Aims and Scope
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Science has always been taught as clearly discreet field in past. However, of late, different subjects are precisely integrated together to develop multidisciplinary arenas. And the upshots of integrative studies resulted in innovations in many areas. As an example, the use of X-ray crystallography for determining the structure of DNA or use of magnetic resonance in medical imaging. The cross-discipline of physics, biochemistry, materials, and biology has provided ground-breaking insights into natural phenomena and has drawn the attention of researchers from varied subjects.

The tenth issue of Biomedical Research Journal contains articles on multidisciplinary research, clinical studies and a commentary on an upcoming area of drug delivery systems.

A clinical study on odontogenic fibroma, a rare benign tumor of mesodermal origin, was diagnosed through Computed tomography (CT). The heterogeneity of the CT density in the tumors helped in accurately revealing the margins of tumors and greatly aided in diagnosis. On a similar line, the use of non-ionizing radiation and optical imaging is progressively bridging the gap between radiology and histopathology and are therefore, now considered as a non-invasive medical diagnosis tool. The sensitivity to molecular, functional and structural content of living cells and their surroundings are well captured by these advanced imaging tools. Among several optical imaging systems, luminescence spectroscopy can be used as an exciting and powerful tool for understanding the intracellular metabolism of metals in living systems. One of our articles focusses on development of a nanophosphor luminescent probe for sensing copper ions. Furthermore, researchers are now able to combine luminescence with other analytical techniques to map metal content in living cells and address fundamental questions about cellular metal homeostasis. Another powerful analytical technique i.e., electrochemistry, which is
a result of rapid evolution of micro- and nanotechnology, has been often used to monitor electroactive species in living organism. The development of electrochemical sensors for selective sensing of neurotransmitters is another breakthrough in medical diagnostics. In particular, the use of graphene as electroactive species has stimulated broader interest in developing nanomaterial based biosensors for disease diagnosis.

Yet another aspect of biomedical research is the development of targeted drug delivery system for specific disease. The focused advantage of such targeted delivery systems lies in concentrating the drug in the tissues of interest rather than spreading throughout the body. Different carrier systems have been developed since long, out of which, the non-ionic surfactant vesicles, called niosomes have particularly been more effective. Niosomes readily form a closed bilayer vesicle in aqueous media and due to presence of hydrophilic, amphiphilic and lipophilic moieties in their structure, they can accommodate drug molecules with a wide range of solubility. A slight manipulation of their structure at atomic level can help in releasing the drug in a controlled manner.

BRJ believes that a surfeit of multidisciplinary aspects will provide the readers a good understanding of the “research on edge”.

Happy Reading!!
Over the years researchers have been attempting to improve the efficiency of utilization of drugs for treatment of various diseases. In this endeavour, drug delivery systems have helped greatly by achieving reduced dose, dosage frequency, and side effects; better patient compliance; and maximum concentration of the drug at the target site. Recent years have seen an unprecedented growth in the use of nanotechnology in designing drug delivery systems. Use of nano-structured drug delivery systems has changed the landscape of pharmaceutical and biotechnology industries. Nanocarriers offer advantages such as, (1) encapsulation and prevention of the drug from degradation, (2) improved delivery of poorly water soluble drugs, (3) targeted drug delivery, (4) co-delivery of multiples drugs with varying solubility or modes of action, (5) controlled release, and (6) production on a large scale (Farokhzad and Langer, 2009).

Drug delivery systems have been synthesized using substances varying from molecules of biological origin to inorganic or chemically synthesized substances. Biological molecules that have been used include, gelatin, albumin and chemical substances include various polymers and solid metal-containing NPs. Organic nanoplatforms include liposomes, polymeric nanoparticles, polymer-drug conjugates, polymeric micelles, hydrogel nanoparticles, protein-based nanoparticles, and dendrimers; whereas inorganic platforms include noble metal nanoparticles, super-paramagnetic nanoparticles, ceramic nanoparticles, carbon-based nanomaterials, and integrated nanocomposite particles (Bamrungsap et al., 2012).
Lipid-based nanocarriers as drug delivery systems

Lipid-based nanocarriers include drug delivery systems such as micelles, liposomes, nanoemulsions, solid lipid nanoparticles, niosomes, and nanostructured lipid carriers. Since these are composed of physiological lipids, they are non-toxic and biocompatible, and hence well tolerated in human body, and are biodegradable (Chuang et al., 2017). Lipid-based nanocarriers can increase the solubility and stability of hydrophobic drugs in aqueous systems and thus eliminate the use of toxic solvents or pH adjustments. These drug delivery systems can also protect labile peptide/protein based drugs such as biologics from enzymatic degradation. Surface modifications of these nanocarriers can help in altering the pharmacokinetic and pharmacodynamics profile of the drugs for passive and active targeting, reducing immunogenicity of the drug/carrier, preventing phagocytosis, and minimizing interaction with blood components. Lipid-based nanocarriers thus have great potential towards improving safety and efficacy of drugs (Lim et al., 2012).

Niosomes as Drug Delivery Systems

Niosomes are primarily non-ionic liposomes that are either unilamellar or multilamellar vesicular structures composed of non-ionic surfactants (Figure 1) instead of phospholipids. Niosomes, as in case of liposomes, have the capability to encapsulate both hydrophobic and hydrophilic drugs. Hydrophobic drugs are entrapped within the lipophilic domain of the bilayer,
whereas hydrophilic drugs get entrapped in the inner aqueous core of the vesicle or get adsorbed on the bilayer surface (Thakkar and Brijesh, 2016). The non-ionic surfactants, being the major component of niosomes, helps in overcoming issues such as susceptibility of phospholipids to oxidation, as observed with liposomes, and thus make niosomes more stable compared to liposomes (Vyas and Khar, 2011). Non-ionic surfactants can also enhance the solubility of poorly soluble drugs and formation of niosomes has been shown to increase the bioavailability of drugs (Rajera et al., 2011).

**Composition of niosomes**

Niosomes, in addition to hydrated non-ionic surfactants, are composed of, in many cases, cholesterol or its derivatives and a charge inducer. To understand the effect of various parameters on the characteristics of niosomes, it is important to know the basic role of each of the components used for their preparation (Kumar and Rajeshwarrao, 2011).

*Non-ionic surfactants*: Non-ionic surfactants act as surface active agents; which provide more stability and compatibility, and lesser toxicity compared to their anionic, amphoteric, or cationic counterparts. They are less irritating to the cellular surfaces and generally can maintain the solution close to physiological pH. They can also inhibit P-glycoprotein, which helps in enhancing absorption of drugs and targeting. Non-ionic surfactants are comprised of both polar and non-polar segments and possess high interfacial activity. The formation of bilayered vesicles, instead of micelles, is dependent on the chemical structure of the components, the hydrophilic–lipophilic balance (HLB) of the surfactant, and the critical packing parameter (CPP).

The HLB value of a surfactant plays an important role in the entrapment efficiency of the vesicle. Several non-ionic surfactants with different HLB values have been used for synthesis of niosomes, e.g., polyglycerol alkyl ethers, glucosyldialkyl ethers, crown ethers, poloxyethylene ethers, and esters such as Brij, Span and Tween. The most commonly used non-ionic surfactants are Span (20, 40, 60, 65, 80, and 85), Tween (20, 40, 60, 65, 80, and 85), and Brij (30, 35, 52, 56, and 58) (Moghassemi and Hadjizadeh, 2014). For non-ionic...
Surfactants, the HLB value ranges from 0–20. Surfactants with low HLB value are more lipophilic, whereas those with high HLB are hydrophilic. Surfactants with HLB value between 14 and 17 are not suitable for formation of niosomes. The highest entrapment efficiency is shown by niosomes formed by surfactant with an HLB value of 8.6, which decreases as the HLB value lowers from 8.6 to 1.7 (Marwa et al., 2013; Kumar and Rajeshwarrao, 2011).

CPP is an important parameter that can help in predicting the type of vesicles formed by the surfactants. Bilayered vesicles are favoured by surfactants with CPP in the range of 1/2 to 1. Another important parameter that can directly affect the entrapment efficiency of a niosome is the phase transition temperature (TC) of the surfactant. Surfactants with high TC exhibit high entrapment efficiency e.g., Span 60 (Moghassemi and Hadjizadeh, 2014).

Cholesterol: One of the most commonly used additives in the preparation of niosomes is cholesterol. Since cholesterol is an important component of the cell membrane, which affects the membrane fluidity and permeability, its incorporation affects surface properties of niosomes such as membrane permeability and rigidity. In addition, it can also affect other important properties such as encapsulation efficiency, storage time, drug release and stability of the formulation. Cholesterol must be added for bilayer formation when the HLB value of the surfactant is greater than 6, and for lower HLB values, it enhances the stability of the vesicles (Kumar and Rajeshwarrao, 2011). It also prevents the aggregation of vesicles by inclusion of molecules that stabilize the system against the formation of aggregates by repulsive steric or electrostatic forces that lead to the transition from gel to liquid phase in niosome systems. Hence, niosomes become less leaky in nature (Rajera et al., 2011).

Hydration medium: Phosphate buffers at physiological pH are commonly used for preparation of niosomes, but the actual pH of the hydration medium depends on the solubility of the drug to be encapsulated.

Additives: Stability of niosomes can be increased by preventing aggregation of the vesicles, which is achieved by addition of charged molecules to prevent coalescence through electrostatic
repulsion. Different types of membrane additives, including negatively charged (e.g., dicetylphosphate and phosphatidic acid), positively charged (e.g., stearylamine and cetylpyridinium chloride), and non-ionic (e.g., cholesteryl poly-24-oxyethylene ether) molecules can be added for preventing aggregation of niosomes (Junyaprasert et al., 2007).

**Types of niosomes**

Based in size, niosomes can be divided into the more common, small unilamellar vesicles (10–100 nm); large unilamellar vesicles (100–1000 nm); and giant unilamellar vesicles (> 1000 nm); and the less common multi-lamellar vesicles. In addition, other specialized forms of niosomes mentioned in literature include proniosomes, surfactant ethosomes, elastic niosomes, polyhedral niosomes, discomes (disk-shaped vesicle), aspasome (ascorbyl palmitate vesicle), surfactant ethosomes, etc. (Chuang et al., 2017; Dolati et al., 2016; Moghassemi and Hadjizadeh, 2014; Pham, 2011).

**Preparation of niosomes**

Preparation of niosomes generally involves evaporation of the organic solvents to produce a lipid film followed by hydration with the aqueous medium (Sankhyan and Pawar, 2012). Several techniques are used for preparation of niosomes that can be classified into the following types:

- **Passive trapping techniques:** Passive trapping techniques involve incorporation of drug into the system during the formation of niosomes. These include methods such as thin film hydration, ether injection, reverse phase evaporation, multiple membrane extrusion, microfluidization, sonication, and the bubble method.

- **Active trapping techniques:** Active trapping techniques involve loading of the drug into the niosomes after they are formed, i.e., during hydration of the niosomes. In these techniques, the drug is added while maintaining pH gradient or ion gradient that can facilitate incorporation of the drug into the niosomes, e.g., trans-membrane pH gradient drug uptake method.

**Niosomes as transdermal drug delivery systems**

In early 1970s, niosomes were widely used for dermatological purpose in the cosmetic industry with L’Oréal being the cosmetic brand that first developed and patented niosomes. Since then their application have now been extended to
the field of drug delivery. Niosomes offer several advantages for transdermal applications due to increased stability, reduced drug toxicity, and modification of pharmacokinetics and bioavailability of the entrapped drugs. However, when using niosome for topical application, it is important to know if the desired effect is local (dermal drug delivery) or systemic (transdermal drug delivery). Niosomes, when applied topically, allows local therapeutic effect in the epidermis and reduces systemic absorption of the drug by increasing the residence time of the drug in the stratum corneum (Cosco et al., 2008). As a result, niosomes have gained immense popularity for use in topical delivery systems. However, for transdermal drug delivery, retention of drug in the stratum corneum can act as a rate limiting step for drug permeation. During the last decade, niosomes have undergone intensive investigation for transdermal drug delivery. Transdermal delivery of drugs offer several advantages over the conventional routes of drug administration as the drugs do not pass through the hepatic first-pass metabolism and avoids gastrointestinal degradation. Transdermal approach also provides a relatively large surface area for absorption, and being non-invasive, it improves patient compliance (Muzzalupo and Tavano, 2015).

However, one of the major challenges for a transdermal delivery agent is the low penetration rate through skin. Very limited number of drugs have been used with transdermal delivery systems due to the selective effect of stratum corneum, allowing only drugs with specific physicochemical properties to cross the skin (Barry, 1991). Several strategies, including use of penetration enhancers, have been evaluated for overcoming the barrier function of stratum corneum and improving the transport of drug across the skin. Penetration enhancers may show their effect via one or more of the mechanisms of the lipid-protein-partitioning theory: alter the intercellular lipid structure between the corneocytes, thereby increasing the diffusivity; and modify intracellular protein domains within the horny layer, thereby increasing the partitioning of the drug into the skin tissue (Karande and Mitragotri, 2009).

**Mechanisms of action of niosomes as permeation enhancers**

Several mechanisms have been proposed by various studies for the ability of niosomes to enhance transfer of drugs across the membrane. These include, (1)
reversible alteration of lipid organization, which affect the barrier function of the stratum corneum, (2) increasing hydration of the stratum corneum by preventing transepidermal water loss, that leads to loosening of the tightly-packed cellular structure, and (3) adsorption and/or fusion of niosomes on the surface of the skin, that causes creates a high thermodynamic activity gradient of drug at the interface (Abdelkader et al., 2014; Manconi et al., 2006). Adsorption of niosomes onto the skin cell surfaces may occur as a result of attracting physical forces or due to the binding of ligands on the niosomal membrane to specific receptors on the cell surfaces, thereby transferring the drug directly from the vesicles to the skin. Fusion of niosomes with the cell membrane, on the other hand, can result in complete mixing of the niosomal contents with the cytoplasm. Endocytosis of niosomes by the skin cells, followed by lysosomal degradation, may also lead to release of the entrapped niosomal content into the cell cytoplasm.

**Niosomes for rheumatoid arthritis**

In case of rheumatoid arthritis (RA), the most common chronic systemic autoimmune inflammatory disease affecting the joints, the conventional drug therapy has been ineffective due to systemic toxicity caused by the drugs, drug resistance and other adverse effects. Nanocarriers have been used for the treatment of RA as they have the potential to provide safe vehicles to increase solubility and stability of hydrophobic drugs and biologics, and reduce the drug-related toxicities through targeted delivery (Chuang et al., 2017; Lim et al., 2012). To achieve targeted delivery of drugs, passive and active mechanisms of targeting of the nanocarriers can be used. Passive targeting can be achieved in inflammatory diseases due to immune response. Targeting of macrophages by nanoparticulate systems has been proven as a powerful approach for the treatment of autoimmune blood disorders such as RA (Chellat et al., 2005). Passive approaches have targeted macrophages due to their increased numbers in inflamed joints and efficient phagocytosis of the nanocarriers by the macrophages, without the requirement of any surface modifications. Passive targeting of macrophages using nanocarriers is based on the key fact that macrophages play a central role in RA, and can help in selective accumulation of
phagocytized nanocarriers into arthritic joints. Systemically, however, the nanocarriers have high chances of clearing by the reticulo-endothelial system (RES). Hence, surface modifications of nanocarriers to delay RES clearing and to actively target other organ systems or immune cells and pathways are constantly being explored (Dolati et al., 2016).

Several studies have evaluated the feasibility of using niosomal formulation via topical route of administration for treatment of RA. The results, though mixed, have been encouraging. Niosomal gel formulation containing anti-rheumatic drugs such as ursolic acid (Mahvish et al., 2015), luteolin (Abidin et al., 2016), etodolac (Asthana, 2016) have been shown to exhibit better skin permeation and skin absorption, with better efficacy of the treatment than the oral formulation. Proniosomal formulations, the liquid crystalline-compact niosomal hybrids that can be converted to niosomes upon hydration, containing curcumin showed lower anti-arthritis activity than marketed indomethacin products (Kumar and Rai, 2012). On the other hand, proniosomal formulations tenoxicam showed higher anti-inflammatory effects compared to the oral marketed tenoxicam tablets (Ammara et al., 2011). Niosomal gel of capsaicin showed higher skin permeation of the formulation resulting in improvement in the cartilage of the knee joints of rats (Jindal, 2008). Novel elastic niosomes were formulated and encapsulated with diclofenac diethylammonium, a salt of diclofenac sodium (Manosroi et al., 2008). The elastic niosomes are prepared by adding ethanol as it acts as an efficient permeation enhancer. As a result of their flexibility they can squeeze themselves through pores which are much smaller than their diameters. The formulations showed physical and chemical stability for three months and can be a promising topical non-invasive treatment for inflammation.

CONCLUSION

Niosomes as a drug delivery system has a promising approach due to the various advantages they offer. Also, they do not require special conditions for handling, protection or storage and industrial manufacturing. Transdermal application of niosomal formulations can be a viable treatment strategy for RA to achieve better drug permeation through skin, as well as sustained therapeutic effect, and reduced side effects compared to oral and invasive therapies.
REFERENCES


Lim SB, Banerjee A, Önükşel H. Improvement of drug safety by the use of lipid-based...


INTRODUCTION

Dopamine is known as an important neurotransmitter which regulate a variety of motivated behaviors involved in several neurological diseases and it modulates many aspects of brain circuitry. Major disorders viz., schizophrenia, Parkinson's disease are caused by abnormal concentration levels of dopamine (Goldberg et al., 1972). Hence, it is very important to have knowledge of exact concentration of dopamine in the body fluid. Several methods including electrochemical techniques and colorimetric assay has been employed to detect dopamine in vivo and in vitro (Sheng et al., 2012). Among these methods, electrochemical techniques which utilize highly selective electrochemical sensor probes, allow to detect very minute concentration of several electroactive biological molecules in vivo and in vitro analysis. Dopamine determination can be done electrochemically through dopamine

**Key words:** Graphene oxide, Cyclic voltammetry, Dopamine.

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Surfactant modified graphene oxide for detection of dopamine oxidation reaction. The reaction proceeds through steps as shown in Figure 1.

Cyclic voltammogram recorded in dopamine solution, typically shows reversible electron transfer process. First, dopamine is oxidized to dopamine-o-quinone in the forward electrolysis (forward scan) at the electrochemical sensor followed by reduction of a resultant product i.e. dopamine-o-quinone (backward scan) to dopamine in the reverse electrolysis. Carbon nanotubes based sensors have been extensively used to detect dopamine in a blood serum (Kumar et al., 2018). However, the sensor response, is limited by the oxidation of interfering agents viz. ascorbic acid and uric acid which is generally present in a large excess in the body fluid. These biomolecules oxidize at the potential very close to the oxidation potential of dopamine and hence it is very necessary to use appropriate sensor probe to distinguish redox processes of dopamine from the interfering species. Britto et al. (1996) used bromoform as a binder to construct a carbon nanotube electrode which was used to study oxidative behaviour of dopamine using cyclic voltammetry. Here, authors observed ideal reversible two-electron oxidation of dopamine to dopamine-o-quinone, and reported significantly better and superior sensor response to that of other reported carbon based electrodes. Wang et al. (2009) reported graphene-modified sensor for the selective determination of dopamine in a linear concentration range of 5 µM to 200 µM in presence of high amount of ascorbic acid. In other report, Kim et al. (2010) reported electro-chemical detection of dopamine at graphene/glassy carbon probe. This sensor showed lower detection limit of 2.64 µM of dopamine and linear working range was found to be 4 µM to 100 µM. Wu et al. (2013) used CTAB to modify graphene, synthesized by modified Hummers' method. Further, Vidya et al. (2015) studied the electrochemical behaviour of dopamine using various surfactants such as SDS, CTAB and Tween-20. Their study demonstrated that the use of SDS in

![Figure 1: Dopamine oxidation reaction.](https://example.com/figure1.png)
graphene paste electrode improves the electrochemical response towards the catalytic oxidation of dopamine. Moreover, Yang et al. (2014) synthesized CTAB/graphene oxide/multi walled carbon nanotubes (MWCNTs) hybrid catalyst and drop-casted on glassy carbon electrode in order to detect dopamine with ascorbic acid and uric acid. The sensor showed linear response in the range of 5.0 to 300 μM (lower detection limit 1.0 μM), 5.0 to 500μM (lower detection limit 1.5 μM) and 5.0 to 800μM (lower detection limit 1.0 μM) for ascorbic acid, dopamine, and uric acid, respectively.

Most of the studies revealed that the use of expensive carbon nanotubes helps in simultaneous detection of dopamine with ascorbic acid and there is not much work done to evaluate the catalytic activity of carbon nanomaterial for the oxidation reaction of dopamine. Herein, we have prepared graphene oxide (GO) using improved Hummer's method and then modified it with two different surfactants: cetyltrimethylammonium bromide (CTAB-GO) and Sodium dodecyl sulfate (SDS-GO). These material where drop-casted on less expensive graphite rod and was used as an electrode to detect dopamine using cyclic voltammetry. Among two, CTAB-GO modified graphite rod sensor showed promising results in the linear concentration range of 500 M to 5 mM dopamine with sensitivity 92.95 A mM$^{-1}$ cm$^{-2}$ in Britton Robinson buffer (pH 7.4) at 27°C. Using classical Butler-Volmer equation we have estimated heterogeneous rate constant for the oxidation reaction of dopamine on CTAB-GO modified graphite rod.

**EXPERIMENTAL**

**Materials**

Graphite powder, dopamine, ascorbic acid were procured from Alfa acer. Cetyltrimethylammonium bromide (CTAB), Sodium dodecyl sulfate (SDS), Potassium permanganate (KMnO$_4$), phosphoric acid, boric acid, acetic acid, hydrochloric acid, sulfuric acid, sodium hydroxide and hydrogen peroxide were purchased from Merck Chemicals. Graphite rod is used as a working electrode for electrochemical measurements. All the solutions were made in double didstilled water.

**Synthesis of Graphene Oxide**

Graphene oxide was synthesized using improved Hummer's method. 3.0 g of Graphite powder and 9.0 g of KMnO$_4$...
was weighed and mixed to 9:1 mixture of concentrated \( \text{H}_2\text{SO}_4 : \text{H}_3\text{PO}_4 \) at 4°C (temperature was maintained using ice bath). The mixture was refluxed at 60°C with 550 RPM for 12 h (Chen et al., 2013; Marcano et al., 2010). Then the solution was kept unstirred for some time to attain room temperature and after that it was poured onto ice cooled water which consists of 30% \( \text{H}_2\text{O}_2 \). This was centrifuged and supernatant was thrown out. The obtained solid brown color residue was washed with distilled water till get neutral pH of the washing supernatant. The compound was then washed with 100 mL 30% HCl, water and 100 mL ethanol. Finally the compound was washed with diethyl ether and dried in oven at 60°C. The product was characterized by using scanning electron microscopy (SEM), EDAX analysis and UV-Vis spectroscopy.

**Modification with Surfactants**

Graphene oxide was dissolved in cetyltrimethylammonium bromide (CTAB) solution (0.04 M). This solution was then refluxed at 80°C at 500 RPM for 2 h followed by centrifugation and washing to get solid product. Further, product was dried in oven at 60°C to get CTAB modified graphene oxide. Same procedure was used to prepare Sodium dodecyl sulfate (SDS) modified graphene oxide and characterized using IR spectroscopy.

**Fabrication of Electrochemical Dopamine Sensor**

In order to make dopamine sensor, graphite rod with dia. 3 mm and length 5 cm was used as a conducting phase. The bare surface of graphite rod was covered with silicon tape by leaving just a graphite disk at the front for sensor paste dropcasting and a 0.5 cm area at the back side for a connection to the potentiostat. Silicon tape was used to restrict the small area for the electrochemical measurement. The exposed disk surface of graphite rod was cleaned by polishing it with fine polish paper and sonicated in ethanol for 2 min. Further, sensor was fabricated by dropcasting mixture of CTAB-GO and 0.5% Nafion solution on the disk of graphite rod followed by drying at 50°C. This electrode was then used as a working electrode in the electrochemical detection of dopamine.

**Electrochemical Measurements**

The electrochemical measurement was carried out using three electrode system with CHI potentiostat (600 D). Ag/AgCl,
3 M KCl, Pt rod (1 mm dia.) and modified graphite rod were used as a reference, counter and working electrodes, respectively. Electrochemical experiments were performed at 25 ± 2°C in Britton Robinson buffer at pH 7.4.

RESULTS AND DISCUSSION
The graphene oxide (GO) synthesized using improved Hummer’s method was characterized by UV-visible spectroscopy, Electron Dispersive X-ray (EDAX) analysis and Scanning Electron Microscopy (SEM). UV–visible spectra of the aq. solution of synthesize GO is shown in Figure 2A. It showed a prominent peak due to the absorption at 230 nm which is ascribed to the π-π* transition of C=C. The feature of the spectrum matches very well with the UV–visible spectrum reported on GO samples in the literature (Chen et al., 2013). The SEM image recorded on the dry powder sample depicts the formation of thick layered graphene sheets as shown in Figure 2B. Besides, EDAX spectrum recorded on the dry GO powder shows the presence of 52 at.% of carbon and 47.9 at.% of oxygen with no other metal impurities (Figure 2B). After confirming the formation of GO, we modified it with two different surfactants: CTAB and SDS.
by chemical method as mentioned in the experimental section. FT-IR spectra of as synthesized GO, CTAB-GO and pristine CTAB is shown in Figure 2D. The absorption band observed at 1134 cm\(^{-1}\) due to C–O–C stretching vibrations in CTAB is diminished in CTAB-GO due to the interaction of CTAB and the epoxy group of GO. In case of CTAB-GO, the characteristic absorption bands were observed at 2924 cm\(^{-1}\) and 2853 cm\(^{-1}\), which are due to C–H stretching vibrations coming from CTAB main chain. The stretching band around 1250 cm\(^{-1}\) to 1300 cm\(^{-1}\) is due to C–N bond present in CTAB. Similarly, FTIR-spectras were recorded on SDS-GO and pristin SDS (Figure 2C) The peak at 2924 cm\(^{-1}\) and 2853 cm\(^{-1}\) observed in pristine SDS were diminished in SDS-GO. Also, a peak at 1220 cm\(^{-1}\) due to S=O stretching of SDS can be seen in SDS-GO. The detailed investigation on both modified GO samples indicate the successful modification of GO surface with CTAB and SDS moities which can be further used in electrochemical investigations on dopamine. Figures 3A and 3B depict cyclic voltammograms recorded at CTAB-GO and SDS-GO modified graphite rods respectively. Britton Robinson buffer at pH 7.4 was used as an electrolyte in which successive addition of dopamine was made to adjust final concentration of dopamine ranging from 250 M to 5 mM. All electrochemical measurements were carried out at 27\(^\circ\)C using three electrode system. The cyclic voltammograms recorded at CTAB-GO graphite rod showed single electron transfer process, where anodic and cathodic peaks were
observed at 0.45 V and 0.15 V (vs. Ag/AgCl), respectively. There is linear increase in anodic as well as in cathodic peak current with little shift in anodic peak potential was observed with successive addition of dopamine at CTAB-GO modified graphite rod electrode (Figure 3A). However, no linear response was observed at SDS-GO modified graphite rod electrode (Figure 3B) due to the poisoning of electrode surface during the proces of dopamine electro-oxidation.

The results demonstrate that the CTAB-GO composite showed promising results for the dopamine oxidation reaction with lower detection of 500 M, linear range: 500 M to 5 mM with sensitivity 92.95 A cm$^2$ mM$^{-1}$ (refer Figure 4). According to the literature reviews, presence of CTAB with carbon nanomaterials helps in simultaneous, distinct detection of dopamine with existence of ascorbic acid. The surfactants like CTAB with positive charge arranged themselves on the negatively charged surface of the graphene oxide which makes modified electrode positively charged. Further, negatively charged ascorbic acid adsorb to the electrode surface but dopamine with positive charge experiences repulsion from the electrode. Hence, due to the presence of CTAB, dopamine oxidation potential shifts to the higher side as compare to ascorbic acid and one can detect both species successfully (Yang et al., 2014).

Thus, surfactants like CTAB can only help to separate electro-oxidation process of dopamine and ascorbic acid by shifting redox potential based on the charge present on the molecules but for the effective detection of these both species it is important to develop sensor with a key catalysts witch can further enhance the oxidation of dopamine and ascorbic acid. Based on this fact, CTAB-GO and CTAB/GO/MWCNTs modified electrodes were reported for the detection of dopamine. Here, incorporation of multiwall carbon nanotubes which are generally having minute quantity of

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**Figure 4:** Calibration curve plot of anodic peak current density at CTAB-GO modified graphite rod electrode (at 0.45 V) vs. dopamine concentration in Britton Robinson buffer (pH 7.4).
metallic impurities remained from their synthesis (Samant et al., 2014), only made it possible to detect ascorbic acid and uric acid simultaneously with dopamine (Vidya et al., 2015; Yang et al., 2014). The metal impurities present within the carbon nanotubes matrix are known to have catalytic activity for the oxidation of ascorbic acid and uric acid (Samant et al., 2014). In order to detect these interfering agents, modification of carbon nanomaterial with Pt, Pd and Au nanoparticles have also been reported (Sun et al., 2011; Yan et al., 2013). Besides, there are few reports which demonstrated that the edge plane defects which are generally distorted sp² hybridized surface (unsaturation on the carbon network) are responsible for the catalytic oxidation of dopamine (Samant et al., 2014; Joshi et al., 2010). In this case, further functionalization of carbon nanomaterials may obstruct the catalytic oxidation of dopamine. Therefore, herein we have tried to estimate approximate value of heterogeneous rate constant, $k^*$ for the dopamine oxidation reaction at the surface of CTAB modified graphene oxide using classical Butler-Volmer model of electrode kinetics (Joshi et al., 2010).

The normalized current accompanying with electrode is given by following equations,

$$i = \frac{1 + e^{-\xi} + e^{-\alpha \xi}}{\Lambda^*}$$

Where, dimensionless potential

$$\xi = \left(\frac{nF}{R \tau}\right) (E - E^0)$$

$$\Lambda^* = \frac{k^* \nu_0}{D} \left[ \frac{\ln \beta}{1 - (1.1 \ln \beta)} \right]$$

$k^*$ is the heterogeneous rate constant of the reaction where factor $\beta$ is given as,

$$\beta = 2 \left( \frac{DRT}{nF \nu_0^2} \right)^{1/2}$$

$E$ and $E^0$ are the applied and the formal redox potentials, respectively. The mass transport limiting current, $i_l$ is given as,

$$i_l = \frac{nFAC^0D}{\eta_\nu \ln \beta} \left( 1 - \frac{1.1}{\beta} \right)$$

Fitting of Eq. (1), in the experimental data obtained from electro-oxidation of dopamine at CTAB-GO modified

**Figure 5:** Experimental data obtained by recording linear sweep voltammetry (LSV) at 2 mV S⁻¹ in a solution of 25 M dopamine in Britton Robinson buffer (pH 7.4) (blue solid line) and orange colour markers indicates its non-linear fitting in Eq. (1).
graphite rod is shown in Figure 5. The approximate fit for $k^0$ and $\alpha$ equal to $8.7 \times 10^{-10}$ cm s$^{-1}$ and 0.45, respectively have been obtained. The reported value of $k^0$ for the oxidation of dopamine on MWCNTs (Britto et al., 1996) and carbon fiber (Joshi et al. 2010) electrode are 0.17 cm s$^{-1}$ and 0.18 cm s$^{-1}$, respectively. The substantially lower value of $k^0$ associates to CTAB-GO modified electrode could be attributed to the lower conductivity, sensitivity of the material due to presence of various functional group moieties on the surface of graphene oxide, which further reduces the defects/edge plane sites which are responsible for the catalytic oxidation of the dopamine (Joshi et al., 2010; Samant et al., 2014). Thus based on our findings, CTAB-GO modified electrode can be used to detect dopamine. Sensor showed linear range in 500 M to 5 mM of dopamine with lower detection limit of 500 M. However, lower $k^0$ value as compare to the pristine carbon nanostructures reported in literature suggests, dopamine oxidation reaction is getting hindered due to the functionalization of the carbon nanostructures. These findings will be useful for the further designing of the highly efficient, selective dopamine sensors.

CONCLUSIONS
We have demonstrated the simple method to fabricate dopamine sensor using less expensive graphite rod and surfactant modified graphene oxide. CTAB-GO modified sensor showed promising results for the detection of dopamine in $\mu$M to mM concentration with lower detection of 500 $\mu$M. Also we have reported first time the electrode kinetics of dopamine oxidation at CTAB-GO modified electrode by estimating approximate value of heterogeneous rate constant. Our findings will be useful for the further designing of the efficient dopamine sensor.

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REFERENCES


Yang YJ, Li W. CTAB functionalized graphene oxide/multiwalled carbon nanotube composite modified electrode for the simultaneous determination of ascorbic acid, dopamine, uric acid and nitrite. *Biosens Bioelectron* 2014;56:300–306.
Ce$^{3+}$ Sensitized YPO$_4$:Tb$^{3+}$ as Luminescent Probe for Selective Detection of Cu$^{2+}$ Ions

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Poly-(acrylic acid) (PAA) modified water dispersible Ce$^{3+}$ (5 at.%) sensitized YPO$_4$, doped with Tb$^{3+}$ (5 at.%) nanocrystals were prepared by polyol method. Structural characterization was thoroughly studied with X-ray diffraction (XRD). Transmission electron microscopy (TEM) image indicate the rod shape morphology of the synthesized material. Fourier transform infrared (FTIR) spectroscopy confirms the surface functionalization of these nanorods. The sample shows strong energy transfer from Ce$^{3+}$ ions to Tb$^{3+}$ ions. The green emission from Tb$^{3+}$ ions could be selectively quenched by Cu$^{2+}$ ions upto $\sim 89\%$ as compared to other heavy metal ions. It is established from the investigation the sensing is through dynamic quenching via resonance type energy transfer. The limit of detection calculated using Stern-Volmer relation is found to be 19 $\mu$M ($\sim$1 ppm). This nanophosphor could be a potential luminescent probe for Cu$^{2+}$ ions sensing.

INTRODUCTION

Lanthanide (Ln$^{3+}$) doped nanophosphors (NPs) has various applications in the fields of lighting, cathode ray tubes, display, laser, scintillator etc. (Blasse et al. 1994; Singh et al. 2017). At present, researchers are exploring to find new applications of these NPs in sensing and bioimaging for biomedical applications. Metal ions are very important for the proper functioning of biological systems. But in excess consumption, they may lead to serious health problems. Metal ions could be quantitatively detected by using atomic absorption spectroscopy, inductively coupled plasma atomic emission spectroscopy and inductively coupled plasma mass spectroscopy. These methods have some major drawbacks such as complexity, time consumption, and are expensive (WHO 2017; Ghosh et al. 2016; Chen et al. 2016; Sarkar et al. 2014). So, detection of metal ions using ligand functionalized quantum dots and Ln$^{3+}$ doped up-conversion NPs (UCNPs) as chemical sensors are reported (Chowdhury et al.).

Key words: Luminescence, Polyol, Nanorods, Quenching, Sensing.

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2018; Resheed et al. 2018). On the other hand, few researchers are working to find the applications of Ln$^{3+}$ doped down-conversion NPs (DCNPs) for sensing of metal ions (Sarkar et al. 2018; Wang et al. 2014). Besides these, there are several efficient techniques such as electrochemical, calorimetric, surface plasmon resonance, peptoids, nanogenerators, however, they are associated with some or the other drawbacks (Bansod et al. 2017; Baskin et al. 2016; Chen et al. 2014; Malek et al. 2016). Advantages of luminescent UCNPs and DCNPs are ease of synthesis or design, economical, selective, stable, long lasting, rapid and quick response toward metal ions (Bargossi et al. 2000; Liu et al. 2017; Sarkar et al. 2014.). Moreover, they can be used as probe for preliminary visual qualitative observation. There are several report on the application of luminescence probes for selective detection of heavy metals, in vivo/in vitro detection of metals ions in blood and living cells, in-depth detection and imaging in biological samples (Nolan et al. 2003; Kim et al. 2016; Lan et al. 2014; Li et al. 2012).

Sensing of Cu$^{2+}$ using Eu$^{3+}$ doped MVO$_4$ (M = Gd, La, P) (Chen et al. 2016; Zhu et al. 2016; Liang et al. 2018; Wangkhem et al. 2018) and KZnF$_3$ (Sarkar et al. 2014) functionalized with poly (acrylic acid) (PAA) and polyvinylpyrrolidine (PVP) have been reported. So far, Sarkar et al. reported the application of Ce$^{3+}$/Tb$^{3+}$ doped SrF$_2$ nanocrystals as fluorescent probe for selective and sensitive detection of Cu$^{2+}$ ions in aqueous solution (Sarkar et al. 2015). The mechanism of sensitive sensing of metal ions is solely due to luminescent quenching via Förster resonance energy transfer (FRET) type energy transfer from the host or/and Ln$^{3+}$ to Cu$^{2+}$. Functionalization of capping agent such as poly(acrylic acid), not only helps to control the morphology and rendering water dispersible particle, it can also act as binding sites of Cu$^{2+}$ ions (Chen et al. 2016; Sarkar et al. 2015).

YPO$_4$:Ln$^{3+}$ (Ln = Ce, Tb, Eu, Sm) is well studied for lighting, color tuning and luminescent switching applications. Usually, solid state, sol-gel, hydrothermal, polyol methods are employed to synthesize YPO$_4$. Capping agents such as citric acid, polyvinylpyrrolidone (PVP), glycerol, are used as surface-functionalizing agents (Dorenbos et al. 2011; Angiuli et al. 2012; Angiuli et al. 2013; Du et al. 2013; Yahiaoui et al. 2018; Debi et al. 2018).
2017, Luwang et al. 2011). Ce\textsuperscript{3+} or Bi\textsuperscript{3+} are used as a sensitizer in YPO\textsubscript{4}:Ln\textsuperscript{3+}. Particularly, Ce\textsuperscript{3+} is utilized as a sensitizer to enhance the luminescence in these hosts doped with Tb\textsuperscript{3+} (Phaomei et al. 2011; Sahu et al. 2014a).

In this article, we report the application of Ce\textsuperscript{3+} sensitized YPO\textsubscript{4}:Tb\textsuperscript{3+} nanorods as a luminescent probe for selective detection of Cu\textsuperscript{2+} in aqueous solution. The sample was synthesized through polyol method using ethylene glycol (EG) as a reaction medium at a low temperature of 150 °C. PAA is used as a capping agent. The particles formed were nanorods and they showed a strong green emission upon UV excitation. YPO\textsubscript{4}:Ce\textsuperscript{3+}/Tb\textsuperscript{3+} showed selective detection towards Cu\textsuperscript{2+} ions out of various metal ions. Luminescence intensity could be quenched up to ~89% in presence of Cu\textsuperscript{2+} ions. The mechanism of selective detection might be due to resonance energy transfer to the metal ions. These YPO\textsubscript{4}:Ce\textsuperscript{3+}/Tb\textsuperscript{3+} nanorods can be a potential luminescent probe for detection of Cu\textsuperscript{2+}.

MATERIAL AND METHODS

Materials

Yttrium(III) nitrate hexahydrate (Y(NO\textsubscript{3})\textsubscript{3}·6H\textsubscript{2}O, 99.9%, Alfa Aesar), ammonium dihydrogen phosphate (NH\textsubscript{4}H\textsubscript{2}PO\textsubscript{4}, 99.999%, Aldrich), terbium(III) nitrate pentahydrate (Tb(NO\textsubscript{3})\textsubscript{3}·5H\textsubscript{2}O, 99.9%, Sigma Aldrich), cerium(III) nitrate hexahydrate (Ce(NO\textsubscript{3})\textsubscript{3}·6H\textsubscript{2}O, 99.9%, Sigma Aldrich) were used as sources of Y\textsuperscript{3+}, PO\textsubscript{4}\textsuperscript{3-}, Tb\textsuperscript{3+} and Ce\textsuperscript{3+} respectively. Poly (acrylic acid) (PAA, Sigma Aldrich), ethylene glycol/EG (C\textsubscript{2}H\textsubscript{4}O\textsubscript{2}, 98.0%, Rankem) and ammonium hydroxide solution (NH\textsubscript{3}OH, ~25% NH\textsubscript{3}, Sigma Aldrich) were also used without further purification.

Calcium(II) nitrate tetrahydrate (Ca(II)(NO\textsubscript{3})\textsubscript{2}·4H\textsubscript{2}O), anhydrous cadmium(II) chloride (Cd(II)Cl\textsubscript{2}), cobalt(II) chloride hexahydrate (Co(II)Cl\textsubscript{2}·6H\textsubscript{2}O), copper(II) acetate monohydrate (Cu(II)(CH\textsubscript{3}COO)\textsubscript{2}·H\textsubscript{2}O), iron(II) sulphate heptahydrate (Fe(II)SO\textsubscript{4}·7H\textsubscript{2}O), manganese(II) sulphate monohydrate (Mn(II)SO\textsubscript{4}·H\textsubscript{2}O), nickel(II) chloride hexahydrate (Ni(II)Cl\textsubscript{2}·6H\textsubscript{2}O), strontium(II) nitrate (Sr(II)(NO\textsubscript{3})\textsubscript{2}) and zinc(II) acetate dihydrate (Zn(II)(CH\textsubscript{3}COO)\textsubscript{2}·H\textsubscript{2}O) were purchased from Merck.

Synthesis

5 at.% Ce\textsuperscript{3+} sensitized YPO\textsubscript{4} doped with 5 at.% Tb\textsuperscript{3+} was synthesized through simple polyol method using EG as reaction
medium and PAA as capping agent at 150°C for 2 h. In this synthesis, 23.8 mg of Ce(NO₃)₃·6H₂O and 23.6 mg of Tb(NO₃)₃·5H₂O were dissolved in 2 mL of de-ionized water (DIW) in a beaker. To this solution, 375.5 mg of Y(NO₃)₃·6H₂O was added and stirred. 100 mg PAA was also added to the above solution followed by the addition of 125 mg of NH₄H₂PO₄ with continuous stirring. Later, 50mL of EG was added and stirred for 5 min. The pH of the solution was adjusted at 10 by adding NH₄OH solution dropwise with continuous stirring. Then, the solution was transferred to a round bottom flask and refluxed at 150°C for 2 h with continuous stirring and allowed to cool down to room temperature naturally. The obtained precipitate was separated by centrifugation for 3 min at 10000 rpm and washed several times with DIW, ethanol and acetone. The precipitate was dried in an oven overnight at 45°C and finally grounded it to powder.

Sample Preparation for Metal Ion Sensing
In this study, a freshly prepared solution of YPO₄·Tb³⁺/Ce³⁺ phosphor, dispersed in DIW with a concentration of 1 mg/5 mL was used. For selective detection study of various metal ions, solutions of 5 mM of each metal ions were prepared. Using a stock solution of 100 mM of Cu(II), smaller concentrations from 1 to 75 mM were also prepared. While studying selective detection of various metal ions, 0.2 mL of 5 mM solution was added to 1.8 mL of YPO₄·Tb³⁺/Ce³⁺ solution to obtain a final concentration of 0.5 mM. In sensitivity studies, the final concentration of the metal ion was varied from 0.01 to 0.75 mM. All solutions were prepared with DIW at room temperature.

Characterization Techniques
The phase identification of the as-prepared sample was performed on an X-ray diffractometer using CuKα radiation (Bruker D8 advance). The Fourier transform infrared spectroscopy (FTIR) spectrum was studied using PerkinElmer. Transmission electron microscopy (TEM) images were recorded using JEOL 2000FX. The photoluminescence (PL) spectra and lifetime were measured using HORIBA make FLUOROMAX-4CP spectrofluorometer with a 150 W Xenon lamp as light source and 25 W μs Xenon flash lamp. All the PL measurement were performed with a slit width of 2 nm at room temperature.
RESULTS AND DISCUSSION

XRD, FTIR and TEM Studies

Figure 1 displays the XRD pattern of the as-prepared 5 at.% Ce\(^{3+}\) sensitized YPO\(_4\) doped with 5 at.% Tb\(^{3+}\). The XRD pattern of the as-prepared sample unambiguously matched with the tetragonal phase of YPO\(_4\) (ICDD#00-011-0254). The presence of other impurity phases could not be observed from the XRD pattern. The average crystallite size was calculated by using the Scherrer’s relation, 

\[ D = \frac{\kappa \lambda}{\beta \cos \theta} \]

where, \(D\) is the average particle size, \(\lambda\) is the wavelength of X-ray radiation used and \(\beta\) is the FWHM (full width at half maximum) and \(\kappa\) is the Scherrer constant. The Scherrer constant (\(\kappa\)) in the formula accounts for the shape of the particle and is generally taken as 0.9. The calculated size is found to be ~24 nm.

The FTIR spectrum of as-prepared YPO\(_4\):Ce\(^{3+}\)/Tb\(^{3+}\) (5 at.% each) is depicted in Figure 2. Bands at 533 and 632 cm\(^{-1}\) are assigned to bending, \(\nu_5\), whereas 1016 and 1087 cm\(^{-1}\) can be assigned to stretching, \(\nu_3\), vibrations of (PO\(_4\))\(^3-\) group. Bands at 1278 and 2935, 2988 cm\(^{-1}\) corresponds to scissoring and stretching vibrations of –CH\(_2\) group form EG (Sahu et al. 2014a). 1456, 1574 and 1722 cm\(^{-1}\) are attributed to –C=O, –C=O and –COO\(^-\) groups of PAA respectively (Sarkar et al. 2014). The band at 3474 cm\(^{-1}\) is assigned to –OH group contributed from both EG and PAA. The presence of these bands confirm the formation of YPO\(_4\):Ce\(^{3+}\)/Tb\(^{3+}\) with the strong attachment of PAA to the surface of nanorods.

The TEM image of Ce\(^{3+}\)/Tb\(^{3+}\) doped YPO\(_4\) shows rod-like structures (Figure
3a) and the HRTEM image Figure 3(b) confirms the crystalline nature of the nanorods. The interplanar distance (d-spacing) 0.34 nm matched with the (200) planes of YPO₄. The average length and diameter distribution of individual nanorods is represented in Figures 3(c) and (d) which was found to be in the range of 20–30 nm and 110–140 nm, respectively.

**Luminescence Studies**

The excitation spectrum of Ce³⁺ (5 at.%) sensitized YPO₄ doped with Tb³⁺ (5 at.%) monitored at 543 nm is presented in Figure 4. The excitation spectrum consists of two absorption peaks at 270 nm and 310 nm. The first peak is associated with a 4f−5d transition in Ce³⁺ from the ²F₅/₂ ground state of 4f to the excited states level of 5d and later peak is assigned to the 4f-4f transition of Ce³⁺.
Upon excitation at 270 and 310 nm, nanorods exhibit strong green emission. The PL emission spectra shows emission bands at 489 (\(\text{D}_1 \rightarrow \text{F}_2\)), 543 (\(\text{D}_1 \rightarrow \text{F}_3\)), 587 (\(\text{D}_1 \rightarrow \text{F}_4\)) and 621 (\(\text{D}_1 \rightarrow \text{F}_5\)) nm (Figure 5(a) and (b)) due to Tb\(^{3+}\). Among these transitions, the strongest emission was observed at 543 nm due to the magnetic dipole transition. Upon excitation at 270 nm, a broad emission peak was observed at \(\sim 360 \text{ nm}\) (Figure 5(a)) due to radiative transitions from the d-level excited states of Ce\(^{3+}\) to its f-level ground state. Efficient energy transfer occurs from the Ce\(^{3+}\) ions absorption to the excited states of Tb\(^{3+}\). In this process of energy transfer, Ce\(^{3+}\) ions act as the sensitizer while Tb\(^{3+}\) acts as the acceptor (Sarkar \textit{et al.} 2015; Paomei \textit{et al.} 2011; Sahu \textit{et al.} 2014a).

**Study of selective detection of Cu\(^{2+}\) metal ions**

The selectivity of YPO\(_4\):Ce\(^{3+}\)/Tb\(^{3+}\) nanorods towards various metal ions have been studied. Different metal ions viz. Ca\(^{2+}\), Cd\(^{2+}\), Co\(^{2+}\), Cu\(^{2+}\), Fe\(^{2+}\), Mn\(^{2+}\), Ni\(^{2+}\), Sr\(^{2+}\) and Zn\(^{2+}\) ions were treated with the nanorod solution (with a final concentration 0.5 mM of each case). The corresponding PL spectra are illustrated in Figure 6(a) and Figure 7(a) under respective excitation of 270 nm and 310 nm.

![Figure 4: PL excitation spectra of YPO\(_4\):Ce\(^{3+}\) (5 at. %)/Tb\(^{3+}\) (5 at. %) nanorods monitored at 543 nm emission.](image)

![Figure 5: PL emission spectra of YPO\(_4\):Ce\(^{3+}\) (5 at. %)/Tb\(^{3+}\) (5 at. %) nanorods under (a) 270 nm and (b) 310 nm excitation.](image)
nm wavelength, respectively.

It is clear that compared to other metal ions, Cu$^{2+}$ shows a strong quenching effect on the emission intensity of YPO$_4$:Ce$^{3+}$/Tb$^{3+}$ nanorods (approximately 89 % of the PL intensity of blank/bare solution decreases). Figure 6(b) and Figure 7(b) show the comparative PL emission intensities in the absence and presence of metal ions under 270 and 310 nm excitation respectively. However, in the presence of other cations such as Ca$^{2+}$, Cd$^{2+}$, Co$^{2+}$, Fe$^{2+}$, Mn$^{2+}$, Ni$^{2+}$, Sr$^{2+}$ and Zn$^{2+}$ have very less quenching effect on the PL intensity. This clearly indicates the selective nature of detection towards Cu$^{2+}$ ions.

To verify the detection sensitivity of YPO$_4$:Ce$^{3+}$/Tb$^{3+}$ towards Cu$^{2+}$ ions, different concentrations of Cu$^{2+}$ ions were
treated with the nanorod dispersion. PL spectra as a function of the different concentration of Cu$^{2+}$ ions under 270 and 310 nm excitation are shown in Figure 8(a) and Figure 9(a), respectively. A gradual decrease in the PL intensity of Tb$^{3+}$ ions was observed with increase in Cu$^{2+}$ ions concentration. In addition, quenching of the intensity of Ce$^{3+}$ ions also increases with an increase in the concentration of Cu$^{2+}$ ions (shown in Figure 8(a)).

To study the nature of PL quenching viz. static or dynamic nature, a Stern–Volmer relationship given below was used.

$$\frac{I}{I_0} = 1 + K_{SV}[Q]$$

\(I_0\) and \(I\) are the PL intensity of Tb$^{3+}$ ions from YPO$_4$:Ce$^{3+}$/Tb$^{3+}$ in the absence and presence of Cu$^{2+}$ ions,
respectively, $K_{SV}$ is the Stern–Volmer constant and $[Q]$ is the concentration of Cu$^{2+}$ ions in the solution. A linear response curve is observed against the concentration of Cu$^{2+}$ ions (0.01 – 0.75 mM) as seen in Figure 8(b) and Figure 9(b), indicating the dynamic nature of the PL quenching.

The limit of detection (LOD) is calculated using the formula:

$$LOD = \frac{3\sigma}{S}$$

where $\sigma$ is the standard deviation of the blank experiment and $S$ is $K_{SV}$, the slope of the calibration (S-V) plot. The calculated value is found to be ~19 μM (~1.21 ppm) at both excitation wavelengths.

Figure 10 shows the attachment of Cu$^{2+}$ ions on the surface of PAA functionalized YPO$_4$:Ce$^{3+}$/Tb$^{3+}$ luminescent probes. The probe and Cu$^{2+}$ ions interact through the capping agent, PAA. Cu$^{2+}$ ions are selectively bounded to free carboxyl groups (–COO$^-$) of PAA on the surface of the nanorods through electrostatic interaction (Sahu et al. 2014b; Sarkar et al. 2015). This enables an efficient energy transfer from the probe to Cu$^{2+}$ ions.

The possible energy transfer mechanism from Ce$^{3+}$ to Tb$^{3+}$ is schematically shown in Figure 11(a). Under 270 or 310 nm excitation corresponding to 4f-5d or 4f-4f transition of Ce$^{3+}$, energy transfer from the $^5D_{3/2}$ state of Ce$^{3+}$ to the excited states of Tb$^{3+}$ occurred. Later, vibrational relaxation takes place from the higher excited states to the lower $^5D_4$ and $^5D_3$ states of Tb$^{3+}$. Thereafter, radiative energy transfer occurs to various lower levels of $^7F_J$ ($J = 0 – 6$). Thus, a strong efficient emission of $^5D_{3/2} \rightarrow ^7F_{5}$, 543 nm in YPO$_4$:Ce$^{3+}$(5 at. %)/Tb$^{3+}$ (5 at. %) nanorods is obtained (Li et al. 2007).

In presence of Cu$^{2+}$, Figure 11(b), the
energy transfer from the \( ^{5}D_{3/2} \) states of Ce\(^{3+}\) also starts to the \( ^{1}D_{1} \) level of Cu\(^{2+}\) ions along with the energy transfer to Tb\(^{3+}\). The relaxation of Cu\(^{2+}\) ions from the excited states to the ground state occurs nonradiatively (Sarkar et al. 2015). Due to this energy transfer from the excited states of Ce\(^{3+}\) to the excited states of Cu\(^{2+}\) at the expense of resonance energy transfer to the excited states of Tb\(^{3+}\) leading to the decrease in intensity of Tb\(^{3+}\) emission. As the amount of Cu\(^{2+}\) increases, the transfer of energy from the Ce\(^{3+}\) to the Cu\(^{2+}\) excited states dominate over the transfer to Tb\(^{3+}\). This is also confirmed from the gradual decrease in the emission intensity of Ce\(^{3+}\) at ~360 nm (Figure 8(a)) and Tb\(^{3+}\) emission as the concentration of Cu\(^{2+}\) increases.

Figure 11 shows the photographs of YPO\(_{4}\):Ce\(^{3+}\)(5 at. %)/Tb\(^{3+}\) (5 at. %) nanorods solution in the absence and presence of Cu\(^{2+}\) ions before and after exposure to UV light. From the images, it is observed that the green emission of the nanorods disappeared with the addition of Cu\(^{2+}\) ions.

The stability of YVO\(_{2}\):Ce\(^{3+}\)/Tb\(^{3+}\) nanorods solution was carried out under 310 nm excitation for 18 h and the
photoluminescence emission intensity was measured every hour. Figure 13 illustrates the emission intensities of each measurement and it can be seen that there is no significant change in the intensity over the entire period of study. Thus, the particles are stable under the suspension in water with a calculated standard deviation of 0.06103.

**Lifetime studies**

PL decay dynamics is concentration independent parameter which is defined by decay lifetime, \( \tau = \frac{1}{k_r + k_{nr}} \), solely due to radiative \((k_r)\) and non-radiative \((k_{nr})\) probabilities. PL decay curves of 5 at.% Ce\(^{3+}\) sensitized YPO\(_4\):Tb\(^{3+}\) (5 at.%) in presence of different concentration of Cu\(^{2+}\) are shown in Figures 14 (a) and (b) with monitoring emission \( ^5\text{D}_4 \rightarrow ^7\text{F}_2 \) at 543 nm and respective excitation at 270 and 310 nm. The decay curves can be fitted to biexponential equation

\[
I(t) = I_1 e^{-\frac{t}{\tau_1}} + I_2 e^{-\frac{t}{\tau_2}}
\]

where \( I_1 \) and \( I_2 \) are intensities at different times and their corresponding lifetimes \( \tau_1 \) and \( \tau_2 \). The average decay lifetime can be calculated using the equation

\[
\tau_{av} = \frac{I_1 \tau_1 + I_2 \tau_2}{I_1 + I_2}
\]

Average lifetime values in the absence and presence of Cu\(^{2+}\) are given in Table 1. The lifetime of YPO\(_4\):Ce\(^{3+}\)/Tb\(^{3+}\) decreases with increase in Cu\(^{2+}\) concentration. This verified the dynamic nature of PL quenching phenomena is through energy transfer.
CONCLUSIONS

Re-dispersible Ce³⁺ (5 at. %) sensitized YPO₄ doped with Tb³⁺ (5 at. %) nanorods were prepared by polyol method using EG as reaction medium and PAA as capping agent. The nanorods show two strong excitation peaks at 270 and 310 nm respectively corresponds to spin-allowed 4f-5d and 4f-4f transitions of Ce³⁺. The nanorods show strong green emission at 543 nm corresponding to ⁵D₂→⁷F₃ of Tb³⁺. This is due to energy transfer from Ce³⁺ absorption to Tb³⁺ excited states. The nanorods show a selective detection of Cu²⁺ out of various metal ions and could quench upto 89 % of the emission intensity. It has been found that the PL intensity decreases with increase in the concentration of Cu²⁺ ions due to luminescence quenching. A linear response of the Stern-Volmer equation confirms the dynamic nature of PL quenching which is also justified from PL lifetime. Selective and sensitive detection has been studied under both excitations at 270 and 310 nm. A limit of detection (LOD) of 19 μM (~1.21 ppm) is found from both excitations. These nanorods could be useful as a luminescent probe for selective detection of Cu²⁺ ions in aqueous solutions.
REFERENCES


Li Q, Yam VWW. Redox luminescence switch based on energy transfer in CePO₄:Tb³⁺ nanowires. Angew Chem Int 2007;46:3486–3489.

Liang Y, Noh HM, Park SH, Choi BC, Jeong JH.


Luwang MN, Ningthoujam RS, Srivastava SK, Vatsa RK. Disappearance and recovery of luminescence in Bi$^{3+}$, Eu$^{3+}$-codoped YPO$_4$ nanoparticles due to the presence of water molecules up to 800°C. *J Am Chem Soc* 2011;133:2998–3004.


Sahu NK, Singh NS, Pradhan L, Bahadur D. Ce$^{3+}$ sensitized GdPO$_4$:Tb$^{3+}$ with iron oxide nanoparticles: A potential biphasic system for cancer theranostics. *Dalton Trans* 2014b;43:11728–11738.


Singh NS, Wangkhem R, Yaba T, Devi S, Luwang MN, Yaiphaba N, *et al.* Multicolour and nearly white light emission in YP$_{0.8}$V$_{0.2}$O$_4$:Sm$^{3+}$ nanorods: controlled energy transfer. *J Alloys Compd* 2017;726:1161–1167.


Wangkhem R, Singh NS, Singh NP, Singh SD, Singh LR. Facile synthesis of redispersible YVO$_3$:Ln$^{3+}$ (Ln$^{3+}$ = Dy$^{3+}$, Eu$^{3+}$, Sm$^3$) nanocrystals: Luminescence studies and sensing of Cu$^{2+}$ ions. *J Lumin* 2018;203:341–348.


Yahiaoui Z, Hassairi MA, Dammak D, Cavalli E, Mezzadri F. Tunable luminescence and energy transfer properties in \( \text{YPO}_4 \cdot \text{Tb}^{3+}, \text{Eu}^{3+}/\text{Tb}^{3+} \) phosphors. *J Lumin* 2018;194:96–101.

Zhu Y, Ni Y, Sheng E. Mixed-solvothermal synthesis and applications in sensing for \( \text{Cu}^{2+} \) and \( \text{Fe}^{3+} \) ions of flowerlike \( \text{LaVO}_4 \cdot \text{Eu}^{3+} \) nanostructures. *Mater Res Bull* 2016;83:41–47.

*Biomed Res J* 2018;5(2):74–89
Case Report

Odontogenic Fibroma of Maxilla: A Rare Clinical Entity

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The odontogenic fibroma (OF) is a rare benign tumor of mesodermal origin characterized by varying amounts of inactive looking odontogenic epithelium embedded in a mature, fibrous stroma. The lesion appears frequently involving the anterior region, when fibroma occurs in the maxilla, whereas they tends to be located in the posterior area, involving the premolar and molar areas, when fibroma occurs in the mandible. We are presenting a case of 36 year old female patient who had cheek swelling and facial disfigurement for 1 year. Biopsy was suggestive of odontogenic tumor. Complete excision was done transorally with sublabial approach and was histopathologically called out as benign odontogenic tumor consistent with an Odontogenic Fibroma. Patient was asymptomatic till 6 months of followup. Desmoplastic fibroma and intra-osseous fibrogenicmyxoma should be considered in the differential diagnosis. The tumor should be managed conservatively with enucleation and curettage.

INTRODUCTION

The odontogenic fibroma (OF) is a rare benign tumor of mesodermal origin characterized by varying amounts of inactive looking odontogenic epithelium embedded in a mature, fibrous stroma (Hammer et al., 1966). Odontogenic fibroma can be divided into central (intraosseous) and peripheral (gingival) types. The central odontogenic fibroma consists of collagenous fibrous connective tissue containing varying amounts of odontogenic epithelium (Allen et al., 1992). The central odontogenic fibroma occurs in the mandible and in the maxilla with equal frequency. The lesion appears frequently involving the anterior region, when fibroma occurs in the maxilla. On the other hand, the lesion tends to be located in the posterior area, involving the premolar and molar areas, when it occurs in the mandible (Covani et al., 2005).

CASE REPORT

A 36-year old woman came with a complaint of left cheek swelling for 1 year, which had an insidious onset and was painless and gradually progressive in

Key words: Odontogenic Fibroma, Gingiva, Retromolar trigone, CT scan, Enucleation.

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nature, with difficulty in chewing and opening mouth. Examination of face revealed left sided single cheek swelling, measuring approximately 10 cm × 8 cm, extending from left angle of mouth medially till angle of mandible laterally, whereas superiorly it was 1 cm below infra-orbital margin and inferiorly till lower border of mandible. The swelling was mobile and non-tender. Oral cavity examination revealed left sided large irregular mucosa covered swelling.
molar trigone area (Figure 1). Computerized tomography (CT) scan showed large multilocular lesion with calcification in the region of maxilla arising from left alveolar process with destruction and extending superiorly into the inferior part of the left maxillary sinus (Figure 2). Biopsy indicated benign odontogenic tumor consistent with odontogenic fibroma. The patient underwent excision of the tumor via sublabial approach. Pre-operatively, the tumor was found to be well encapsulated, with origin from left premolar and first molar, and going superiorly in maxillary sinus area. Premolars and first molar teeth, along with large expansile outer part, were therefore removed as single specimen and remaining part involving maxillary sinus was removed separately. Drilling was done in maxillary antrum to ensure complete removal of the tumor, and was sent as another specimen (Figure 3). Final histopathology report indicated benign odontogenic tumor consistent with odontogenic fibroma (Figure 4). The ideal time for follow-up, to look for any recurrence, in such cases is at least 6 months post-op. In this particular case, the patient did not report any fresh complaint during the last follow-up visit, six months after the operation (Figure 5).
DISCUSSION
The reported incidence of odontogenic tumor is 3–7% of all odontogenic tumors (LeDoussal et al., 1981). It is subclassified by the WHO into two subtypes: (1) the WHO variant (epithelial rich/complex type) and (2) the non-WHO variant (epithelial poor/simple type) (Barnes et al., 2005). The WHO variant, considered a mesenchymal odontogenic tumor is comprised of two distinct cell types, a fibrous element and an epithelial element that resembles the dental lamina or the rests that are seen in normal dental follicles. While, non-WHO variant lacks an epithelial component, being a monomorphic fibroblastic tumor purported to be of odontogenic mesenchymal origin (Lewis et al., 2011). There is no clear cut separation between the two types at the microscopic level in that one of the patterns may be predominant with the other being present focally. Our case belonged to the non-WHO variant of odontogenic fibroma (i.e., epithelial poor/simple type). More commonly seen in the second to fourth decades, and found to arise more often in the anterior regions of the gingiva. The radiographic appearances are similar to other peripheral odontogenic tumors such as traumatic bone cyst, ameloblastoma, odontogenic cyst and central giant cell granuloma (Ramer et al., 2002). Main treatment modality for odontogenic Fibroma is enucleation and curettage with no tendency for recurrence (Eversole et al., 2011).

CONCLUSION
Odontogenic Fibroma is a benign mesenchymal tumor with good prognosis. Though rare it should be considered in the differential diagnosis of various jaw swellings. Correct diagnosis and management can be done with multidisciplinary approach involving otolaryngologist, dental surgeon, radiologist and pathologists.

CONFLICT OF INTEREST
There is no conflict of interest regarding this case report.

ETHICS CLEARANCE
Ethics clearance was obtained from the Ethics Committee of Government Medical College and Hospital, Chandigarh, India. All procedures were carried out after taking informed and written consent from the patient.
REFERENCES
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