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Disulfiram and Its Copper Chelate Attenuate Cisplatin-Induced Acute Nephrotoxicity in Rats Via Reduction of Oxidative Stress and Inflammation

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Abstract
The use of cisplatin (CP) in chemotherapy of resistant cancers is limited due to its dose-dependent nephrotoxicity. Disulfiram (DSF), the aversion therapy for alcoholism, has recently emerged as an anticancer and chemopreventive agent. Its anticancer activity is potentiated in the presence of copper. However, such use of copper leads to several adverse effects. In the present study, the protective effect of DSF and its copper chelate (Cu-DEDC) against CP-induced nephrotoxicity in rats was evaluated. Nephrotoxicity was induced by a single intraperitoneal injection of CP (5 mg/kg). The treatment groups included control (vehicle treated), CP (CP-treated), CP + DSF (CP followed by DSF), CP + DSF + Cu (CP followed by DSF and $CuCl_2$), CP + Cu-DEDC (CP followed by Cu-DEDC), and CP + AMF (amifostine pre-treated and CP-treated). The DSF, Cu-DEDC, and $CuCl_2$ were administered orally at 50 mM/kg/day dose for 5 days post CP injection. AMF served as a standard chemo protectant, administered intravenously 30 min prior to CP. The markers of oxidative stress, inflammation, and kidney function estimated on the 6th day revealed that both DSF and Cu-DEDC significantly attenuated the CP-induced rise in the serum/urine creatinine and blood urea nitrogen (BUN). The CP-induced rise in serum alkaline phosphatase (ALPase) was reversed by these drugs. Both drugs reduced the levels of malondialdehyde and nitric oxide (NO) in kidney tissues. These drugs reversed CP-induced depletion of SOD, catalase, and GSH in the kidneys. There was a significant reduction in the CP-induced TNF-α and IL-1β production along with prevention of histological alterations. Above observations indicate that DSF and Cu-DEDC may have significance as adjuvants to protect against CP-induced nephrotoxicity.

Keywords Cisplatin · $Cucl_2$ · Cu-DEDC · Cytokines · Disulfiram · Nephrotoxicity

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Introduction

Cisplatin (CP) is widely used as a chemotherapeutic agent in the treatment of several cancers including head, neck, testis, ovary, breast, bladder, esophageal, and cervical cancers. However, its clinical use is restricted due to its adverse effects like nephrotoxicity, ototoxicity, and neurotoxicity [1–4]. Accumulating evidences suggest a need for the development of therapeutic strategies to prevent the CP-associated organ toxicities while retaining its anticancer activity. Intravenous administration of amifostine (AMF) prior to CP injection is a currently available therapy against CP-induced nephrotoxicity. Therefore, research to identify and develop suitable nephroprotective adjuvants to chemotherapy is warranted.

Disulfiram (DSF) is in use since the last five decades as an aversion therapy for alcoholism [5]. Recently, DSF is re-emerging as an anticancer and chemopreventive agent for the treatment of various cancers [6, 7]. DSF has been reported

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PHYSICAL CHEMISTRY OF NANOCLUSTERS AND NANOMATERIALS

Eco-Friendly In Situ Fabrication of Reduced Graphene Oxide Gold Nanocomposites for Catalysis and Dye Degradation[1]

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Abstract—The invention represents a development of robust eco-friendly method use for water waste management and polluted water. The inadvertent role of peanut peels extract helps to simultaneously convert and form reduced graphene oxide gold nanocomposite (rGO@AuNCs) in single step. Fabricated nanocomposite was evaluated for its catalytic performance using reduction of 4-nitrophenol to 4-aminophenol as well as elimination of methylene blue (MB) and malachite green (MG) dyes from water. Graphene oxide (GO) and rGO@AuNCs, were synthesized using simplified approaches and preliminary characterization was done using UV–Vis spectrophotometer and Fourier transform infrared spectroscopy. Least concentration of rGO@AuNCs is required to eliminate MB and MG around 77 and 93%, respectively. Furthermore, surface morphology and elemental analysis of rGO@AuNCs confirm successful fabrication methods as well as X-ray diffraction pattern confirms the crystalline behavior of nanocomposite. The study illustrates an environment-friendly and cost effective in situ fabrication rGO@AuNCs from industrial agro waste for an environmental remediation.

Keywords: graphene oxide, industrial-agro waste, methylene blue, malachite green, 4-nitrophenol, environmental remediation

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INTRODUCTION

Single-layer of graphene oxide (GO) is usually produced by the chemical oxidation of graphite, which is a harsh chemical reaction in presence of H_2SO_4 and $KMnO_4$. Exfoliated graphite forms a stable dispersion in water and different organic solvents such as ethanol, dimethyl sulfoxide, etc. [1]. A synthesized material at nanoscale shows enormous structural and functional properties. These advancements in nanotechnology deals with the exploration and exploitation of nanomaterials with their synthesis, characterization, evaluation, etc. [2]. Conventional composite materials unable to show such efficient properties thought the nanocomposite owing to their unique desirability and surface, structural properties shows significant progress in 21st century. The significant aspect for exploring the research of the graphene-based nano composites is the yearning to combine the promising properties of graphene with other fundamental nanomaterials [3]. Applications and recent needs of energy and environmental remediation approaches as well as to check the possibilities attension has been made towards fabrication of graphene based nanocomposites [4].

Metal nanoparticles–graphene nanohybrid systems become highly important in catalysis and dye removal because of their large surface area, high electronic transport capacity and extraordinary chemical stability [5]. The interest in the use of graphene-based materials in the field of catalysis is due to the activity and stability of graphene-based catalysts through tailoring its structures/morphologies, catalytic performance, and design for synthesis, catalytic mechanisms [6]. Textile industries are using dyes in larger amount and their wastage is also been increasing, synthetic dyes are less costly but produces toxicity to aquatic animals and humans. The rate of degradation of dyes is much slower due to complex chemical structure and difficult in decomposition. Several methods have been reported previously for the treatment of dye bearing effluents, but they are generally inefficient for the complete removal of dyes. Adsorption and removal of dyes using metal nanoparticles–graphene nanohybrid is the method of choice for the treatment of waste water [7].

Peanut (*Arachis hypogaea*) is an important food crop grown in over 100 countries with a total produc-

[1] The article is published in the original.

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Design and development of thiolated graphene oxide nanosheets for brain tumor targeting

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ABSTRACT

The present investigation emphasizes on synthesis and characterization of thiol functionalized reduced graphene oxide (TrGO) as a novel platform for loading of anticancer drug methotrexate (TrGO-MTX), through amide bonding. Thiolation of graphene oxide (GO) was achieved by transesterification process. The introduction of sulfur containing chemical groups and the partial reduction of GO to TrGO were proven by analytical techniques. Thiol content was found to be 6.98 mM by Ellman's method in a quantitative manner. Furthermore, antineoplastic action of TrGO-MTX against human glioblastoma astrocytom U-373 MG cell line was studied, wherein TrGO-MTX demonstrated significant inhibition rate as compared with pure MTX.

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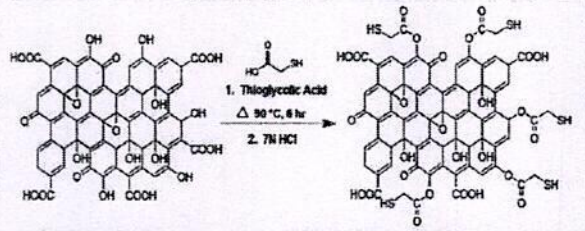
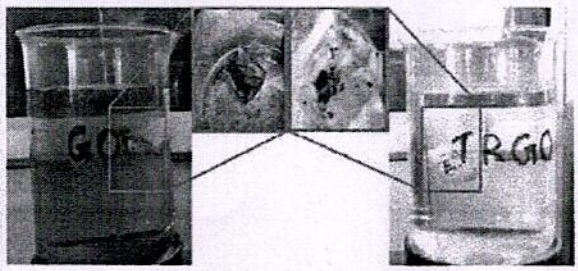
KEYWORDS
Brain tumors; graphene oxide; methotrexate; mucoadhesion; mucociliary clearance; thiolation

GRAPHICAL ABSTRACT



Graphene Oxide (GO) Thiolated Reduced Graphene Oxide (TrGO)



Mucoadhesive Property of GO and TrGo

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Graphene-based nanocomposites for sensitivity enhancement of surface plasmon resonance sensor for biological and chemical sensing: A review

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ABSTRACT

Surface plasmon resonance (SPR) offers exceptional advantages such as label-free, *in-situ* and real-time measurement ability that facilitates the study of molecular or chemical binding events. Besides, SPR lacks in the detection of various binding events, particularly involving low molecular weight molecules. This drawback ultimately resulted in the development of several sensitivity enhancement methodologies and their application in the various area. Among graphene materials, graphene-based nanocomposites stands out owing to its significant properties such as strong adsorption of molecules, signal amplification by optical, high carrier mobility, electronic bridging, ease of fabrication and therefore, have established as an important sensitivity enhancement substrate for SPR. Also, graphene-based nanocomposites could amplify the signal generated by plasmon material and increase the sensitivity of molecular detection up to femto to atto molar level. This review focuses on the current important developments made in the potential research avenue of SPR and fiber optics based SPR for chemical and biological sensing. Latest trends and challenges in engineering and applications of graphene-based nanocomposites enhanced sensors for detecting minute and low concentration biological and chemical analytes are reviewed comprehensively. This review may aid in futuristic designing approaches and application of graphenenous sensor platforms for sensitive plasmonic nano-sensors.

1. Introduction

From its inception, surface plasmon resonance (SPR) technique plays a prevailing role in the field of optical sensors. The SPR has evolved from a moderately impenetrable physical phenomenon to an optical tool that is widely used in chemical and biological investigations (Slavík et al., 1999; Yamamoto, 2008; Zeng et al., 2014) to study the binding events between two molecules of interest. Since its first intervention in 1990 by a Biacore group (GE Healthcare), the technology has established exponential growth in the last years, which is evident from the increase in the number of publications as well as the number of the methodology developed, till 2019, total of 24,148 papers are published as per PubMed search database (Fig. 1).

SPR technique is advantageous in terms of an *in-situ*, label-free methodwitheconomical and ease of fabrications as compared with the electrochemical and other methods (Merwe, 2001). The SPR phenomenon occurs in between the metal surface of sensorgram with specific molecule recognition element and a medium either vacuum/air or liquid. Whenever there is recognition of the particular molecule specific to the site/scaffold/receptor of this element, it results in the change of the surface of the metal, causing an angle shift as shown in Fig. 2(i). The shift resulted due to the changes in the refractive index (RI) at the surface of the metal. A usual SPR sensor either works in the angular interrogation mode or the wavelength interrogation mode. At the resonance wavelength or angle, the dispersion relation of the incident light matches with that of the surface plasmon, at which the reflectance shows a dip as seen in Fig. 2 (ii). The reflectance dip is attributed to the transfer of energy possessed by the photons incident to the surface plasmon and is more sensitive to the changes in the dielectric medium adjacent to the sensor surface (Ekgasit et al., 2004; Vasić et al., 2013).

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19-20

DEVELOPMENT AND CHARACTERIZATION OF SUBLINGUAL FILM CONTAINING ROPINIROLE HYDROCHLORIDE

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ABSTRACT

In the present work films of ropinirole hydrochloride were prepared by using polymers such as hydroxy propyl methyl cellulose (HPMC E-15) and polyethylene glycol (PEG-400) as plasticizers, by a solvent casting method, for treatment of Parkinson's disease. HPMC E-15 was used as film forming agent in the range of concentration 50 mg – 600 mg and PEG-400 was used as plasticizer in the range of concentration 0.3-1.0 mL for solvent casting method. The optimized concentration of film forming agent was 400 mg and plasticizer concentration was 0.7mL. By using optimized concentration, Ropinirole Hydrochloride mouth dissolving films (MDFs) were prepared by additionof other excipients. The formulated MDFs were evaluated for different physical characteristics like uniformity of weight, thickness, folding endurance, drug content uniformity, percentage elongation, and tensile strength, disintegration, *in vitro* drug release studies and provided agreeable results. The FTIR and DSC studies confirmed that no physicochemical interaction in between drug and excipients accured. Mouth dissolving film of Ropinirole Hydrochloride containing HPMC E-15 as polymer showed 97.66 % drug release at 30 min. Mouth dissolving films of ropinirole hydrochloride containing HPMC E-15 showed better tensile strength (70.56 ± 0.9 g/mm2), percentage elongation (33.33 ± 2.88 %), folding endurance (168± 2.081 numbers of folds), *in vitro* disintegration time (35± 3.511 sec.) and thickness (0.4± 0.17 mm).

Keywords: Ropinirole hydrochloride, Parkinson's disease, solvent casting method, tensile strength, mouth dissolving film

INTRODUCTION

Since time immemorial, oral drug administration is one of the most suitable and commonly accepted routes of delivery for most therapeutic agents. Conventionally, oral formulations refer to tablets, capsules and liquid preparations which are taken orally, swallowed and transit through the gastrointestinal tract (GIT) for post buccal absorption. For the last few years, investigators have been developing intraoral drug delivery systems (IODS) that can produce desirable drug exposure for optimum therapeutic effect. The intraoral formulations include fast dissolving dosage forms (tablets, films, wafers), sublingual tablets, buccal/gingival patches, microparticles, Periodontal fibres, solutions and sprays, chewing gums, dry powders, topical gels, topical pastes, bioadhesive tablets, topical ointments, local injections, dissolvable lozenge etc and more[1].

New developments of orally fast dissolving dosage form such as the fast dissolving tablet or fast dissolving films have advantages of ease of dosing and convenience of dosing in the absence of any fluid and water. Most of the existing fast-dissolving drug delivery systems are in the form of tablets and designed to dissolve or disintegrate in to the mouth within a few seconds or minutes, without any need to swallow or chew. The films overcome the risk of choking and the development of a fast dissolving film also brings an opportunity for a line extension into the market place; an extensive range of drugs (e.g., neuroleptics, cardiovascular drugs, antiasthmatic, analgesics, antihistamines, and drugs for erectile dysfunction have been developed)[2].

Recently, mouth dissolving film (MDF) is one of the most extensively used marketable product because of its quick onset of action, fast dissolution, and fast disintegration in a few seconds'. Therefore Mouth dissolving film is also widely used as local anesthetics for toothaches, headache, body pain, migraine, hypertension, oral ulcers, cold sores and treatment of psychological

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Synthesis of mesoporous alumina: an impact of surface chemistry on release behavior

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ABSTRACT

The present investigation describes the successful synthesis of mesoporous alumina (MeAl) nanoparticles for controlled drug delivery *via* a soft template route have been adopted using hexadecyltrimethyl ammonium bromide as template and aluminum chloride as precursor. The obtained Langmuir type II isotherm for MeAl showed P/Po 0.1 at 10 cm^3/G STP. The Brunauer-Emmett-Teller study revealed the formation of uniform morphology and mesoporous structure. The fourier transform infrared spectroscopy study confirmed the presence of characteristic peaks of mesoporous alumina. Elemental analysis demonstrated the substantial Al and O peak supported with nanosized crumb with cluster by field emission scanning electron microscopy. The transmission electron microscopy indicates wormhole strikingly inter connected pore system assigned to functionalized MeAl. X-ray diffraction pattern suggests the formation of γ-Aluminum oxide. The particle size and surface charge of synthesized MeAl were successfully analyzed to assess the surface charge. The drug loading was confirmed by spectroscopic study with eloquent extension in drug release was found to be 74.44% attributed to release by control manner. In present study, synthesized MeAl holds an excellent compassionate impact on particle size and exterior chemistry for sustained release of model drug.

KEYWORDS

Mesoporous; FESEM; adsorption; functionalization; particle characteristics

1. Introduction

Mesoporous Alumina (MeAl), a novel member of molecular sieve family kindled worldwide resurgence in the field of inorganic solid mesoporous materials. Porous material plays fundamental role in a variety of scientific and industrial operations such as adsorption, separation, host-guest encapsulation and catalysis etc (Liu et al. 2013). The architecture and remarkable properties of unique mesoporous structure of MeAl have fascinated ample attention in the former decades due to promising biomedical applications and rapid expansion in an area such as tissue engineering, DNA sequencing, photonics etc (Zhang et al. 2009; Biumen, Cheng, and Ramos 2007). In consonance to International Union of Pure and Applied Chemistry (IUPAC), pores are categorized as micropore, mesopore and macropore depends on their varying particle sizes(<2 nm, between 2 nm and 50 nm,> 50 nm) (Zdravkov et al. 2007). The nature of porous material may be inorganic, organic or possesses both properties with technological significance. The porous material represents capability to link with atoms, molecule or ions to load the solid, liquid or gaseous chemical entities (Zhao 2006). Based on above dominance, mesoporous material emerged as talented host for extensive range of companion molecules like proteins (Vinu et al. 2004; Vinu, Murugesan and Hartmann 2004) drugs (Regi, Ramila and Del 2001) and smaller biological molecules(Anderson, Rosenholm and Areva 2004). Conventionally, High-surface-area transition alumina or activated alumina have been used as a porous alumina. However, the limited performance of MeAl identified may be due to deactivation during catalysis have been by pore plugging or coke formation in micropores. Therefore, the requirement was to synthesize alumina having ordered, uniform and tunable pore diameter. Thus, the successfully synthesized alumina showed remarkable properties such as controlled porosity, high thermal and mechanical stability, chemical inertness and tunable surface chemistry has made MeAl as excellent host for large drug loading and controlled release in an area of biomedicine (Kim et al. 2003; Ramli and Saleh 2008). The swift evaluation of sol-gel approach during former two decades has drive electric breakthrough in deliberate synthesis of porous materials. Sol-gel is an inexpensive method serves straightforward tailor substitute for traditional synthesis method. In comparison to traditional procedure, this lenient method provides outcome of mixed oxides with low cost and enhanced homogeneity. The sol-gel method produced

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Fabrication and characterization of colon specific eudragit coated graphene oxide microsphere for sustained delivery of tramadol hydrochloride

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ABSTRACT

Present investigation reports a straight forward method for synthesis of graphene oxide (GO) followed by fabrication of graphene oxide microsphere (GMS) using water in oil (w/o) emulsification technique. For colon specific drug delivery, enteric coating is desirable, which was done using Eudragit S100 and characterized by Fourier transform Infrared Spectroscopy (FTIR). The surface morphology of fabricated microsphere was confirmed using scanning electron microscopy (SEM). Drug loaded microspheres demonstrated a high payload capacity for model drug tramadol hydrochloride (TmH). The comparative *In-vitro* drug release showed around 72.37% release from uncoated microspheres, whereas eudragit coated microspheres retarded the drug release upto 10 h.

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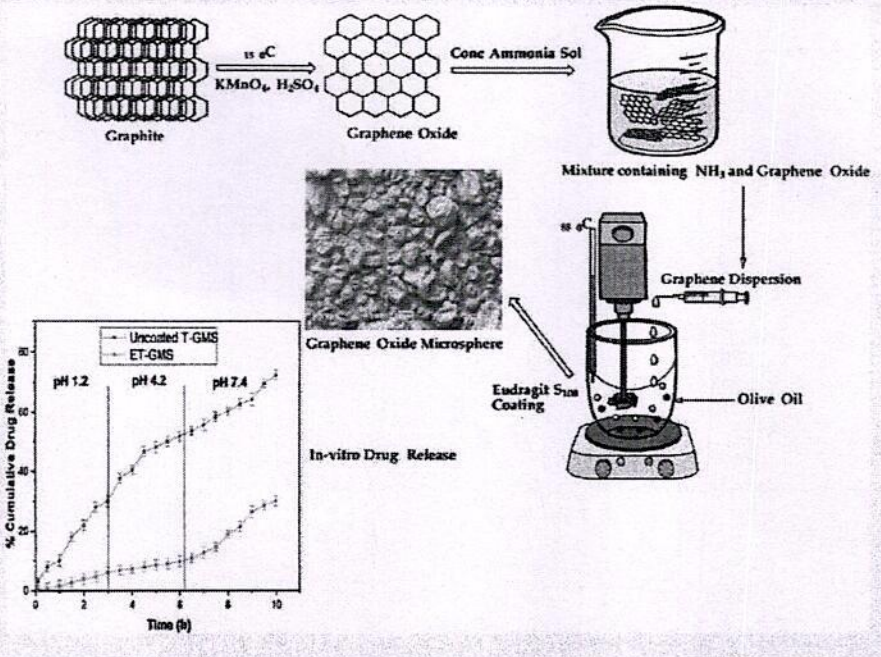
KEYWORDS
Graphene oxide; microsphere fabrication; colon targeted drug delivery system; irritable bowel disease



1. Introduction

An inflammatory Bowel disease (IBD) intensifies in many traumatic conditions such as ulcerative colitis, Crohn's disease, amebiosis, colonic cancer, etc. Specifically, IBD is most common functional disorder in colon region.[1] Due to many transportation barriers such as acid reach environment in stomach, differential pH condition and larger micro flora in small intestine, therapeutic agent is unable to reach at the colon site.[2] It seems to be very difficult for

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