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Flow Injection Analysis of Ellagic Acid in Cosmetic Skin-Whitening Creams Using a Dendritic Nanostructured Copper-Gold Alloy Plated Screen-Printed Carbon Electrode

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A copper-gold co-deposited alloy modified screen-printed electrode (SPE/{Cu-Au}$_{nano}$) coupled flow injection analysis (FIA) was developed for sensitive and selective detection of ellagic acid (EA) in cosmetic products. SEM characterization of the working electrode revealed nanostructured dendritic morphology for the alloy on the SPE surface. Cyclic voltammetric response of the SPE/{Cu-Au}$_{nano}$ showed well defined and stable oxidation current signal at 0.1 V vs Ag/AgCl in 0.05 molL^{-1} NaOH due to complexation of EA with the {Cu-Au}$_{nano}$ alloy particles. Control experiments with Cu or Au modified SPE have failed to show any such marked oxidation response at 0.1 V vs Ag/AgCl. Interrelated FIA parameters including applied potential, flow rate and the electrolyte concentration were systematically optimized for sensitive and selective detection of EA. Under an optimal condition, SPE/{Cu-Au}$_{nano}$ electrode shows a linear calibration plot for EA detection in the window of 0.2—200 mgL^{-1} with a sensitivity and detection limit value of 0.0657 µA/mgL^{-1} and 4.1 µgL^{-1} respectively. A relative standard deviations of 3.95, 3.36 and 3.60% were obtained for ten consecutive injections (n = 10) of 1, 50 and 100 mgL^{-1} EA, respectively in FIA. Finally, a practical application of the proposed electrode was successfully demonstrated by the quantitative analysis of EA in skin whitening creams with good agreement to that of the labeled values along with appreciable recovery.

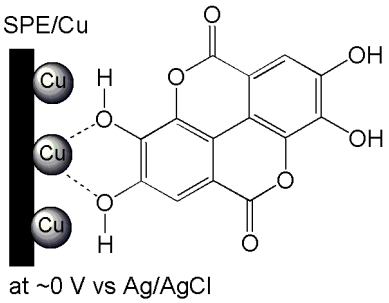
Keywords: copper-gold alloy; dendritic nanoparticles; screen-printed electrode; cosmetic ellagic acid; flow injection analysis

1. INTRODUCTION

Ellagic acid (2,3,7,8-Tetrahydroxy-chromeno[5,4,3-cde]chromene-5,10-dione, EA, Scheme 1) is a polyphenolic phytochemical, found in several fruits and vegetables including blackberries, raspberries, strawberries, cranberries, walnuts, pecans, pomegranates, wolfberry and other plant foods etc [1-5]. It has strong anti-proliferative, antioxidant and anti-aging properties [3-5].

Scheme 1(a).

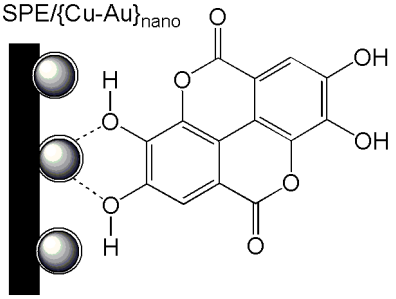
Cu-EA complexation (Unstable)



at ~0 V vs Ag/AgCl

Scheme 1(b).

$\{Cu\text{-}Au\}_{nano}$-EA complexation (stable)



at ~0 V vs Ag/AgCl

Scheme 1. A and B corresponds to the Cu-EA complexation structures on SPE/Cu and SPE/{Cu-Au}nano systems

Recent literature stated that consumption of EA containing fruits can reduce the blood pressure [1]. EA's antioxidant and anti-aging behaviors provide excellent defense against cancer and reduction in the immunity which are the two major health risks among the elderly people [2]. In addition, EA acts as a remarkable depigmentation agent that inhibits the melanin production [3] and hence it has been formulated with many cosmetic skin-whitening formulations in the form of creams and lotions. For instance, a commercial product called Proleva contains the highest concentration of EA available (70% extract) [6]. EA is also available as tablet in the form of general health care product with a prescribed dosage of 1000 mg twice daily [7].

Considering the above vital applications of EA, selective and sensitive detection of the compound in real samples is of significant research interest in analytical chemistry. Various conventional detection methods such as UV-Vis spectrophotometric and high performance liquid chromatographic (HPLC) methods were reported previously [8-13]. Note that the separation based detection techniques require large amounts of high purity organic solvents, long system stabilization time and special off-line sample preparation protocols. UV-Vis technique currently in use as a detector for the separation of the analytes by HPLC or capillary electrophoresis has poor sensitivity. For instance, a detection limit value of 1.5 mgL^{-1} with a recovery error up to ~10 %, was noticed for HPLC-UV diode-array detection at 360 nm for EA [14]. Shui et al updated the procedure and improved the detection limit up to 0.29 mgL^{-1} [15]. Meanwhile, in order to perform sensitive and separation-less detection of EA in ppb level, EA- Cetyl trimethylammonium bromide (CTAB)

surfactant assisted fluorescence [16] and Gemini surfactant-EA coupled resonance light [8] detection methodologies were also reported. In recent times electrochemical techniques are found to be excellent choice for analytical chemists, due to its portability in the instrumentation, on-site measurements and can be extended to low cost disposable type screen-printed electrodes for the assays [17]. Our group, demonstrated a preliminary electro-analytical assay for EA using pre-anodized screen-printed carbon electrode (SPE*, * = pre-anodized) surface at an applied potential of 0.4 V vs Ag/AgCl with 0.025 M NaOH as an eluent by flow injection analysis (FIA) previously [18]. Even though the method has been successfully demonstrated for cosmetic EA real sample analysis, we faced some practical difficulty in preparation of the reproducible SPE*. The SPE* has strong tendency to irreversible adsorption of polyphenolic organic compound (catechol) on the surface, and we have encountered a problem in reproducing the EA's electrochemical behavior by cyclic voltammetry (CV) in our previous work [18,19]. However, no such adsorption complication was encountered during FIA, which may be due to electrolyte-hydrodynamic approach of the system, where the continuous flow of the electrolyte can assist to wash away the adsorbed species from the electrode surface [18]. Note that damage to the carbon based electrode surface is also possible upon extensive pre-anodization [19]. Most importantly, interference from arbutin and green tea, which are the important cosmetic ingredients [20,21] where the arbutin acted as co-skin whitener and green tea as a natural anti-oxidant in the formulation [22], which couldn't be eliminated by the above SPCE*/FIA method [18]. Our continued research interest for the search of new and advanced analytical methodology for EA analysis, lead to fabrication of metal (Cu, Au) plated SPEs, since the preparation of the reproducible metallized SPE is relatively easier than the SPE*. Our group members are successful in preparation of copper based screen-printed electrodes, where copper layer is modified on the SPE by electroplating methodology (SPE as base) or bulk copper-ink printing approaches for electro-analytical applications [23-25]. We have demonstrated selective detection of catechol and its derivatives such as dopamine and pyrogallol on a copper plated SPE, utilizing the selective complexation property of the 1,2 dihydroxy phenol with copper metal and in turn its complexation current as an analytical signal at ~0.1 V vs Ag/AgCl [26]. Since EA has polyphenolic structure, initially we have chosen copper plated screen-printed carbon electrode (designated as SPE/Cu) as working electrode for the EA analysis by CV in this work. Unfortunately, the SPE/Cu was found to be unstable towards EA which may be due to the EA exhibiting strong complexation behavior with the Cu, which in turn plugs-off certain portions of the plated copper metal from electrode to solution. We have solved the above mentioned problem by replacing copper with copper-gold alloy as a plating system on SPE, and successfully demonstrated for sensitive and selective EA analysis using FIA in the latter part of this work.

Bimetallic nanostructured materials show enhanced electrocatalytic performances with high activity, selectivity, and stability compared to their individual components with well-controlled physical property [27]. Few reports were available for preparation of bimetallic Au-Cu modified electrodes by successive or simultaneous co-deposition methods and utilized for determination of amino acid [28], glucose [29] and salicylic acid [30], however, there is no report available till now for the determination of the EA with them. In this manuscript, we are presenting a preparation of beautiful dendritic structured Cu-Au alloy plated SPE (designated as SPE/$\{Cu\text{-}Au\}_{nano}$) as a working electrode

for EA analysis with a detection limit value of 4.1 μg L^{-1} at 0.1 V vs Ag/AgCl applied potential. Finally, couple of cosmetic real samples analyses was successfully demonstrated.

2. MATERIALS AND METHODS

2.1. Reagents and instruments

EA, ascorbic acid (AA), ascorbic acid 2-glucoside (A_2G), magnesium ascorbyl phosphate (MAP), kojic acid (KA), copper sulphate ($CuSO_4$) and arbutin (Sigma-Aldrich, USA), sodium hydroxide and gold atomic absorption standard solution (Showa, Japan) were used as received. All reagents were of analytical reagent grade and prepared with de-ionized water.

Cyclic voltammetric (CV), and amperometric experiments were performed using a CHI800c electrochemical workstation (Austin, TX, USA). Scanning electron microscopy (SEM) coupled with energy-dispersive X-ray spectroscopy (EDX) (Topcon ABT-150S, Japan) and Electron Spectroscopy for Chemical Analysis (ESCA) (ULVAC-PHI, PHI5000, ST Instrument, Netherlands) were used to detect the morphological and elemental properties of Cu-Au alloy system. SPE with an area of 0.196 cm^2 was purchased from Zensor R&D (SE100, Taiwan). The flow injection analysis system consisted of a Cole-Parmer microprocessor pump drive (PM-92E, BAS, Austin, TX, USA), Rheodyne 7125 sample injection valve (20 μL loop) with interconnecting teflon tube and an electrochemical detector. The EA oxidation peak signal was uniformly taken as a quantitative parameter.

2.2 Modified electrodes preparation

The SPE/$\{Cu\text{-}Au\}_{nano}$ was prepared by electrochemical co-deposition of 100 mgL^{-1} each of Au and Cu as $CuSO_4$ dissolved in 1 N H_2SO_4 at an applied potential of -0.6 V vs Ag/AgCl under hydrodynamic condition (300 rpm) for 600 s using screen-printed carbon electrode (SPE) as working electrode (optimal). Control electrodes such as copper and gold alone modified SPE's (SPE/Cu and SPE/Au) were also prepared in method similar to the above electrodeposition conditions except with its respective individual metal solution in the preparation bath.

2.3 Flow Injection Analysis

Flow injection analysis (FIA) was performed by a Rheodyne 7125 sample injection valve (20 μL loop) and equilibrated in 0.05 $molL^{-1}$ NaOH carrier solution at +0.10 or +0.3 V vs Ag/AgCl until the current became constant, which took approximately 5 minutes at room temperature (25±1 ˚C). SPE compatible with FIA instrument was purchased from Zensor R&D, Taichung, Taiwan, and general operation procedures of the instrument as per our previous reported procedures [23,24]. Base-line corrected EA oxidation peak current in FIA was taken as a quantitative parameter.

2.4 Preparation of sample solutions

Cosmetic cream samples; #1 and #2, which contains variable EA contents were purchased from local supermarkets. Labeled EA values in the cosmetic products taken for analyses are 0.4 % and 0.5 % (w/w) respectively for the samples. Other ingredients present in the real sample are as follows: sample #1- β-carotene, glycolic acid, dithiaocatanediol, glycerin, propylene glycol, bacillus ferment, mulberry exact, hyaluronic acid, squalane, nanotech cordyceps sinensis, orchid extract, α-bisabolol, avocado oil, dimethicone, tricetеareth-4 phosphate, methylparaben, propylparaben, acrylate/C10-30 alkyl acrylate crosspolymer, deionized water and fragrance and sample #2- octyl methoxycinnamate, titanium dioxide, avocado oil, α-Bisabolol, mulberry extract, nano-tech ganoderma lucidum, orchid extract, hyaluronic acid, C12-15 alkyl benzoate, cetyl dimethicone, xanthan gum, methylparaben, propylparaben, deionized water and fragrance.

Test solutions of the commercial samples were prepared by dissolving 0.2413 g (sample #1) and 0.2204 g (sample #2) in 100 ml of supporting electrolyte and mixed through ultrasonication for 5 min. The mixture solutions were then filtered through a 0.22 µm filter paper to remove the suspended particles. Finally, the filtered solutions were diluted suitably to the concentration required for the FIA.

3. RESULTS AND DISCUSSION

3.1 Physicochemical characterization

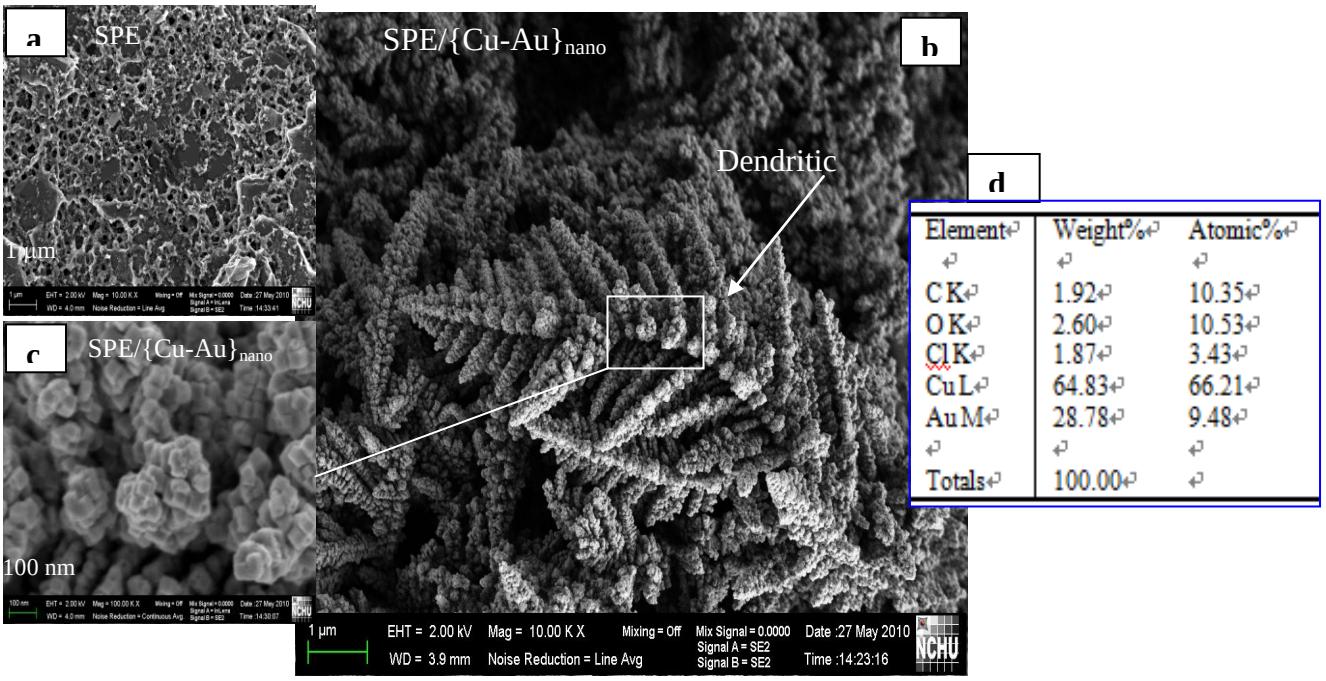


Figure 1. SEM pictures of (A) bare SPE (B and C) SPE/{Cu-Au}$_{nano}$ with dendritic structure and at magnifications and (D) elemental analysis of SPE/{Cu-Au}$_{nano}$ by energy dispersive X-ray analysis.

In our previous works, we did several SEM characterizations for bare SPE and copper modified SPE (SPE/Cu) systems where the 100 mgL^{-1} of Cu was electrochemically deposited in 0.1 $molL^{-1}$ HNO_3 medium.

Highly porous and agglomerated type structure-morphologies were noticed for the SPE/Cu [25]. Figure 1a-c shows the SEM pictures of SPE/$\{Cu\text{-}Au\}_{nano}$ at different magnifications, in this work. Interestingly, a clear dendritic structure with a central trunk and multiple branches extending symmetrically in three directions are noticed. The branches of dendritic structure are measured to be approximately 1 μm in length with 100 nm particles within that. In literature, few electrochemical and hydrothermal deposition methodologies were reported for the dendritic Cu-metal preparations [31-36]. First time in this work, we are reporting the formation of a dendritic structure of Cu-Au alloy on a screen-printed carbon electrode support. Presence of Cu and Au within the $\{Cu\text{-}Au\}_{nano}$ have been confirmed by energy dispersive X-ray and X-ray photoelectron spectroscopy as shown in the Online Resource 1 characterizations. Calculated [Cu]/[Au] atomic ratio value with the SPE/$\{Cu\text{-}Au\}_{nano}$ electrode is 6.98 (by EDX, Fig. 1d). Exact mechanistic details for the formation of the dendritic $\{Cu\text{-}Au\}_{nano}$ structure is unknown for us now. It is expected that highly porous nature of the SPE and choosing of H_2SO_4 as a bath condition, are the influencing factors for the dendritic morphological structure. The SPE/$\{Cu\text{-}Au\}_{nano}$ was found to be quite suitable for stable analysis of EA.

3.2 Cyclic voltammetry

Figure 2a-c illustrate comparative CV responses of copper modified SPE (SPE/Cu) (A), gold modified SPE (SPE/Au) (B) and the Cu-Au alloy co-deposited SPE (SPE/$\{Cu\text{-}Au\}_{nano}$) (C) without and with 50 mgL^{-1} of EA in 0.05 M NaOH.

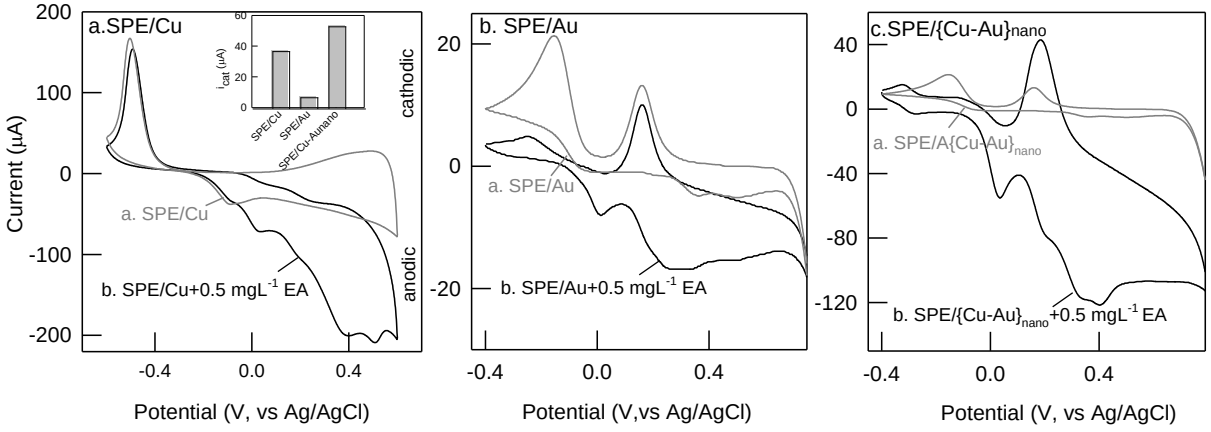


Figure 2. CV responses of (A) SPE/Cu (B) SPE/Au and (C) SPE/$\{Cu\text{-}Au\}_{nano}$ at v=50 mV s^{-1} in the potential window of +0.6 V to -0.6 V vs. Ag/AgCl in 0.05 $molL^{-1}$ NaOH.

As can be seen in the figure 2a and b, in presence of EA, decrease in the anodic peak current (negative shift) and very feeble increase the current responses at ~ 0 V vs Ag/AgCl with respect to its corresponding blank responses for the respective working electrodes were observed; while in the case of alloy system, SPE/{Cu-Au}$_{nano}$, marked enhancement in the anodic peak current with the EA, was noticed. Earlier, two different types of current signals, namely complexation (reversible) and electro-catalytic oxidation (irreversible) at -0.2 to +0.2 V and > 0.2 V vs Ag/AgCl with 1,2 dihydroxy and amino acids have been reported [19,25,26]. In the complexation approach, 1,2 dihydroxy group from the analyte can form weak co-ordination bond with copper active site [25,26], whereas in the electrocatalytic approach, the 1,2 dihydroxy group get oxidized as respective ortho-quinone compound [19,25,26]. Based on the above information and since EA has 1,2, dihydroxy structure, the current signal at 0 V vs Ag/AgCl in this work can be taken as a measure of Cu-EA complexation current (Scheme 1a&b). Hence, the reason for the negative shift in the current signal of SPE/Cu electrode at 0 V vs Ag/AgCl with EA (Fig. 2b, Scheme 1a) might be due to instability of the Cu-EA complex. The Cu-EA complexation mechanism may plug-off the copper atom from the electrode surface to solution phase. On the other hand the SPE/{Cu-Au}$_{nano}$ electrode as displayed in Fig. 2c, showed positive increase in the current signal at 0 V, which indicates no such instability problem mentioned early, occurred with the present system (Scheme 1b). Considering the cost, stability, reproducibility and low working potential the SPE/{Cu-Au}$_{nano}$ was chosen as optimal working electrode for further EA analysis by FIA.

3.3. Flow injection analysis

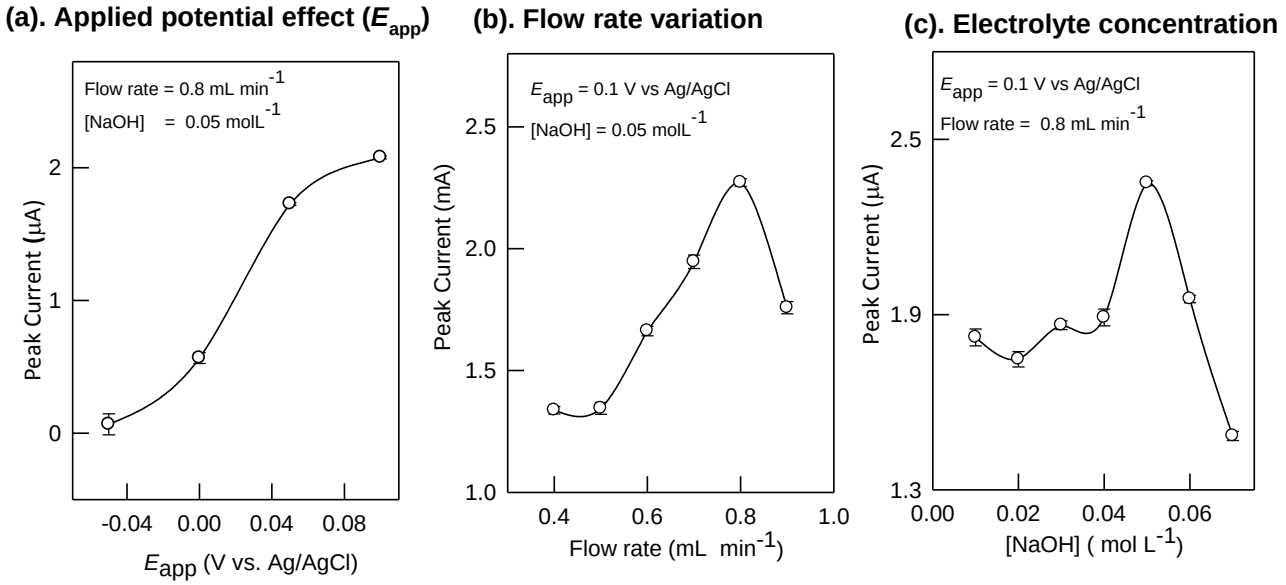


Figure 3. Optimization of FIA parameters for the detection of 50 mgL^{-1} ellagic acid with SPE/{Cu-Au}$_{nano}$ working electrode. Effects of (A) applied potential (B) flow rate and (C) NaOH concentration

Interrelated hydrodynamic parameters such as applied potential (E_{app}), flow rate and electrolyte concentration were systematically optimized as shown in Fig. 3.

By keeping the flow rate as 0.8 mL min^{-1} and concentration of NaOH ([NaOH]) 0.05 $molL^{-1}$ constant, E_{app} was varied from -0.05 to 0.1 V vs Ag/AgCl, for the detection of 50 mgL^{-1} of EA in the FIA. The FIA currents increased with increase in E_{app} and saturates at 0.1 V. The observation of the saturation potential at 0.1 V vs Ag/AgCl with the working electrode, SPE/{Cu-Au}$_{nano}$ indicates the detection current mechanism through complexation approach as mentioned in the previous section. Effect of flow rate variation in the window of 0.4 - 0.9 mL min^{-1} was studied as shown in Fig. 3c. A systematic increase of up to 0.8 mL min^{-1} and a decreased FIA response was noticed. Possible reason for the reduction in the peak current is due to the limitation in the electrode complexation kinetics up to 0.8 mL min^{-1}. Finally, effect of NaOH concentration (0.01 -0.07 $molL^{-1}$) for the detection of EA at E_{app} = 0.1 V and at flow rate of 0.8 mL min^{-1} was tested as shown in Fig. 3c. A peak like response, with minimum peak current at 0.04 $molL^{-1}$ and a maximum response at 0.05 $molL^{-1}$ of NaOH, was obtained. The peak maximum may be due to the maximum existence of Cu(I)/Cu redox species, which is the key form of active site that can bind with the EA and in turn results to complexation current signals.

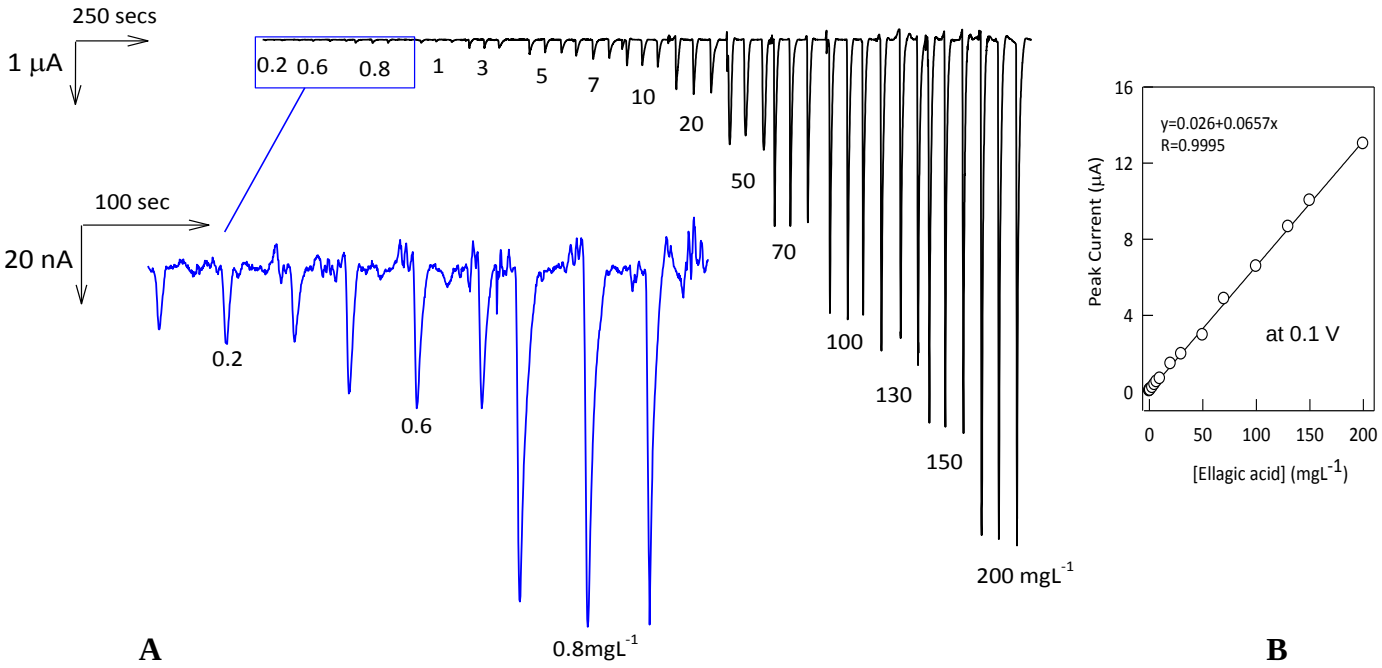


Figure 4. (A) FIA response of SPE/{Cu-Au}$_{nano}$ at different ellagic acid concentrations under an optimal condition and (B) Plot of peak current versus [EA] from the figure 4A. Flow rate = 0.8 mL min^{-1}; E_{app} = 0.1 V vs Ag/AgCl and [NaOH] = 0.05 $molL^{-1}$

Fig. 4a shows the FIA peak current responses for increasing EA concentrations varying from 0.2—200 mgL^{-1} under the optimized FIA condition. A linear regression coefficient of 0.999 for detecting EA was obtained (linear equation y=0.026+0.0657x) as seen in Fig. 4b with a calculated detection limit of 4.1 μgL^{-1} (S/N=3). Ten repeated EA detection experiments with 1, 50 and 100 mgL^{-1} concentrations resulted in relative standard deviation (RSD) values of 3.95, 3.36 and 3.60 % respectively (Fig. 5).

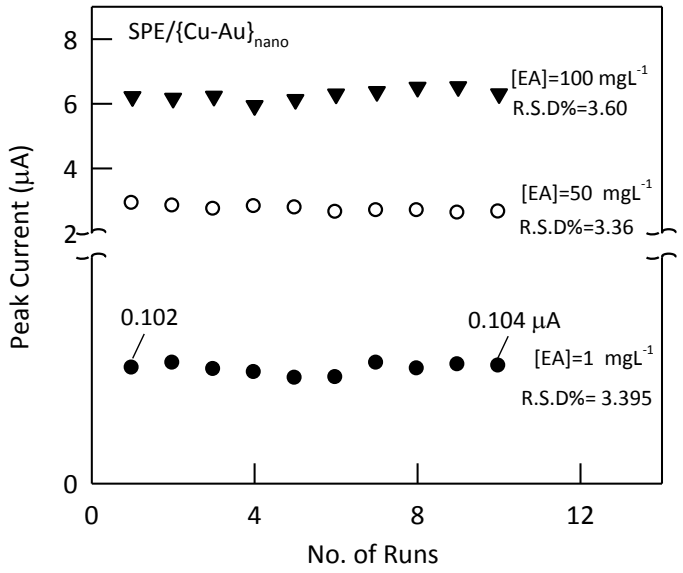


Figure 5. Plot of no. of runs vs FIA's peak current for the detections of three different concentrations of EA using APE/{Cu-Au}$_{nano}$ at 0.1 V vs Ag/AgCl. Other FIA conditions are as in the Fig. 4

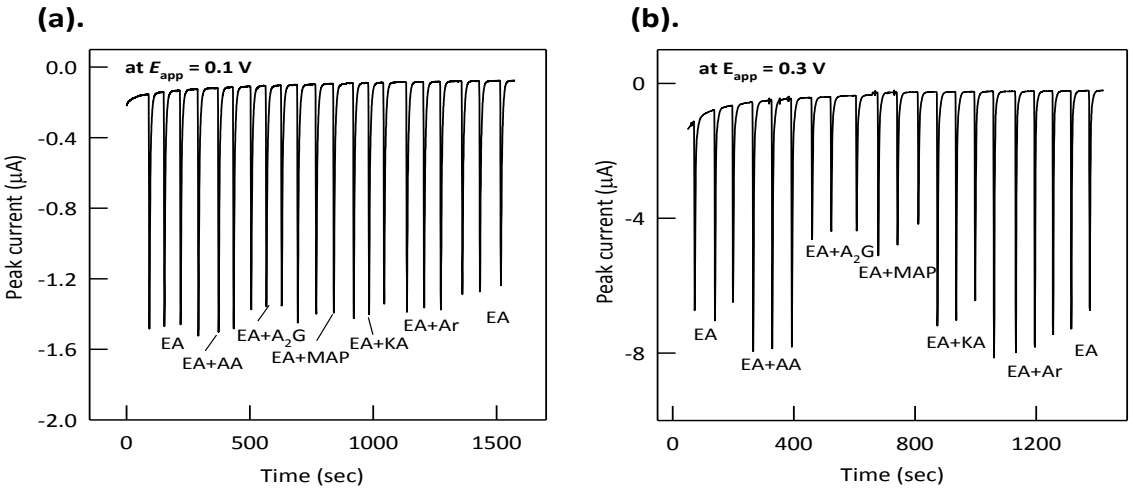


Figure 6. Effect of interference on the detection of 50 mgL^{-1} each of EA and co-existing cosmetic ingredients at two different applied potentials; 0.1 and 0.3 V vs Ag/AgCl by FIA using SPE/{Cu-Au}$_{nano}$ working electrode. Other FIA conditions are as in the Fig. 4

The repeated EA detection experiments with 50 mgL^{-1} concentrations of Au and Cu to form SPE/Au and SPE/Cu respectively resulted in RSD values of 3.34% and 10.91%, but the response current of SPE/Au was 10 times less than the SPE/$\{Cu\text{-}Au\}_{nano}$ (reason for the reduction in the current may be the absence of complexation mechanism for Au with that of EA). The detection limit obtained in the current work is lesser than the earlier reports using the chromatographic techniques and the spectrometry technique which are in mgL^{-1} scale for the EA containing solution [10,12,13]. In addition, the detection limit (4.1 μgL^{-1}) value is about three times lower than that of our previous preanodized screen printed carbon based working electrode (4.1 μgL^{-1}) [18].

Table 1. Comparison of analytical parameters for the electrochemical FIA of EA by two different methods.

Parameters	Pre-anodized electrode [18]	SPE/$\{Cu\text{-}Au\}_{nano}$ [This work]
1. Applied potential	0.4 V	0.1 V
2. Flow rate	0.3 mL min^{-1}	0.8 mL min^{-1}
3. Supporting electrolyte	0.025 $molL^{-1}$ NaOH	0.05 $molL^{-1}$ NaOH
4. Intra assay (R.S.D.%)	1mgL^{-1} : 4.37% (n=10) 50 mgL^{-1} : 3.90% (n=10) 20 mgL^{-1} : 4.00% (n=30) 20 mgL^{-1} : 7.23% (n=40)	1 mgL^{-1} :3.95% (n=10) 50 mgL^{-1} :3.36% (n=10) 100 mgL^{-1}:3.60% (n=10)
5. Inter assay (R.S.D.%)	4.70% (n=5)	2.99% (n=5)
6. Linear range	0.1—50 mgL^{-1}	0.2—200 mgL^{-1}
7. Selectivity (Kojic Acid, Arbutin, A_2G, MAP and green tea)	Arbutin and green tea are serious interferents	None
8. Detection limit	12 μgL^{-1}	4.1 μgL^{-1}
9. Regression coefficient (R^2)	0.998	0.9995
10. Linear function	y=0.0177x + 0.0218	y=0.0657x+0.0260

Fig. 6 shows the interference study of 50 mgL^{-1} each of EA, AA, A_2G, MAP, KA and arbutin at two different applied potentials namely 0.3 and 0.1 V vs Ag/AgCl where electrocatalytic and complexation mechanisms are occurring respectively. As can be seen in the Fig. 6a at 0.1 V applied potential no interference was noticed with the compounds tested, whereas from Fig. 6b we could find the AA, A_2G, KA, and MAP all showed serious interferences with the EA determination, when the detection potential was fixed at 0.3 V, which is similar to the case of SPE* working electrode [18]. Thus, it is clear that present working electrode allows detection of EA at less operation potential without any interference from other co-existing cosmetic ingredients. Table 1 provides a comparison of 10 different analytical parameters for the electrochemical FIA sensing of EA using present SPE/$\{Cu\text{-}Au\}_{nano}$ and our previous pre-anodized screen-printed carbon based electrode [18]. It is clear that the present system is superior in the detection parameters.

3.4 Analytical applications

The analytical application of SPE/{Cu-Au}$_{nano}$ sensor was tested in detecting EA concentration in skin whitening creams (#1 and #2). Analytical parameters for the analysis of the cosmetic samples were given in Table 2. Original calculated values are 9.1 and 10.4 mgL^{-1} respectively for the samples. After correcting the dilution factor, the values are 0.38 % and 0.51%. Note that the labeled EA values in the creams were 0.40 % and 0.50%, which is closer to the electrochemical analysis data. Present method provides good recovery values in the range from 102.36 to 104.10% and 97.90 to 103.19% respectively. These results suggest that the SPE/{Cu-Au}$_{nano}$ electrode coupled with FIA is a reliable detection method for EA in commercial cosmetic products without any separation technique that is necessary to be utilized with the chromatography technique.

Table 2. Real samples analysis of EA in cosmetic formulations using SPE/{Cu-Au}$_{nano}$ electrode by FIA.

Real Sample[a]	Original detected value (mgL^{-1})	Spike (mgL^{-1})	Detected value after spike (mgL^{-1})	Recovery (%)
# 1	9.05±0.088	10	19.45±0.65	103.89±6.46%
		20	29.31±0.70	101.32±3.51
		30	39.19±0.27	100.46%±0.91
# 2	10.37±0.19	10	20.63±0.42	102.57±4.22%
		20	30.64±1.19	101.37±5.96
		30	40.18±0.33	99.36%±1.10

a. Dilution factors for the samples #1= 414 and #2= 490.

4. CONCLUSIONS

New copper-gold alloy nanoparticles modified SPE (SPE/{Cu-Au}$_{nano}$) with dendritic structure was demonstrated for a low potential detection of ellagic acid (EA) without any separation technique by flow injection analysis. The Cu-Au alloy modified electrode showed a specific complexation current with EA at 0.1 V, which was found to be stable compared to that of the Cu or Au modified SPE that resulted in unstable Cu-EA or Au-EA complexation current. The SPE/{Cu-Au}$_{nano}$ exhibited three times higher sensitivity and lower detection limit respectively than that of preanodized SPE (SPE*) working electrode reported previously at higher applied potential (0.4 V vs Ag/AgCl) for EA detection. Further, the FIA analysis showed highly selective detection of EA at 0.1 V vs Ag/AgCl through complexation mechanism without any interference from other co-existing cosmetic ingredients such as ascorbic acid, ascorbic acid-2-glucoside, magnesium ascorbyl phosphate, kojic acid and arbutin. Finally, the fabricated SPE/{Cu-Au}$_{nano}$ electrode was successfully utilized for the detection of EA from different cosmetic real samples with good agreement to that of the labeled and appreciable

recovery values. The proposed SPE/{Cu-Au}$_{nano}$ electrode can be extendable for further EA detection from fruits and pharmaceutical samples apart from the cosmetic products.

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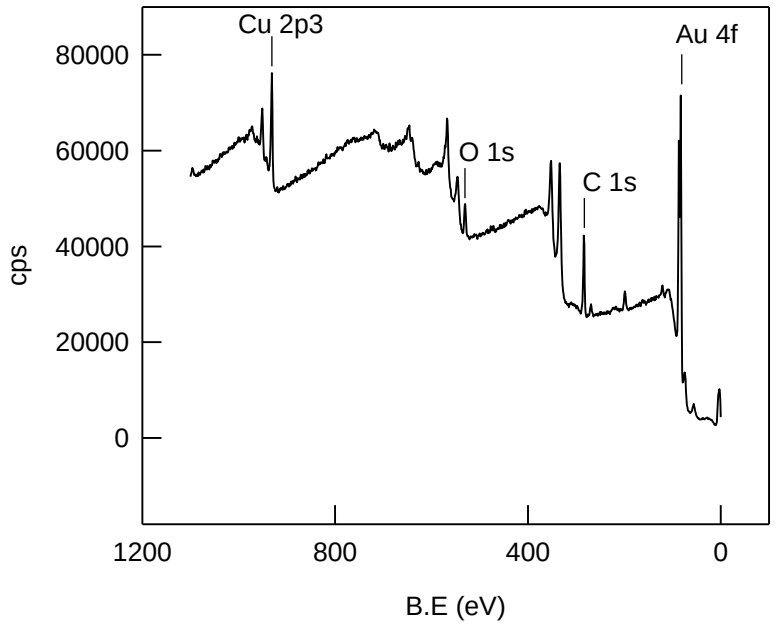
Supplementary Data:

Flow injection analysis of ellagic acid in cosmetic skin-whitening creams using a dendritic nanostructured copper-gold alloy plated screen-printed carbon electrode



ESM 1. X-ray photoelectron spectroscopy survey scan of SPE/{Cu-Au}$_{nano}$ electrode.

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