH 7.0 and hence, this pH was chosen as the optimum pH for further electrocatalytic applications.

## 3.3. Electrocatalytic oxidation of 4-AP at Fc-PAA-AuNPs/GCE

The electrocatalytic oxidation of 4-AP at a Fc-PAA/GCE and a Fc-PAA-AuNPs/GCE in 0.1 M phosphate buffer (pH 7.0) was investigated by cyclic voltammetry at a scan rate of 50 mV s<sup>-1</sup>. The results obtained are depicted in Fig. 4A and B, respectively. Initially, cyclic voltammetry of 0.5 mM 4-AP at a bare GCE and a PAA/GCE was performed and the results obtained are presented in the inset to Fig. 4A and Fig. 4B, respectively. It is evident that both bare GCE and PAA/GCE have shown a low oxidation peak current for the oxidation of 4-AP.

Interestingly, Fc-PAA/GCE has shown good electrocatalytic activity upon sequential addition of 0.1 mL aliquots of 0.01 M 4-AP, as evidenced by the increasingly larger oxidation peak at 0.420 V in the cyclic voltammograms in both Fig. 4A and Fig. 4B. These results indicate that the modified electrode has the ability to electrocatalytically oxidise 4-AP. Further, inclusion of AuNPs into the Fc-PAA dendritic network (Fc-PAA-AuNPs/GCE) yielded a 188% increase in the oxidation current of 4-AP compared to that at a Fc-PAA/GCE. On applying the oxidation potential of 0.427 V, Fc in the Fc-PAA-AuNPs/GCE was electrochemically oxidised to ferrocenium ion  $(Fc^+)$ , which in turn chemically oxidizes the target analyte 4-AP to guinoneimine and gets reduced to Fc. The electrochemical oxidation of Fc to Fc<sup>+</sup> and the chemical oxidation of 4-AP by Fc<sup>+</sup>, occur in a cycle as long as the analyte is available at the electrode surface, which result in an increased current response for every addition of 4-AP. Noticeably, this mediated electrocatalytic oxidation of 4-AP occurred at a moderately low onset potential with a larger oxidation current at the Fc-PAA-AuNPs/GCE than at the Fc-PAA/GCE. The increased current response for Fc-PAA-AuNPs/GCE could be again due to the incorporation of a large number of AuNPs in the highly branched Fc-PAA dendritic network, leading to a 23% increase in the electrode surface area, as well as sensitivity by improving the conductivity of the developed sensor.

Fig. 4C depicts the amperometric response of 0.45 V in the presence of increasing 4-AP concentration at a bare GCE (black), a Fc-PAA/GCE (red) and a Fc-PAA-AuNPs/GCE (blue) modified electrodes in a continuously stirred 0.1 M phosphate buffer (pH 7.0). Initially, the operating potential for the amperometric measurements has been optimized by performing experiments at various potentials from 0.40 V to 0.55 V (Fig. S4). The response current towards the detection of 4-AP at Fc-PAA-AuNPs/GCE was found to increase with the working potentials up to 0.45 V. While a marginally improved response was attained even beyond 0.45 V, the increase in current was non-linear at higher potentials and thus we have chosen 0.45 V as optimum potential for the detection of 4-AP. It can be observed that the bare GCE displays a small and nonlinear current response after each addition of 4-AP. On the other hand, Fc-PAA/GCE and Fc-PAA-AuNPs/GCE showed a rapid increase in current after successive addition of 4-AP, which stabilized within 3 s, indicating



**Fig. 4.** Cyclic voltammograms obtained at (A) Fc-PAA/GCE and (B) Fc-PAA-AuNPs/GCE after sequential addition of 0.1 mM 4-AP to 0.1 M phosphate buffer (pH 7.0). Inset to Fig. 4A & B: Cyclic voltammograms of 0.0 and 0.5 mM 4-AP at a bare GCE and PAA/GCE. (C) Amperometric i-t response of Fc-PAA-AuNPs/GCE (blue), Fc-PAA/GCE (red) and bare GCE (black) for different concentration of 4-AP in 0.1 M phosphate buffer (pH 7.0) at +0.45 V. (D) Corresponding calibration plot for detection of 4-AP.

the superior electrocatalytic behaviour of the newly assembled electrodes. Fig. 4D displays the calibration plot for the determination of 4-AP, wherein the sensitivity was estimated from the slope (*m*) of the calibration plot and LOD (S/N = 3) was calculated using the formula  $3\sigma$ /m, where ' $\sigma$ ' denotes the standard deviation of the blank. Fc-PAA-AuNPs/GCE and Fc-PAA/GCE showed linear current response with

better sensitivities of 87.8  $\mu$ A mM<sup>-1</sup> cm<sup>-2</sup> and 72.2  $\mu$ A mM<sup>-1</sup> cm<sup>-2</sup>, whereas the bare GCE exhibited a low sensitivity of 35.9  $\mu$ A mM<sup>-1</sup> cm<sup>-2</sup>. The higher current response observed with Fc-PAA-AuNPs/GCE could be attributed to the inclusion of AuNPs into the dendritic network, which improved their surface area and enhanced their electronic conductivity. Moreover, Fc-PAA-AuNPs/GCE showed a wide linear range

#### Table 1

Comparison of the performances of different 4-AP electrochemical sensors.

Electrodes	Methods	Linear range (µM)	Sensitivity $\mu A \ m M^{-1} \ cm^{-2}$	LOD (µM)	Ref.
Pt/ZnO/ITO	AP	-	12.55	4.11	[61]
AuPt/ZnO/ITO	AP	-	14.31	3.60	[61]
G-PANI/CPE	AP	50-500	-	15.68	[7]
CS/Au/Pd/rGO/GCE	DPV	1-300	-	0.12	[8]
ZnO/NPC/GCE	AP	5-120	31.02	0.014	[9]
RGO/P-L-GSH/GCE	AP	0.4-200	27.2	0.023	[13]
MoS <sub>2</sub> /GCE	DPV	0.04-17	4.278	0.05	[62]
CuO-Au/MWCNTs/GCE	DPV	0.5-1.6	35.84	0.1	[25]
ZIF-67/MWCNT-COOH/Nf/GCE	DPV	0.2-200	14.60	0.01	[63]
VMSF/ITO	DPV	0.5-400	-	0.32	[64]
MoS <sub>2</sub> @NHCSs/GCE	DPV	0.05-20	-	0.013	[20]
Fc-PAA-AuNPs/GCE	AP	30-1064	87.8	7.61	This work

TTO – Indium tin oxide, PANI – Polyaniline, CPE – Carbon paste electrode, rGO/RGO – Reduced graphene oxide, NPC – Nitrogen doped porous carbons, P<sub>-L</sub>-GSH – poly-L-glutathione, ZIF-67 – Zeolitic imidazolate framework – 67, VMSF – Vertically-ordered mesoporous silica-nanochannel films. 3

2

0

-1

-2

3

2

1

0

0

Current / µA

0.0

0.1

50

100

Current / µA

2

for the electrocatalytic determination of 4-AP from 30 to 1064  $\mu$ M with a high sensitivity and low limit of detection (LOD). The sensitivity and LOD were found to be 87.8  $\mu$ A mM<sup>-1</sup> cm<sup>-2</sup> and 7.61  $\mu$ M, respectively. Table 1 compares the obtained parameters such as linear range, LOD and sensitivity of the proposed electrochemical sensor with the recently published 4-AP sensor and it is found to be comparable or better than the previous reports. The improved performances in terms of current response and rapidity of Fc-PAA-AuNPs/GCE could be attributed to the covalently attached Fc as well as encapsulation of AuNPs in the PAA network. The covalent attachment of Fc would have afforded enhanced electrical wiring for better electron transport and the AuNPs encapsulated in the highly branched dendritic network is expected to provide increased surface area and conductivity and thus resulting in better sensing performance.

## 3.4. Selectivity, stability and reproducibility of Fc-PAA-AuNPs/GCE

Stability of the fabricated sensor was evaluated by continuous potential cycling at a scan rate of 50 mV s<sup>-1</sup> in 0.1 M phosphate buffer (pH 7.0). Fig. 5A displays 50 consecutive cyclic voltammograms of 0.1 M phosphate buffer at the Fc-PAA-AuNPs/GCE. Evidently, there were no obvious changes in the peak behaviour with respect to peak current and peak potential in these repeated scans. Furthermore, long

Absence of 4-A

Presence of 4-AF

0.2

0.3

Potential / V vs (Ag/AgCI)

2-AP

150

Time / s

0.4

cate that it is promising sensor for the detection 4-AP. Further, the selectivity is an imperative parameter for the any developed sensors in real time monitoring and other practical utilizations. To

Presence of 4-AP

4

Absence of 4-AP

2

4-AP

Glu

AA

DA

3

No. of Electrode

UA

2-NP

2-AP

CC



250

(A)

50 scans

0.6

(C)

0.5

A C R

200

6

Current / µA

2

0

0.6

0.4

0.2

0.0

Current / µA

1



regular interval of time in the absence and presence of 0.4 mM 4-AP

(Inset to Fig. 5A). These studies revealed that the fabricated Fc-PAA-

AuNPs/GCE retains 97.8% and 93.6% of its initial response in the absence

to be 2.83% in the presence of 4-AP and 1.78% in the absence of 4-AP, in-

dicating the excellent reproducibility among the individually developed

sensors. Further, the repeatability of the developed Fc-PAA-AuNPs/GCE

modified electrode was tested using cyclic voltammetry in the presence of 0.4 mM of 4-AP (5 times) with the same modified electrode (Fig. S5).

The RSD was found to be 2.13%, which suggested good repeatability of

the developed modified electrode. The prolonged storage and cyclic stability along with excellent reproducibility of Fc-PAA-AuNPs/GCE indi-

(B)

5

PA

CP

QR

(D)

#### Table 2

Determination of 4-AP spiked in water samples.

Samples	Spiked (µM)	Found (µM)	Recovery (%)	RSD <sup>a</sup> (%)
Lake water	75	73.08	97.4	2.55
	150	154.61	103.1	2.30
Tap water	100	101.97	102.0	1.85
	200	200.06	100.0	1.20

<sup>a</sup> Three replicates were performed.

evaluate the effect of interference at the Fc-PAA-AuNPs/GCE, amperometry was performed (Fig. 5C) in the presence of 0.1 mM of 4-AP with 10 times excess concentrations of the coexisting species at an operating potential of 0.45 V and their current response is presented in Fig. 5D. Reagents that are commonly found in pharmaceutical industries and environmental samples including glucose (Glu), dopamine (DA), ascorbic acid (AA), uric acid (UA), 2-nitrophenol (2-NP), 2aminophenol (2-AP), catechol (CC), paracetamol (PA), chlorophenol (CP) and quercetin (QR) were chosen for this investigation. It is observed that, except 2-AP and CC, other coexisting species did not show any interference towards 4-AP determination. Even the interference caused by 2-AP (6.5%) and CC (8%) were very minimal and would not cause any appreciable change in the determination of 4-AP. But still, attempts are underway in our laboratory to minimise the interference from 2-AP and CC. These results suggest that Fc-PAA-AuNPs/GCE based sensor has established substantial selectivity for 4-AP detection.

## 3.5. Analysis of real-life samples

The efficacy of a Fc-PAA-AuNP/GCE-based sensor in real time analysis was evaluated by applying the fabricated sensor to the detection of 4-AP spiked in real-life lake water sample and tap water sample (Fig. S6). The water samples were collected from a nearby lake in Vellore and a normal tap water. A standard addition method was followed by spiking known concentrations of 4-AP into the electrochemical cell, which was then quantified by amperometry and the obtained recoveries are presented in Table 2. The recoveries were found to lie between 97.4 and 103.1%, indicating that the fabricated electrochemical sensor has the ability to quantify the concentrations of 4-AP in real-life samples.

## 4. Conclusion

Redox-active ferrocene terminated PAA dendrimers encapsulated with AuNPs have been developed for the electrochemical sensing of 4-AP. Ferrocene carboxaldehyde was covalently anchored to amine terminated PAA dendrimer through Schiff base condensation reaction. Further, AuNPs were encapsulated in the pores of Fc-PAA dendritic network to enhance the conductivity and surface area of the newly developed platform. The fabricated Fc-PAA/GCE exhibited a pair of redox peaks representing the Fc/Fc<sup>+</sup> redox couple and further, encapsulation of AuNPs in Fc-PAA (Fc-PAA-AuNPs/GCE) revealed a 91% increase in peak current compared to that obtained at a Fc-PAA/GCE. Further, the fabricated sensor has shown several advantages such as facile fabrication, good electrocatalytic activity, low detection limit, reliable reproducibility, appreciable sensitivity and good selectivity for determination of 4-AP. The covalent immobilization of Fc on PAA, improved the storage and operational stability and inclusion of AuNPs in the dendritic network enhanced the sensitivity of the developed sensor, which makes it a suitable candidate for the electrochemical determination of 4-AP.

## **Credit Author Statement**

Mari Elancheziyan: Investigation, Methodology, Validation, Writing – original draft. Sellappan Senthilkumar: Conceptualization, Writing – review & editing, Project administration, Supervision.

## **Declaration of Competing Interest**

The authors declare that there is no conflict of interest.

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## Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi. org/10.1016/j.molliq.2020.115131.

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