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Synthesis of Organoclay and its Applications in Electrochemical Detection of Paracetamol

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ABSTRACT

The aim of this work is to synthesize by cationic exchange reaction organoclays by exfoliation after modification of clay with cetyltrimethylammonium ions (CTA^+) and their use as an electrode material for the detection of Paracetamol. The physicochemical properties of modified and unmodified clay mineral are first analyzed by particle size analysis, XRD, BET, FTIR, thermal analysis (TGA and DTA), ^{29}Si NMR, ^{27}Al NMR and TEM. The results showed that the surface of clay successfully reacted with cetyltrimethylammonium bromide (CTAB) and this significantly enhanced electrochemical reactivity. This electrochemical sensor exhibited excellent analytical performance for Paracetamol detection at physiological pH with detection limit of 23 µM, linear range of 10-80 µM (R^2=0.9825).

Keywords: Cetyltrimethylammonium ions, Electrochemical sensor, Organoclays

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INTRODUCTION

Modification of clay minerals surface has received attention because it allows the creation of new materials and new applications. The synthesis of organoclays has opened new perspectives with those composites that have interesting and diverse applications in materials science. Modified clays have varied applications such as in the agro-food industries, in the cosmetics, water and air, control agents, etc.

In electrocatalysis, the modified clays are used as catalytic support and also as modifying electrodes for the detection of certain pharmaceutical compounds thus opening the way to the development of the new types of electrochemical sensors. Furthermore, its applications in pharmacy, adsorbents, and ion exchangers are also reported in the literature [1,2]. These last applications are particularly useful for the development of electrochemical sensors [3,4].

In recent years there has been considerable progress in the field of electrodes modified by organoclays [5-10]. The organoclays can be synthesized by several routes including the postsynthesis grafting of functionalized organosilane onto the clay surface [11-14], the one-step preparation by the sol-gel process [15,16] and the intercalation of quaternary ammonium-based organic cations in the interlayer region of the clay [17-20]. The new chemical properties exhibited by the electrode surfaces when coated by the clays are indicative of the catalytic power of the modified clays. In the latter case (intercalation of quaternary ammonium cations), the novel properties are exploited for applications such as ion exchange coatings, or (electro)-chemical sensors [21,22].

The previous work has been based more on the formation of organoclays by reaction with silane groups [9]. For example, the treatment of montmorillonite with trichloro and trialkoxysilanes has been reported, resulting in organic loadings of up to 25 wt %, with the intended application of hazardous material remediation [23]. No increase in the clay's basal spacing has been observed, suggesting that the organic compounds are bound to the outer clay edges. The trialkoxysilanes apparently linked the clay sheets together, making them non dispersible, while monoalkoxysilanetreated clays are dispersible in water. In another report, protonated amino alkoxysilanes and end-terminated alkoxysilanes are used to create clay monoliths by cross-linking clay particles together with their edges [24]. Also, the surface of magadiite, a layered sodium polysilicate containing silanol groups, is reacted with different lengths of aliphatic alcohols and is able to be cast into transparent nanocomposite films [25]. Surfactant-treated montmorillonite was further modified with a trialkoxysilane-terminated epoxy to improve clay compatibility and properties of poly(L-lactide) and poly(L-lactide)/poly(butylene succinate) blends [26-28].

Quaternary ammonium ions have been frequently used to prepare organoclays thus changing the hydrophilic properties of clays [29]. Falaras and Petridis have also reported the preparation of Clay-Modified Electrodes (CME) by the coating of cetyltrimethylammonium bromide, which are successfully used for the incorporation and binding of anionic species [30]. Recently, Heidarimoghadam et al. [31] reported the successful application of graphene oxide in the presence of cetyltrimethylammonium bromide to the determination of testosterone in biological fluids and drug. In the case of smectites, the adsorption of neutral molecules is due to various interactions. The presence of the hydroxyl functions on the surface of these clays therefore allows the grafting reactions [32]. The organoclays are generally prepared in solutions by cation exchange reaction or by solid-state reaction.

Paracetamol is a widely used antipyretic and analgesic drug [33]. It is an effective and safe analgesic agent used worldwide for the relief of mild to moderate pain associated with headaches, backaches, arthritis and post-operative pains. It is also used for reduction of fevers of bacterial or viral origin [34]. Paracetamol has no toxic effect on human health, but its misuse can cause adverse effects, excessive doses can cause skin rashes, liver disorders, nephrotoxicity and inflammation of pancreases [35]. Presence of Paracetamol has been extensively studied in human plasma and urine, but is also being studied in the aquatic environment with levels of up to 10 μg/L in natural water as reported by Kolpin [36]. Therefore the development of rapid and simple methods is a clinical requirement. Several techniques, namely liquid chromatography [37,38], electrophoresis [39,40], spectrophotometry [41] and electrochemical methods [42-44], are employed for the determination of drugs such as Paracetamol in pharmaceutical preparations. However, spectrophotometric and chromatographic methods usually require sample pretreatment (e.g., extraction, complex formation) that is laborious and time consuming. To overcome these defects, electrochemical techniques have received more attention in detection of Paracetamol due to the presence of electroactive groups of hydroxyl and acetamid in Paracetamol molecule. Conventional electrodes do not give a satisfactory response, which is why the development of new electrodes modified with organoclay composites emerged, opening the way to the promotion of electrochemical sensors [45-47].

In this work, the organoclays were synthesized by exchanged cationic reaction with cetyltrimethylammonium bromide. The characterization techniques such as analysis of particle size, XRD, BET, FTIR, TGA/DTA, ^{29} Si and ^{27} Al NMR and TEM were used to explain the physical and chemical properties of composites. The film layer of the organoclays was used to modify the surface of the glassy carbon electrode. The electrochemical behavior of the modified electrode was analyzed and its response to the electrochemical detection of Paracetamol was evaluated.

MATERIALS AND METHODS

Materials

Paracetamol was purchased from Sigma-Aldrich. N-Cetyl-N,N,N-trimethyl ammonium bromide ($C_{19}H_{42}BrN$) Assay was obtained from Himedia Laboratories Pvt. Ltd, India. Sodium chloride (NaCl) was procured from Merck specialties Privates Limited Mumbai, India (≥ 99.0%). Potassium phosphate monobasic (99%), Sodium hydroxide and Hydrochloric acid were purchased from Sisco Research Laboratories Pvt. Ltd, India.

The soil samples were taken in a dry river bed situated between the center and Makabaye quarter of Maroua town (Cameroon) in the far-north region of Cameroon. The system coordinates of this area is 10°34.393N and 014°16.895 E. The chemical and mineralogical compositions of the clay were studied elsewhere [48]. The clay was purified according to the protocol described in the literature [49]. After these treatments, the clay slurry was centrifuged; settled clay was washed with distilled water (2-3 times) and dried at 100-110°C. Dried clay was ground using a mortar and pestle, and sieved to collect particles with less than 2 μm fraction. The purified clay is designated as Clay Ma. Its cation exchange capacity (CEC), 63 meq/100 g, was determined by NH4+ method as described in the literature [50].

Modification of Clay

Preparation of Organoclays

The preparation of organoclay complex was obtained by very slow addition of 500 mL of the corresponding CTAB solution at 0.5 CEC (initially homogenized by stirring for 1 h). At the end of this addition, which is under rapid and permanent agitation, the resulting mixture was allowed to stand for 24 h at room temperature to promote insertion of the cationic surfactant. After 24 h, the organoclay complex obtained was separated by centrifugation at 7000 rpm for 30 min. The pellet obtained was washed several times with deionized water until the disappearance of excess surfactant (no foam). After drying at 40°C in an oven, the material obtained was ground in a porcelain mortar. The solutions were decanted and suction filtered. The precipitate was washed with 100 mL of deionized water, stirred for 1 h, and suction filtered again. Washing and filtration were repeated up to 10 times to remove any residual CTAB. After each wash cycle the waste solutions were checked for Br ions (free CTAB molecules) by adding some drops of 0.5 M $AgNO_3$. After the last filtration, the filtrate was dried in an oven at 80°C overnight, crushed to a fine powder in a mortar, and stored in a sealed container for further studies. This organoclay sample was labeled as CTAMa.

Preparation of the working electrode

The glassy carbon electrodes (GCE) were previously polished with alumina slurries of different size (1, then 0.05 µm) on billiard cloth. They were then placed in an acetone solution and properly cleaned in a sonicator for 10 min to eliminate any remaining alumina particles. The thin clay mineral film working electrode was prepared by "drop coating" 10 µl of the aqueous dispersion of CTAMa on the active surface (3 mm in diameter) of the GCE. The clay mineral modified electrodes, denoted GCE/CTAMa, were stored at room temperature for about 6 h to ensure their complete drying before use.

Characterization techniques

Analysis of the particle size of sodium saturated clay and modified clay in aqueous solution was carried out at room temperature using Nanotrac equipped with Microtrac FLEX 10.5.2 software for data processing. The particle size distribution curves were obtained with organoclays samples prepared by the wet chemical method. For all the measurements, 0.0015 g each sample was sonicated in 20 ml millipore water about 10 minutes beforethe sample was subjected to particle size analysis.

The X-ray diffraction (XRD) patterns of the starting clay mineral and organoclays were recorded at room temperature using a Panalytical (Model: PW3040/60 X'pert PRO, Netherlands) equipped with a Cu anode (kα radiation, λ=1.54056 Å) and using a voltage of 40 kV and a current of 30 mA.

Specific surface areas and pore volumes were evaluated by the B.E.T. method from N_2 adsorption–desorption experiments performed at 77.35 K in the relative pressure range from 10^{-5} to 0.99, using an Autosorb iQ Station 2 (model Quantachrome Instruments). Prior to each measurement,the sample was degassed at 105°C under vacuum for 16 h.

IR spectra were scanned using KBr pellets in the region 4000 to 400 cm^{-1} with a resolution of 0.125 cm^{-1}, on a spectrometer (model Tensor 27, Brucker Optik GmbH, Germany) equipped with the Opus TM software which provides an intuitive interface and facilitates the analysis of scans.

Differential thermal analysis (DTA) and thermogravimetric analysis (TGA) were recorded using a SDT Q600 V8.3 Build 101 simultaneous DSC-TGA instrument. Approximately 5.2600 mg of clay material was placed on the microbalance of the STA analyzer, which was purged with nitrogen gas. The measurements were recorded from room temperature to 1100°C under nitrogen flow (100 ml min^{-1}) with a heating rate of 20°C/min. Data analysis was performed using Universal V4.7A TA software package.

Solid state NMR spectra were recorded using a BRUKER AVANCE DMX 400 MHz spectrometer operating at the frequencies of 104.229, 105.8 MHz for $^{27}Al(I=5/2)$,^{23}Na (I=3/2), quadrupolar nuclei and 79.460 MHz for ^{29}Si (I=1/2), respectively.

Transmission electron micrographs of the functionalized clays were taken in FEI, the Netherlands (Model: Tecnai20) transmission electron microscope with an accelerating voltage of 200 keV. Ultrathin sections of bulk specimens (~100 nm thickness) were obtained at -85°C using an ultra-microtome fitted with a diamond knife.

Analytical measurements

Cyclic voltammetry (CV) on all prepared GCE/CTAMa as well as on an unmodified GCE was performed on CHI 6084C electrochemical analyzer (USA). A three-electrode measurement cell equipped with a GCE/CTAMa (working), an Ag/AgCl (saturated KCl) reference electrode and a Pt wire auxiliary electrode was used for all measurements. Phosphate Buffer Solution 0.1M (pH=7.4) was used as electrolyte solution.

RESULTS AND DISCUSSION

Structural characterization of clays

The X-ray diffraction of the purified clay (**Figure 1**) shows the presence of several characteristic peaks of each mineral. The natural clay of Makabaye is thus made up of illites, chlorites, quartz, kaolinite, Feldspar (**Table 1**). After modifying the clay with the surfactant (CTAB), the intensities of the peaks decreased, which could probably be due to the exfoliation of the interlayer layers. The approach of the intercalation is no more observable in this study because of the small amount of surfactant used which has been proven in previous work [51].

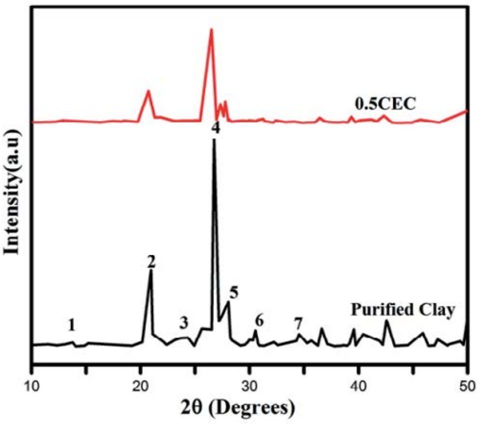

Figure 1: XRD patterns of purified clay and organoclay.

Table 1: Reflections of purified clay

Peak number	2θ (°)	d-spacing (Å)	Minerals
1	9.129	9.6790	Illite (001)
2	21.013	4.2243	Quartz (100)
3	25.635	3.4722	Chlorite (004)
4	26.955	3.3050	Quartz (101)/ Illite (003)
5	27.616	3.2275	Kaolinite (002)/ Feldspar
6	30.422	2.9359	Illite
7	34.422	2.5941	Goethite

Porosity measurements

The adsorption-desorption isotherms for the organoclays are reported in **Figure 2**. They are typical of clay materials containing smectites [52]. The nitrogen adsorption-desorption isotherms for Organoclay are shown in **Figure 2**; the isotherms are type IV according to the I.U.P.A.C. classification and have an H1 hysteresis loop which is representative of mesopores [53]. The low value of the specific surface area (**Table 2**) is due to the presence of the organic molecules at the clay surface thus preventing the adsorption of nitrogen.

Characterization of Purified Clay and Organoclay by FT-IR spectroscopy

The FTIR spectra of the purified clay mineral and of organoclay are presented in **Figure 3**. They were found to coincide well with those reported in the literature for similar materials [54]. The two intense bands at 1025.15 and 1033.03 cm^{-1} were attributed to the Si–O stretching vibrations. The additional bands at 3695.54 and 3445.21 cm^{-1} due to hydroxyl stretching vibrations were attributed to free and interlayer water molecules, and 1638.44 cm^{-1} was related to the (H–O–H) bending vibrations of the water molecules adsorbed on the clay mineral. Other weak bands at 916.89 and 777.89 cm^{-1} were assigned to the bending vibrations of Al–Al–OH and Al–Mg–OH hydroxyl groups on the edges of the clay mineral layers [55]. The Si–O–Al **(octahedral Al)** and Si–O–Si bending vibrations were detected at 534.95 and 466.67 cm^{-1}. After reacting with the CTAB solution, the organoclay exhibited new bands in the 2800-2950 cm^{-1} region, corresponding to antisymmetric and symmetric stretching of CH_2 groups at 2912.45 and 2847 cm^{-1}, respectively [56]. The characteristic band of the C-N stretching vibration (ν CN) of CTAB was present at 1471 cm^{-1} [57].

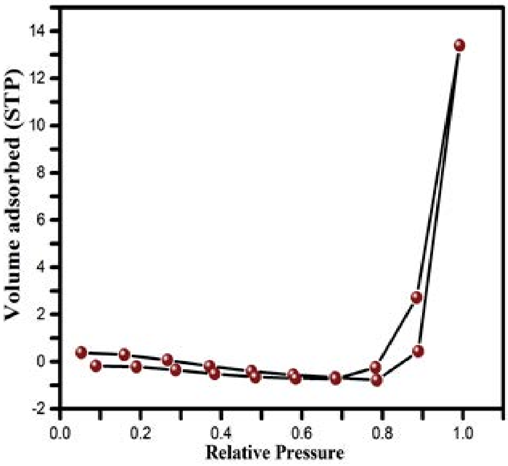

Figure 2: Nitrogen adsorption and desorption isotherms at 77K for Organoclay.

Table 2: Textural characterization of clays

Sample	Pore radius (Å)	Specific surface area (m²/g)	Pore volume (cm³/g)
CTAMa	69.895	2.658	0.007

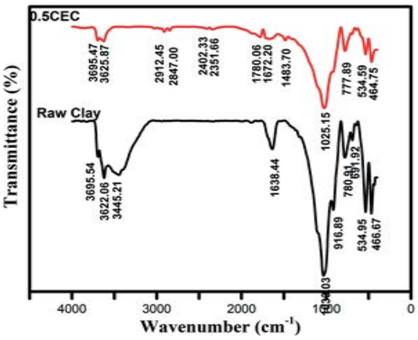

Figure 3: The FTIR transmission spectra of purified clay and organoclay.

Thermal analysis

TGA and DTA thermograms of Organoclays are shown in **Figure 4**. The TGA curves indicate that there are three major steps during decomposition of the surfactant [58]. The corresponding TGA-DTA thermograms in the range of 25 to 1000°C revealed the loss of carbon from the organoclay in the 200-555°C region as indicated by three discrete "peaks" with mass-loss maxima at 203.68, 273.68, and 551.54°C. All these results are confirmed in DTA thermograms. The lowest temperature peak at 92.56°C is due to water loss from the surface (dehydration) and interlayers. The second at 315.68°C is due to degradation of CTAB in interlayers of clay, while the highest temperature peak at 705.54°C is due to dehydroxylation of the clay layers [59].

^{27}Al and ^{29}Si NMR Analysis

^{27}Al and ^{29}Si MAS NMR provides information about the inorganic framework. ^{27}Al MASNMR spectra of Organoclay and Purified Clay samples are presented in **Figure 5.** In Purified Clay sample, one resonance line of the ^{27}Al nuclei is observed at 66.64 ppm and one resonance line is observed at 55.25 ppm for Organoclay. This is related to tetrahedrally coordinated aluminum (IV) ions which occur in the octahedral layers of the clay. The interaction of tetrahedral layers with water molecules in the clay galleries was due to the generation of IV-coordinated aluminum ions in octahedrons [60,61].

The ^{29}Si MAS NMR spectra of purified clay (**Figure 6**) contained a single, symmetric ^{29}Si resonance at -86.27 ppm [62], corresponding to the unique Si environment in the sample, consisting of Si atoms surrounded by three SiO_4 tetrahedra-Q_3(0Al) according to Liebau nomenclature [63]. The position of this signal does not change much with the treatment (-85.13 ppm), although an increase in the FWHM value was observed (**Figure 6**), indicating a progressive disorder in the local environment of the Si nuclei of the remnant montmorillonite particle [64-66].

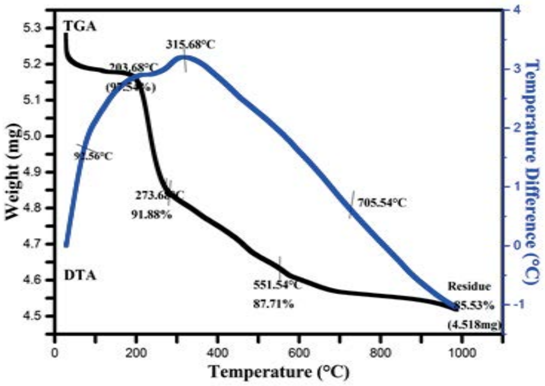

Figure 4: Thermal analysis data (TGA and DTA) of Organoclay.

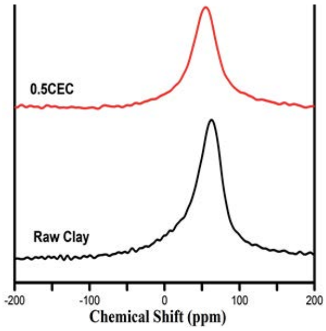

Figure 5: ^{27}Al NMR Solidstate spectra of purified Makabayeclay and Organoclay.

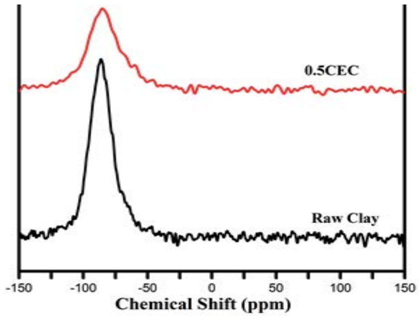

Figure 6: ^{29}Si NMR Solidstate spectra of purified clay and Organoclay.

Transmission Electronic Microscopy imaging of Organoclay morphology

TEM images of **Figures 7** and **8** shows the morphology of the Purified and Organoclay samples and seem identical. The presence of the interlayer silicates is observable with particles of hexagonal shape and dimensions of the order of 100 nanometers (**Figures 7 and 8**). The Organoclay particles have a bimodal distribution. The selected area electron diffraction shows the single crystallite diffraction for non-modified clay (**Figure 7a**) and the polycrystallite diffraction for Organoclays (**Figure 8b**).The image of **Figure 7b** shows the exfoliated layer.

Application

Electrochemical behavior of paracetamol at CTAMa modified electrode

The voltammetric behavior of paracetamol on GCE/CTAMa was examined using Cyclic Voltammetry (CV) (**Figure 9**). One peak of oxidation at 415.3 mv and another peak of reduction at 128.9 mV, corresponding to quasi-reversible electrochemical reaction of paracetamol, can be seen. The remarkable voltammetric response of paracetamol on the GCE/CTAMa can be reasonably ascribed to the electrocatalytic activity of organoclays, which improves the adsorption efficiency and electrochemical reactivity of paracetamol. It is suggested that, owing to its high adsorptivity, CTAB

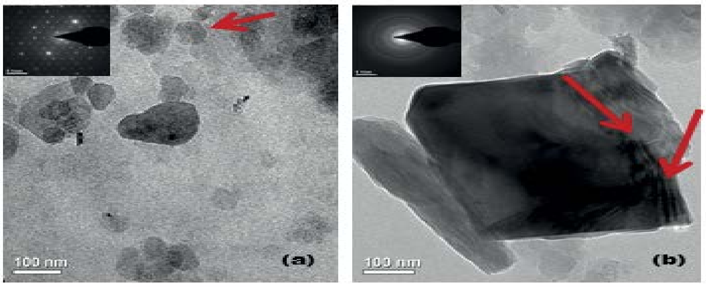

Figure 7: TEM images of (a) Purified clay (b) Organoclay at high magnification.

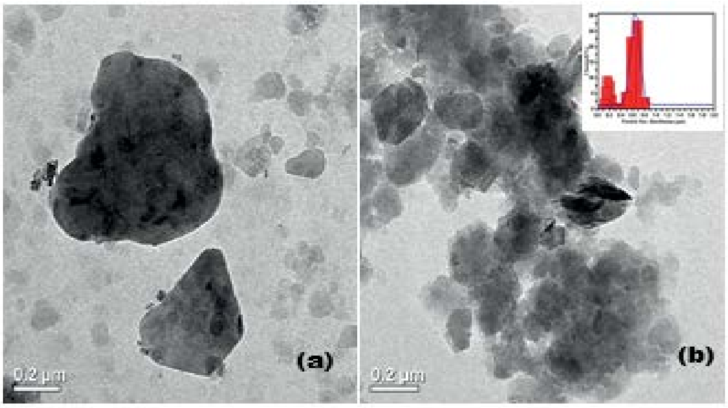

Figure 8: TEM images of (a) Purified Clay (b) Organoclay at low magnification (Particle size distribution).

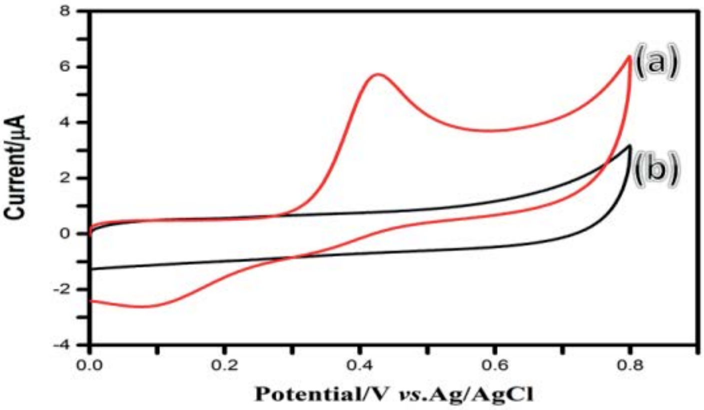

Figure 9: CVs of 3.5x10-5M Paracetamolon the (b) bare GCE, (a) GCE/CTAMa in 0.1M PBS (pH=7.4), at scan rate of 50 mVs−1.

effectively modifies the surface chemistry of clay sheets, which provides an efficient interface and microenvironment for the electrochemical reaction of paracetamol.

The redox mechanism of Paracetamol on GCE/CTMa

The effect of scan rate on the anodic and cathodic peak current of paracetamol on the GCE/CTAMa was investigated. As shown in **Figure 10**, the anodic and cathodic peak currents increase linearly as the scan rate grows from 30 to 230 mVs^{-1}. The linear relationship between the peak current and the scan rate was obtained with the linear regression equation as: $Ipa/\mu A=61.12+ 187.70\ v/mVs^{-1}$ ($R^2=0.9907$) and $Ipa/\mu A=-22.12\ -185.90\ v/mVs^{-1}$ ($R^2=0.9944$), respectively (**Figure 10**). This result indicates that the electrochemical reaction of paracetamol on the CTAMa film is a surface-controlled process [67].

The effects of pH on oxidation of paracetamol on GCE /CTAMa have been studied in 0.1 M PBS in the pH range of 2.10-10.45 (**Figure 11**). With the increase of pH from 2.10 to 7.4, there has been significant increase in peak currents with an optimum pH at 7.4, followed by decline in peak currents from pH 7.4 to 10.45; the pH 7.4 is therefore chosen for the subsequent determinations. Furthermore, both oxidation peak potentials are shifted positively with increase in pH, confirming that protons participate in the oxidation processes of Paracetamol. The peak potentials are proportional to the pH values in the range of 2.10-10.45 (**Figure 11**) and the linear regression equations: $E_pa/V=0.7137-0.0484$ pH ($R^2=0.9862$).

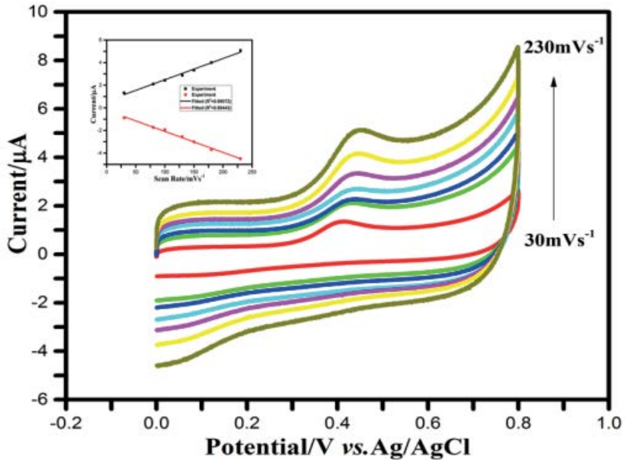

Figure 10: CVs of 3.5 × 10-5M Paracetamol on GCE/CTAMa at different scan rates in 0.1M PBS (pH=7.4).

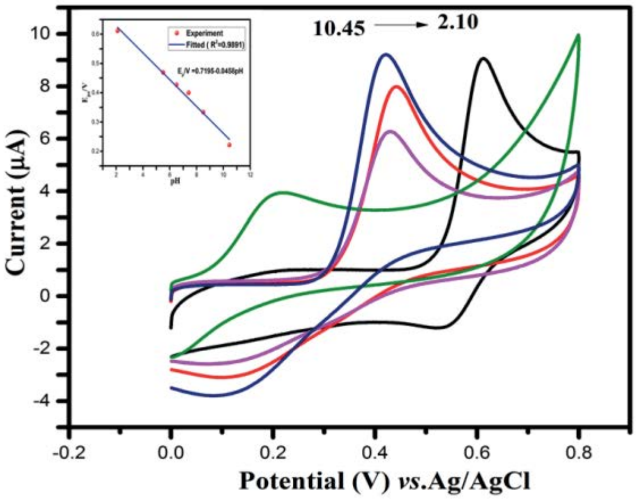

Figure 11: CVs of 3.5 × 10-5 M Paracetamol on GCE/CTAMa in 0.1M PBS with pH values of 2.1, 5.0, 7.0, 8.0 and 10.45. Scan rate: 50 mVs−1

According to the formula dEpa/dpH=2.303 mRT/nF

Where m is the number of protons; n, the number of electrons; and R, T and F have their conventional scientific meanings, the ratios of m/n were found to be 1.066 for paracetamol, suggesting the electrochemical oxidation of paracetamol two protons **[68].** This is confirmed by the linear slopes of 48.49 mV/pH that are close to the theoretical value of 59 mV/pH.

Voltammetry determination of Paracetamol

The voltammetric determination of paracetamol was carried out in 0.1 M PBS (pH 7.4) using cyclic voltammetry at the GCE/CTAMa (**Figure 12**). The oxidation peak current increases linearly with the concentration of paracetamol within the range of 10-80 µm. The equation of the straight line is Ipa (µA)=5.0035+57.2139$C_{paracetamol}$ ($R^2=0.9862$) (**Figure 12**). The detection limit is calculated by using the formula 3σ/b where σ is the standard deviation of the blank and b is the slope of the calibration curve. The detection limit of the modified electrode towards paracetamol is found to be at 23 µm.

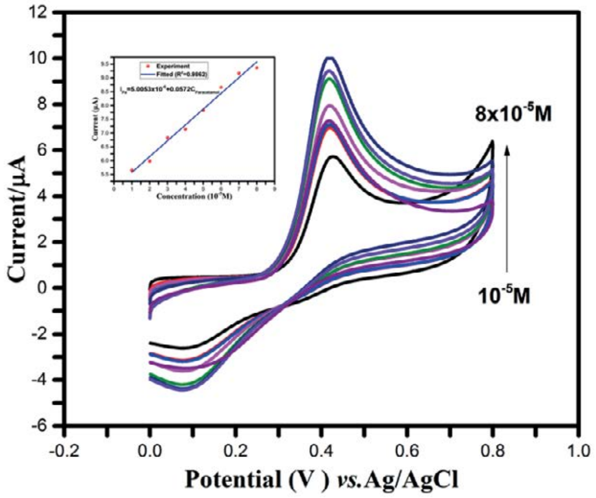

Figure 12: CVs response of CTAMa/GCE at different added concentration of Paracetamol in the electrolytic medium.

CONCLUSION

In this work, organoclays with CTAB and natural clays were synthesized. Their physicochemical structure, morphology and thermal properties were explored using various experimental techniques. The results indicated the exfoliation after modification of natural clay with CTAB. It was found that the organoclays nanocomposite could provide a favorable interface and microenvironment for the electrochemical detection of paracetamol. The composite film modified electrode was successfully employed for the voltammetric determination of paracetamol with low detection limit, wide linear range and good selectivity. The application of GCE/CTAMa for paracetamol detection in commercial tablets with satisfactory results was also demonstrated.

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