H. R. Patel Institute of Pharmaceutical Education and Research, Shirpur

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RESEARCH ARTICLE

Preparation, Characterization and *In Vivo* Assessment of Repaglinide Nanosuspension for Oral Bioavailability Improvement

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Abstract: ***Aims and Background*:** The objective of the study was to improve the bioavailability of poorly soluble repaglinide (RPG) by preparing nanosuspension with poloxamer 188 using high pressure homogenization (HPH). The recent patents on nanocrystals (US20150337006A1) facilitated selection of drug and polymer.

***Methods*:** Suspensions containing dissimilar sized particles were prepared by ultrasonication and HPH. The prepared aqueous suspensions were lyophilized and then characterized. Further, the dried aqueous suspensions were evaluated for drug content, solubility, *in vitro* dissolution, oral bioavailability study and stability study.

***Results*:** RPG nanoparticles size, polydispersity index (PDI) and zeta potential were found to be 280.8 ± 15 nm, 0.279 ± 0.04 and - 25.81 ± 1.6mV, respectively. DSC and XRD results showed that RPG particles in aqueous suspensions were present in a crystalline state; however, RPG nanoparticles exhibited decreased lattice energy due to smaller particle size. Nanoparticles prepared by HPH exhibited significant improvements in solubility and dissolution rate. Oral bioavailability was found to be enhanced by 1.93 fold in comparison with that of plain RPG. The nanosuspension was found to be stable when stored at 5°C ± 3°C.

***Conclusion*:** The outcomes of the study revealed significant enhancement in dissolution rate and oral bioavailability of RPG due to size reduction to nano range by HPH.

Keywords: Repaglinide, nanosuspension, high pressure homogenization, solubility enhancement, dissolution rate enhancement, oral bioavailability enhancement.

1. INTRODUCTION

Bioavailability and dissolution rate governs the therapeutic success of a poorly soluble drug. Dissolution is the most important constraints for pharmacological action by attaining anticipated absorption of the drug in systemic circulation [1]. Numerous restrictions like growing the dose, increase in the frequency of administration and the considerable incidences of the side effects are associated with the poorly soluble drugs. Absorption of poorly water soluble drugs in the gastro intestinal fluids is governed by the dissolution rate of such drugs. Improvement in the solubility and dissolution rate of poorly soluble drugs thus improves the oral bioavailability.

Repaglinide (RPG) is a meglitinide derivative aimed at managing type 2 diabetes mellitus [2, 3]. RPG was developed in an effort to succeed in dealing with the adverse effects such as hypoglycemia, cardiovascular side effects, and secondary failure of the existing antidiabetic compounds [4]. The blood glucose lowering mechanism by RPG involves binding to a receptor site different from that of sulfonylurea and stimulating the release of insulin. Poor solubility with relatively low and variable bioavailability of RPG is a constraint for good therapeutic prospective [2]. High inter-individual inconsistency in plasma concentrations in clinical trials has been shown by RPG [5-7]. Dissolution rate and bioavailability enhancement of RPG is thus, a valued tactic for improving its therapeutic efficacy.

During last 2 decades, a novel tool for decreasing drug particle size has been established. Pure solid drug particles with a mean particle size below 1 µm are called as drug nanocrystals. Nanosuspensions are the liquid dispersions of the drug nanocrystals stabilized with surfactants or polymeric stabilizers [8]. Enhanced bioavailability is attained by nanosuspensions by improving the saturation solubility and dissolution rate of poorly soluble drugs [9]. Drug nanosuspensions can be prepared by top down process, bottom up process and the combination of these two processes. Amongst these technologies top down process involving HPH is commonly used because of the lack of organic sol-

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Physicochemical characterisation and anti-inflammatory activity of ayurvedic herbo-metallic *Tamra bhasma* in acute and chronic models of inflammation

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ABSTRACT

Current study was aimed to validate traditional claim of *Tamra bhasma* (*TB*) as an antinflammatory agent by investigating the preclinical anti-inflammatory activity of *TB*. Initially, *TB* was characterised by some traditional and modern parameters including scanning electron microscopy (SEM), energy dispersive x-ray analysis (EDAX) and X-ray diffraction (XRD). Subsequently, its anti-inflammatory activity was evaluated in carrageenan, cotton pellet and complete Freund's adjuvant (CFA) model. The % inhibition of paw oedema and granuloma tissue, blood and tissue related pharmacological evaluations were performed for assessment of anti-inflammatory activity. The SEM, EDAX and XRD confirmed presence of nanoparticulate copper as its sulfide or oxide form in *bhasma*. The changes produced by carrageenan and CFA in animals were reversed significantly in *TB* treated animals throughout the study. The results suggest that *TB* has a potential anti-inflammatory activity.

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KEYWORDS
Tamra bhasma; anti-inflammatory activity; physicochemical characterization; *Ayurvedic bhasmas*; preclinical activity

Introduction

The growing recognition of Ayurveda worldwide in recent years has drawn the attention of budding researchers as well as patients from modern medicine to alternative therapies. *Bhasmas* (incinerated ash) are unique metal/mineral/herbal based ayurvedic medicines that have been used to treat numerous chronic ailments since ancient times without any toxicity. Adopting unique set of procedures namely *Shodhan* (purification); removal of toxicity and *Maran* (incineration); produces ash [1] which is a key to safety and maximum therapeutic effect of *bhasmas*. Although *bhasmas* have been used in clinical practice since ancient times, their use is limited in the present era because of safety concerns [2]. In this regard, several recent studies proved they are nontoxic upto certain doses [3,4]. Furthermore, preclinically *bhasmas* possess haematinic [5], antidiabetic [6], anticataleptic, antianxiety, antidepressant [7] activities.

Tamra bhasma (TB) is an ash of metallic copper. According to the ancient literature, *TB* is used to cure *Pandu* (anaemia), *Udara* (ascites), *Svasa* (asthma), *Amlapitta* (hyperacidity), liver disorders, old-age disorders, leucoderma, arthritis [8], *Sotha* (inflammation) and *Sula* (pain) [9]. Several biological studies also reported that it have antihyperlipidemic [10], free radical-scavenging [11] and hepatoprotective activity [12].

To date, only two *bhasmas*, namely Muktashoukti [13] and Raupya [14] reported to possess anti-inflammatory activity. Copper is well known for its anti-inflammatory property stated in many books belongs to ancient cultures of India, Egypt and China [15]. Several published reports suggested that copper has anti inflammatory properties [15–17] and copper complexes of non-steroidal anti-inflammatory drugs (NSAIDs) preclinically exhibit enhanced anti-inflammatory activity and improve gastric protection [18,19]. As available literature supports anti-inflammatory claim of copper, its biological evaluation needs to be performed. The current study focused on pharmacological evaluation of *TB* to check its anti-inflammatory activity.

Materials and methods

Drugs and chemicals

TB was procured from Baidyanath, Nagpur, India. CFA and λ-Carrageenan were purchased from Sigma Aldrich. Rat TNF-α and IL-1β ELISA kits were procured from Krishgen Biosystems, Mumbai, India. All the other chemicals utilized in the study were of analytical grade.

Preparation, dose, and route of TB

The study doses of *TB* were calculated from its specified clinical dose (60–120 mg/day) as per Paget and Barnes, 1964 [20]. The therapeutic equivalent dose (TED) for animal is 5.5 mg/kg. Other study doses were 2.25-(TED/

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Controlled synthesis of blue luminescent graphene quantum dots from carbonized citric acid: Assessment of methodology, stability, and fluorescence in an aqueous environment

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HIGHLIGHTS

- Carbonized Citric acid forms self assembly structure at controlled condition.
- Graphene Quantum dots (GQDs) demonstrated efficient and stable fluorescence.
- GQDs has high luminescence at variable pH and Temperature.
- Reproducible fluorescence for prolonged period of time at ambient temperature.

ARTICLE INFO

Keywords:
Graphene quantum dots
Scientific microwave
Blue luminescence
Aqueous synthesis
Carbonization

ABSTRACT

The present investigation deals with a comparative assessment of various techniques for the synthesis of blue luminescence Graphene Quantum Dots (GQDs) using various equipments like furnace, domestic microwave synthesiser and scientific microwave synthesiser using citric acid as a precursor. A bottom–up method was adapted to develop photoluminescent (PL) GQDs and assessed for luminescence intensity of GQDs at different environmental conditions. The methodology requires very less concentration of NaOH to disperse GQDs. The present approach is advantageous over other conventional organic solvent mediated synthesis, as it requires less time, easy to reproduce and disperse in water, furthermore it produces stable fluorescence for a longer period of time at ambient temperature conditions. The synthesized GQDs are primarily characterized by UV for detection of the fluorescence intensity and simultaneously Ultraviolet–Visible (UV–Vis) spectroscopy and Fourier Transform Infra Red (FTIR) Spectroscopy to assess the up conversion from the precursor molecule. Apart from these techniques, Particle Size and Zeta Potential, Scanning Electron Microscopy (SEM), Elemental Analysis (EDX), Raman Spectroscopy and Fluorescence spectrophotometry were used to characterise synthesized GQDs.

1. Introduction

From last few decades when the nanotechnology starts exploring at the edge; becoming a new area that represents small sized materials, structures, devices, and systems. Nanometer scale size ranging between 1 and 100 nm is considered the most promising application in nano-medicine and other technical approaches [1]. Novel technical aspects can be possible with help of Nanomaterials to produce an efficient system with wide range of applications such as drug delivery systems; performance based medical devices, diagnostic materials, etc. [2,3].

The demand of nanomaterials has increased in recent years, due to their unique properties and structural features. The application area is going to increase day by day with varying its phases or in different types of areas such as catalysis, biomedical, drug delivery and many more areas are still exploiting. Few of these materials includes the carbon-based luminescent nanomaterials (CLNMs), carbon quantum dots (CQDs) [4], nanodiamonds [5], Carbon nanotubes (CNTs) fragment and surface functionalized CNTs [6,7], Graphene quantum dots (GQDs) to name a few, are exploring more due to low toxicity, high luminescence, robust material, chemically inertness and ease for

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Mixed micelles for bioavailability enhancement of nelfinavir mesylate: *In vitro* characterisation and *In vivo* pharmacokinetic study

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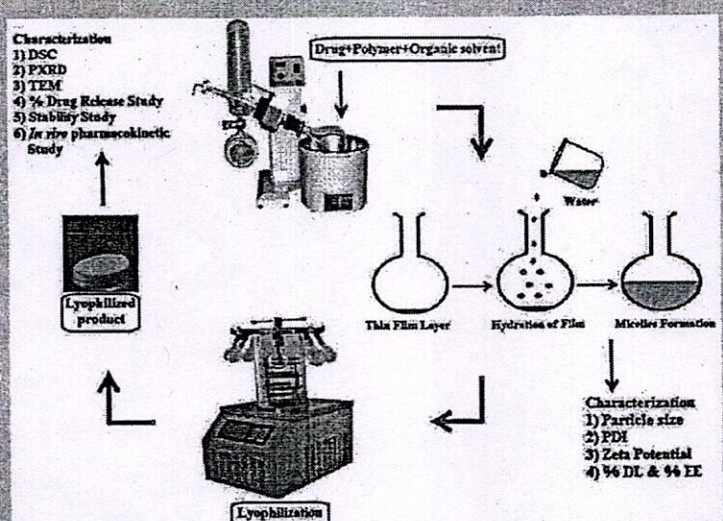
ABSTRACT

The present investigation deals with the fabrication of Nelfinavir mesylate loaded mixed micelles (NFM-MM) to enhance its oral bioavailability. NFM is a Human Immunodeficiency Virus-1 protease inhibitor having poor oral bioavailability and pH-dependant aqueous solubility leading to frequent dosing. Mixed micelles of Pluronic F127 and D-α-tocopherol polyethylene glycol 1000 succinate were prepared by thin film hydration technique. Results of *in vitro* characterisation showed that NFM-MM exhibited particle size 104.1 nm, polydispersity index (PDI) 0.127, zeta potential −10.6 mV, % entrapment efficiency 99.76 ± 1.20 and % drug loading 19.51 ± 1.02. DSC and P-XRD studies confirmed that NFM was encapsulated inside the mixed micelles. The *in vitro* release studies revealed that NFM-MM showed sustained release for upto four days. These mixed micelles were spherical or elliptical in shape as revealed by TEM study. On oral administration of NFM-MM; the relative bioavailability was enhanced about 1.94 fold as compared to NFM suspension. Thus, it can be concluded that PF127/TPGS mixed micelles can be used as a promising delivery system for NFM with increased bioavailability and sustained drug release.



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KEYWORDS
Nelfinavir mesylate; Pluronic F127; TPGS; mixed micelles; bioavailability enhancement

Introduction

World Health Organisation reported that approximately 35 million humans have died of HIV until 2016 and millions are still dwelling with this dreadful virus. The number of newly registered cases every year is stagnant despite the available treatment like highly active antiretroviral therapy (HAART) and efforts taken by the government organisations [1]. However, the biggest challenge for HAART is that the virus remains dormant to ARVs as it generates intracellular and anatomical reservoirs. Also, poor bioavailability of ARVs is a reason for the failure of HIV treatment [2].

NFM, a mesylate salt form of nelfinavir, is a synthetic antiviral agent [3]. NFM inhibits the HIV viral proteinase enzyme which inhibits gag-pol polyprotein bifurcation, ensuing in a non-infectious, undeveloped viral particle [4]. As per the Biopharmaceutical Classification System (BCS), NFM belongs to class IV (drugs with both low permeability and solubility). It is highly lipophilic, almost insoluble at pH 3.5 and 7.4 and non-ionisable in water [5]. The usual dosing regimen of NFM by conventional

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ORIGINAL RESEARCH

Performance overview of an artificial intelligence in biomedics: a systematic approach

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Abstract Artificial intelligence and technological advancements are exceptionally influenced the entire society and mankind. Unprecendented and extensive use of social media, mobile phones and the internet has resulted in accumulation of huge amount of data. Most of this big data are available in unstructured form and it is beyond the capability of traditional systems to manage, maintain, supervise, keeping and analyse the data within a limited time span. Effective analysis and interpretation of health care data provides new insights in the condition of patients and suggest the most appropriate treatment opportunities. Discovery and invention of vital information in medical data helps the health care professionals to arrive at appropriate clinical decisions and improvement of quality of life in a variety of patients. In this article, we have discussed various issues and addressed them with the updated information on big data sources, big data management, big data processing and big data analysis through various tools and techniques. We have also analysed and interpreted the recent applications and advancements in artificial intelligence and big data in the health care technology and m-Health domain.

Keywords Artificial intelligence · Big data · Big data analytics · Health care · m-health · Machine learning

1 Introduction

Artificial intelligence (AI) is a branch of Computer Science and Engineering that deals with the computational understanding of intelligent behaviour and the creation of artefacts exhibiting such behaviour [61]. The main idea of AI suggests the capability of learning and reasoning through a computerized system [23]. AI has the capability to analyse the complex medical data. It involves an understanding of mechanisms of intelligent behaviour and thought along with their personification in machines [23, 61]. As, AI finds the solutions of complex problems through the use of judgmental knowledge, it can contribute to medical practice. The use of various AI tools and techniques implies the organization of knowledge in such a way that resembles the reasoning techniques of an intelligent human [66]. It is evident that there is a possibility of efficient analysis of medical data and making diagnostic predictions through AI [44, 61, 68]. AI is used in clinical setting either as clinical decision making expert systems or as a knowledge based systems implanted within laboratory instrumentation. Efforts have been made to develop the software architectures that imitate human intelligence [56].

Artificial neural networks, fuzzy logic systems and Bayesian belief networks are AI techniques that involve mathematical models based on human thinking and neuronal architectures. Rather than just making an assumption based on statistical distributions, AI tools generates the

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Fabrication and In-vitro Drug Release Characteristics of Magnetic Nanonanocellulose Fiber composites for efficient delivery of Nystatin

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Abstract

In the present study, one pot fabrication process was used for the synthesis of magnetic nanocellulose fiber composite (MCFNCs), wherein *In-situ* co-precipitation methodology contains reaction of iron with ammonia in controlled temperature environment and cellulose fibers acts as a capping and stabilizing agent. The crosslinked cellulose fibers helps to dissociate Fe ions and avoid aggregation during the nucleation stages. The Nystatin (Nyst) was used as a model drug for studying the release characteristics of MCFNCs. The preliminary confirmation was done by comparing the FTIR spectra of synthesized MCFNCs with its precursor. The fabricated MCFNCs was characterized by X-ray Diffraction, Vibrating Sample Magnetometry, Particle Size, etc. The surface morphology and internal structure were identified by Scanning and Transmission Electron Microscopic observation of respective samples. It shows porous aggregated structure of synthesized nanocellulose, BET surface area and BJH pore size was determined simultaneously and found to be 13.42 m^2/g and 104.48 Å respectively. Due to the porous nature of nanocellulose fiber, it has high loading capacity i.e. around 17.8% amongst porous material category. *In-vitro* drug release characteristics of Nyst loaded MCFNCs compared to pure drug showed sustained deliver for up to 8h time period. The Antifungal activity was evaluated on *Candida Albicans* and showed prominent inhibitory activity. The biocompatible nature of synthesized nanocomposites obtained from the natural nanocellulose fiber has a huge prospective in magnetically guided drug delivery in various parasitic diseases and have a potential of biomedical applications.

Keywords: Nanocellulose Nanofiber, Nanocomposites, Antifungal Activity, Controlled Release, Drug Delivery System

1. Introduction

Nanocellulose based fibers containing Iron oxide composites have gained significant interest in recent years due to interim potential pharmaceutical and bio-medical applications by virtue of their biocompatibility and biodegradability [1, 2]. Nanocellulose based magnetic composites find more promising application as antifungal and antimicrobial activity when studied in combination with silver nanoparticles [3, 4], agents for a hyperthermia based killing of parasites [5], drug delivery [6], vectors for magnetically-assisted active targeting in diseases such as cancer [7, 8], etc. The impressive characteristics of nanocellulose fibers have increased its relevance in different fields due to high specific surface areas and aspect ratio

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Development of graphene-drug nanoparticle based supramolecular self assembled pH sensitive hydrogel as potential carrier for targeting MDR tuberculosis

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ABSTRACT

The *Mycobacterium tuberculosis* (MTB) resides in mononuclear phagocytes (macrophages) hence selective targeting at the molecular level using Graphene Oxide (GO) Air Dried Hydrogel (ADH) is investigated in present investigation. The GO has capability to form supramolecular self assembly, due to $\pi - \pi$ stacking and hydrogen bonding interactions between surface groups of GO and oppositely charged drug molecule in presence of water. The hydrogel was fabricated using GO and Para-aminosalicylic acid (PAS) in solution phase. The fabricated hydrogel was lyophilized to obtain air dried hydrogel (ADH). The ADH showed potent antimicrobial activity and *in-vitro* cytotoxicity against *S. Aureus* and *E. Coli*, and MCF –7 cells respectively. The Alamar blue assay demonstrated the invasive characteristics of ADH in MTB (H37Rv). From the results obtained so far we lead to conclude that ADH is more invasive compared to the equivalent amount of pure PAS.

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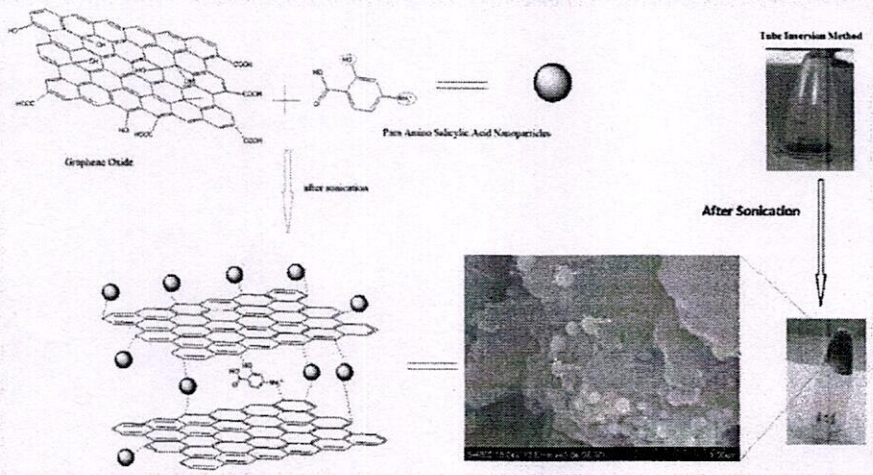
KEYWORDS
Tuberculosis; macrophages; supramolecular hydrogel; antitubercular activity; para amino salicylic acid; cytotoxicity



Introduction

Tuberculosis (TB) is contributing major cause of death amongst global health population Smith [1]. It was considered diseases of the past but eventually about 30% of the global population are affected with TB. The world wide diseases burden comprises major causes of morbidity and mortality is related to TB [2]. It is a chronic, contagious [3], airborne [4], prototypic [5] and fatal respiratory bacterial infection. TB is caused by the rod-shaped, obligate [6], non–spore-forming aerobic bacterium [7]. In 1993, World Health Organization (WHO) declared that TB is a global threat for health community [8].

'Super Carbon' denotes the potential applications of Graphene, it is one-atom thick honeycomb lattice structure, two-dimensional (2D) sheet of carbon atoms and is considered as the potential revolutionary material with electronic potential of zero band gap semimetal [9]. Graphene Oxide (GO), also known as graphitic acid, was discovered long time back [10]. The GO has large number of

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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-

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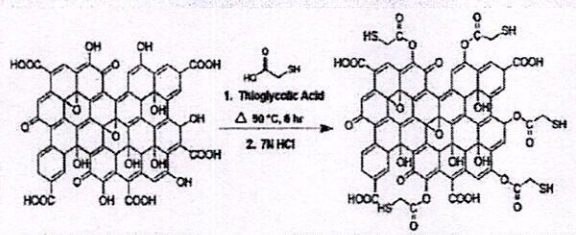
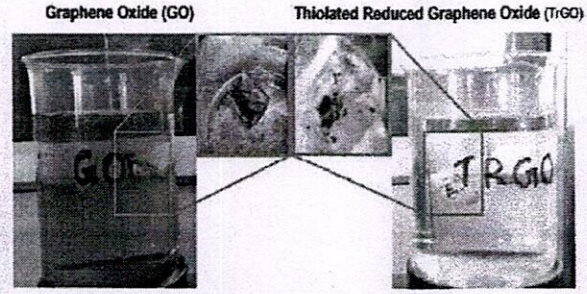
Brain tumors; graphene oxide; methotrexate; mucoadhesion; mucociliary clearance; thiolation

GRAPHICAL ABSTRACT



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



Mucoadhesive Property of GO and TrGo

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Color versions of one or more of the figures in the article can be found online at www.tandfonline.com/gpom.

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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 grapheneous 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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