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

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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 anti-inflammatory 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.

ARTICLE HISTORY

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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-1 β 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/

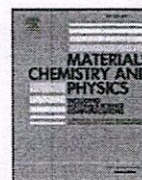




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Controlled synthesis of blue luminescent graphene quantum dots from carbonized citric acid: Assessment of methodology, stability, and fluorescence in an aqueous environment



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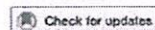
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Development of graphene-drug nanoparticle based supramolecular self assembled pH sensitive hydrogel as potential carrier for targeting MDR tuberculosis

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ABSTRACT

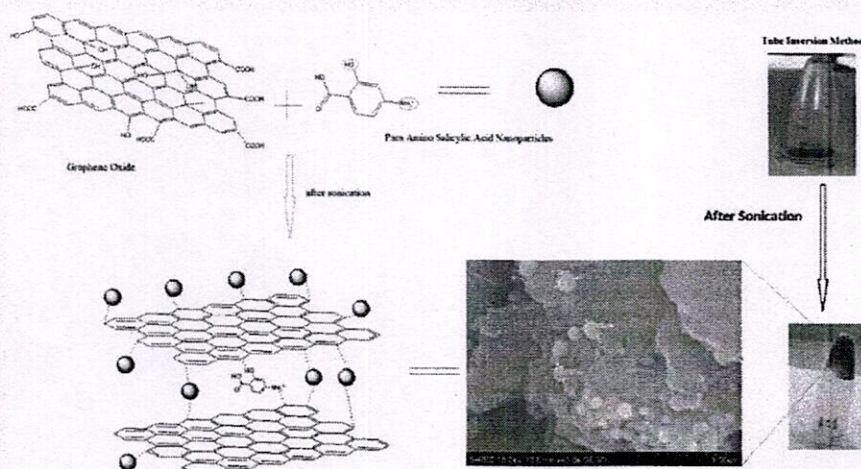
The *Mycobacterium tuberculosis* (MTB) resides in mononuclear phagocytes (macrophages) hence selective targeting at the molecular level using Graphene Oxide (GO) Air Dried Hydrogel (ADH) is investigated in present investigation. The GO has capability to form supramolecular self assembly, due to $\pi - \pi$ 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

Shraddha I. Khairnar¹ · Umesh B. Mahajan¹ · Kalpesh R. Patil² · Harun M. Patel³ · Sachin D. Shinde¹ · Sameer N. Goyal^{1,4} · Sateesh Belemkar⁵ · Shreesh Ojha⁶ · Chandragouda R. Patil¹

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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-DEDIC) 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 CuCl₂), CP + Cu-DEDIC (CP followed by Cu-DEDIC), and CP + AMF (amifostine pre-treated and CP-treated). The DSF, Cu-DEDIC, and CuCl₂ 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-DEDIC 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-1 β production along with prevention of histological alterations. Above observations indicate that DSF and Cu-DEDIC may have significance as adjuvants to protect against CP-induced nephrotoxicity.

Keywords Cisplatin · CuCl₂ · Cu-DEDIC · 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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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 astrocytoma U-373 MG cell line was studied, wherein TrGO-MTX demonstrated significant inhibition rate as compared with pure MTX.

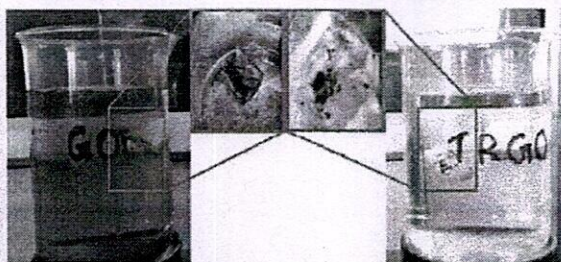
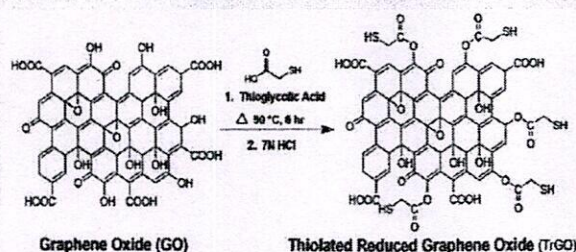
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Brain tumors; graphene oxide; methotrexate; mucoadhesion; mucociliary clearance; thiolation

GRAPHICAL ABSTRACT



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 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 (Slavik 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 method with economical 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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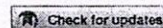
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Synthesis of mesoporous alumina: an impact of surface chemistry on release behavior

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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 cm³/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; Biemen, 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

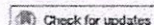
companion molecules like proteins (Vinu et al. 2004; Vinu, Murugesan and Hartmann 2004) drugs (Regi, Ramila and Del 2001) and smaller biological molecules (Anderson, Rosenholm and Areva 2004). Conventionally, High-surface-area transition alumina or activated alumina have been used as a porous alumina. 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

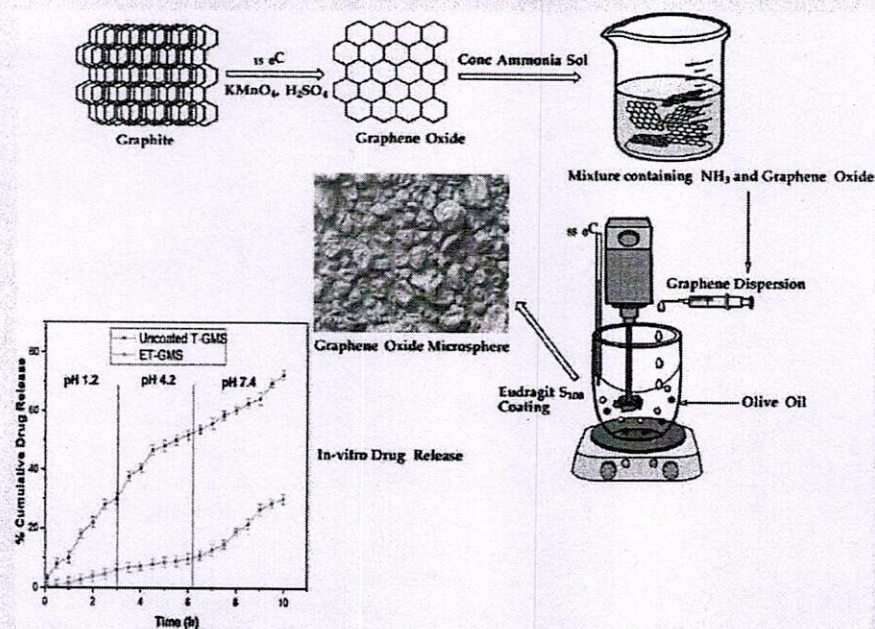
Present investigation reports a straight forward method for synthesis of graphene oxide (GO) followed by fabrication of graphene oxide microsphere (GMS) using water in oil (w/o) emulsification technique. For colon specific drug delivery, enteric coating is desirable, which was done using Eudragit S100 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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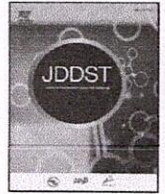
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Fabrication of efavirenz loaded nano-formulation using quality by design (QbD) based approach: Exploring characterizations and *in vivo* safety

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ABSTRACT

Quality by design (QbD) approach was practically applied in fabrication of nanostructured lipid carrier (NLC) encapsulating efavirenz (EF) to ensure the quality in product. Initially, risk factors were categorized based on risk priority number (RPN) using risk identification and assessment tools. A central composite rotatable design (CCRD) was employed to assess the influence of critical process parameter (CPP) (pressure of high pressure homogenizer) and critical material attributes (CMAs) (combination of solid lipid and oil; combination of stabilizers) on responses such as particle size, dispersity and entrapment efficiency. ANOVA was applied to evaluate the data for confirmation of statistical significance ($p < 0.05$). The optimum formulation was decided by setting criteria of responses to achieve desired quality product. This formulation was subsequently lyophilized to evaluate solid state characterization. TEM shows spherical particle shape of NLC. The transformation in amorphous state of NLC from crystalline EF was observed by DSC and PXRD. Lack of molecular interactions and intermolecular hydrogen bonding with lipidic atmosphere revealed by FTIR and ¹HNMR respectively. *In vitro* drug release 91.21% was obtained at the end of 24 h with Higuchi-matrix mechanism. *In vivo* pharmacokinetic studies improved relative bioavailability 2.95 fold with lower liver toxicity of EF encapsulated in NLC. In conclusion, QbD based approach clearly proved its usefulness to build quality in product resulting high drug encapsulated potential nanocarrier to enhance bioavailability and confirms safety of EF-NLC with promising acceptable criteria.

1. Introduction

Efavirenz (EF) is a leading drug molecule in the regimen of highly active antiretroviral therapy (HAART) for the treatment of human immunodeficiency virus (HIV). Orally active EF was official by FDA in 1998, belongs to the class of non-nucleoside reverse transcriptase inhibitors (NNRTIs) mostly prescribed to treat HIV-1 infection [1,2]. However, its pharmacokinetic is unpredictable when taken orally. This could be due to poor aqueous solubility, low gastro-intestinal (GI) absorption and rapid first-pass metabolism disappointing *in vivo* pharmacokinetic results [3]. Moreover, it is highly lipophilic (Log *P* = 5.4, intrinsic water solubility = 3–9 µg/mL) drug and categorized in biopharmaceutical classification system (BCS) class II (i.e. poor solubility and high permeability) results in low oral bioavailability of 40–45% [4,5]. The development of hepatotoxicity due to prolong administration is another increasingly important issue limiting the clinical applications [6–8].

Therefore, there is necessitate to develop a strategy which

modulates to improve solubility and bioavailability issues of EF. The few works on such issues have been reported. For example, EF loaded nanoemulsion improved bioavailability with dosage adjustable formulation for HIV therapy [9]. Nanosuspension containing EF prepared and characterized β-cyclodextrin (β-CD) based polymeric nanosuspension (PNS) to enhance aqueous solubility and dissolution rate as compared to pure drug [10,11]. The optimized Eudragit E100-Efavirenz loaded polymeric nanoparticles developed to increase in dissolution, drug distribution, and bioavailability, which ultimately implies better control over the therapeutic dosing; and physicochemical evaluation confirmed the formulation stability of nanoparticles [12,13].

SLNs prepared for lymph targeting delivery system to understand chylomicron blocking mechanism approach [14], and NLCs engineered for brain targeted delivery through intranasal route [4]. However, no reports have been addressed on issues of hepatotoxicity which develops on prolong oral administration of EF. Therefore, our prime objective was to develop the EF loaded NLCs to augment biopharmaceutical properties.

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Aloin protects against arsenic trioxide–induced myocardial membrane damage and release of inflammatory cytokines

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Naunyn-Schmiedeberg's Archives of Pharmacology **393**, 1365–1372 (2020)

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Abstract

Aloin exerts concentration-dependent pro-oxidant and antioxidant effects when tested in vitro. Such duality of effects has not been investigated through in vivo studies on aloin. We evaluated the effects of aloin at doses ranging between 1 and 125 mg/kg against the arsenic trioxide (As_2O_3)–induced cardiotoxicity in mice. As_2O_3 (5 mg/kg/day) was intraperitoneally administered for 10 days. Aloin was administered through oral gavage at 1, 5, 25, and 125 mg/kg/day. As_2O_3 induced rise in ST height and QT interval in ECG, increased oxidative stress, and depleted the antioxidative defense. As_2O_3 increased inflammatory cytokine concentrations in the heart. Aloin dose dependently inhibited the As_2O_3 -induced cardiotoxicity. There was no evidence of increased oxidative stress in the low-dose aloin-treated mice receiving As_2O_3 . Our results indicate that aloin possesses cardioprotective potentials and its pro-oxidant effects are not evident in vivo at tested doses.




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Heterogeneous surface architected metal-organic frameworks for cancer therapy, imaging, and biosensing: A state-of-the-art review



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ABSTRACT

With recent progress in inorganic material based nanoplateforms for cancer therapy and imaging, multiple nano vehicles have been developed and evaluated. These recent advancements in material science led to the development of metal organic frameworks (MOFs) and nano MOFs (nMOFs) as the potential and versatile delivery platforms for cancer theranostic. With a vast amount of ongoing research on MOFs, various surface architected MOFs for with variable properties have been developed and tested. The concept of subcellular targeted therapy of cancer has also been employed using MOFs which demonstrated significantly enhanced anticancer therapy. These MOFs have been developed in a way to provide them stimuli-responsive drug release property which can be utilized for externally guided therapy of cancer. Apart from cellular and subcellular targeted platforms and stimuli-responsive platforms, MOFs have also been explored in the field of bioimaging and biosensing. Multiple types of biosensing platforms based on MOFs and nMOFs have been proposed for biosensing of biomolecules related to cancer for sensing and early detection. The bioimaging probes based on MOFs have been employed for multiple diagnostic platforms. The review gives the recent updates for the abovementioned topics along with the toxicity aspects of MOFs for human use. The review overall gives a detailed overview of research done to date in the field of MOFs based nanoplateforms for cancer theranostics.

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Development of amine-functionalized superparamagnetic iron oxide nanoparticles anchored graphene nanosheets as a possible theranostic agent in cancer metastasis

Mahesh P. More^{1,2} · Prashant K. Deshmukh¹

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Abstract

The major objective of the present investigation was to assess the targeting potential of a designed system for breast cancer at metastatic phases with imaging ability. In a nutshell, we have developed surface-engineered graphene oxide (GO) nanosheets by covalent linking with amine-functionalized iron oxide nanoparticles (IONPs) (GOIOIs). Gefitinib (Gf) was selected as a model drug and entrapped in between exfoliated GO sheets (GOIGF) via π - π^* stacking before functionalization with IONPs. Preliminary characterization of GO, IONPs, GOIOI, and GOIGF was performed using UV-visible and Fourier transform infrared spectroscopy. Scanning and transmission electron microscopy studies confirmed successful surface engineering of GO with IONPs. The in vitro drug release study demonstrated sustained release of Gf. The magnetic behavior of IONPs and GOIOI demonstrated a sigmoidal-shaped hysteresis loop with superparamagnetic properties. The in vitro cell cytotoxicity assay was carried out on MDA-MB-231 breast cancer adenocarcinoma cell lines. The cell cytotoxicity assay showed 61.18% inhibition of cell growth with 30 ppm concentration containing 64% of the drug, whereas 100% of the pure drug revealed only 56% of inhibition. In the near future, GOIOI could be tailored further for theranostic research, especially for metastatic cancers.

Keywords Carbodiimide chemistry · Gefitinib · π - π^* stacking · MDA-MB-231 breast cancer adenocarcinoma cell lines · Magnetic graphene · Drug delivery

Introduction

Cancer is the most devastating disease in human; one out of six deaths is because of cancer, and the estimated death count may increase up to 13.1 million by 2030. It is the major cause of morbidity and mortality at present. In females, breast cancer is the leading site of cancer followed by cancer of the cervix and uteri [1].

Chemotherapy [2], gene therapy [3], radiotherapy [4], surgery [5], photodynamic [6], photothermal therapy [7], hyperthermia [8], or a combination thereof have been used for the treatment of cancer. Unfortunately, no effective therapy could successfully eradicate cancer to date. Theranostic nanomedicine is the latest approach under investigation, which could systemically provide simultaneous diagnosis and treatment at a specific site of infection. This could avoid interaction with normal cells, and only cancer tumor cells get destroyed using suitable carrier molecules [9]. The survival rate in cancer patients was dismal from 5 to 15% from developing to developed countries, respectively. Mutation of cancer cell specifically in the epidermal growth factor can be characterized to identify 50% of adenocarcinomas [10].

With the emergence of 2D materials, graphene has gained attention for its use in various biomedical applications including cancer. Graphene is an allotrope of carbon in the form of a single layer of atoms in a two-dimensional hexagonal lattice in which one atom forms each vertex [11, 12]. There are numerous methods available for the synthesis of graphene oxide (GO), an oxidized counterpart of graphene such as mechanical

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Medicinal Chemistry & Drug Discovery

Exploring Quinazolinones as Anticonvulsants by Molecular Fragmentation Approach: Structural Optimization, Synthesis and Pharmacological Evaluation Studies

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In recent years, design and synthesis of anticonvulsants effective against multiple seizures has attracted much attention of medicinal chemists. In an attempt to find novel anticonvulsants, herein we have reported structurally optimized sixteen different substituted quinazolinones explored through molecular fragmentation approach. The anticonvulsant activity of synthesized compounds was assessed by using predictable seizure models in mice. Two most promising analogues **8d** ($ED_{50} = 35.1$ mg/kg, MES, mice, *i.p.*; $ED_{50} = 41.5$ mg/kg, scPTZ test, mice, *i.p.*) and **8i** ($ED_{50} = 21.2$ mg/kg, MES, mice, *i.p.*; $ED_{50} = 32.4$ mg/kg, scPTZ test, mice, *i.p.*) exhibited broad spectrum anticonvulsant action in preclinical models of seizures. Com-

ound **8i** was also shown profound activity against pharmacoresistant limbic seizures produced in 6 Hz test. Most of the synthesized molecules exhibited moderate to high anticonvulsant activity in all seizure models with no symptoms of neurotoxicity and hepatotoxicity. We have also used *in-silico* protocol for prediction of physicochemical and pharmacokinetic properties of synthesized quinazolinones. The promising anticonvulsant activity of synthesized analogues, *ex-vivo* toxicity, *in-silico* molecular docking, physicochemical and pharmacokinetic predictions make us to anticipate emergence of synthesized quinazolinones as valid leads for the treatment of convulsive disorder.

Introduction

Epilepsy is a grievous and chronic neurological disorder affecting over 65 million individuals worldwide.^[1] An epileptic seizure is abnormal, excessive or synchronous neuronal activity in the brain.^[2] Around 1% of world population at any time is afflicted by epilepsy. This number increases every year by about 2.4 millions.^[3] Antiepileptic drugs (AEDs) therapy is mainstay of treatment for many patients with epilepsy. Development of new AEDs resulted into increased treatment options for patients with epilepsy but making drug selection a more complex task.^[4] Despite decades of research, it is still not clearly understood how AEDs act to control seizures. Unfortunately, at

a present time, there are no AEDs that are significantly effective at different forms and degrees of convulsive disorders.^[5]

Ligand based and random screening protocols have been used by many medicinal chemists to design and synthesize potential anticonvulsants.^[6-7] Due to insufficient knowledge and complex pathogenesis of human epilepsy; it is difficult to develop novel AEDs using routine methodologies. Ligand based protocol for design of anticonvulsants is focused on utilization of pharmacophores present in clinically effective and reported AEDs.^[8-9] Methaqualone and its synthetic analogues proved as good anticonvulsants. The chloro analogue of methaqualone has shown 1.5 times more potency than phenytoin in MES test and 10 times more efficacy than troxidone in scPTZ model.^[6,10-12] Some of the potent anticonvulsants with quinazolinone nucleus are depicted in Figure 1. The substitution of quinazolinone by electron withdrawing halogens at 6th, 7th or 8th positions resulted derivatives with optimum anticonvulsant activity and lower toxicity than phenytoin.^[12-13] Ralitolone is a recently reported AED, found effective in both MES and kindling models of seizures with rodents.^[14] Ralitolone has *N*-(2,6-dimethylphenyl)acetamide as pharmacophoric fragment and shown paramount importance in anticonvulsant potency. Retigabine is an anticonvulsant (ezogabine) approved by the United States Food and Drug Administration (USFDA) and/or by the European Medicines Agency (EMA) in 2011. Retigabine consists of *N*-(2-amino-phenyl)acetamide fragment as critical part of its structure and have vital role in its anticonvulsant activity.^[15] Careful incorporation of these pharmacophoric fragments from reported potent anticonvulsants into designed molecules may boost

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Topical Review

Recent advancements in bioprecursor derived graphene quantum dots: synthesis, characterization and toxicological perspectives

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Abstract

Graphene quantum dots (GQDs), impressive materials with enormous future potential, are reviewed from their inception, including different precursors. Considering the increasing burden of industrial and ecological bio-waste, there is an urgency to develop techniques which will convert biowaste into active moieties of interest. Amongst the various materials explored, we selectively highlight the use of potential carbon containing bioprecursors (e.g. plant-based, amino acids, carbohydrates), and industrial waste and its conversion into GQDs with negligible use of chemicals. This review focuses on the effects of different processing parameters that affect the properties of GQDs, including the surface functionalization, paradigmatic characterization, toxicity and biocompatibility issues of bioprecursor derived GQDs. This review also examines current challenges and the ongoing exploration of potential bioprecursors for ecofriendly GQD synthesis for future applications. This review sheds further light on the electronic and optical properties of GQDs along with the effects of doping on the same. This review may aid in future design approaches and applications of GQDs in the biomedical and materials design fields.

Keywords: bioprecursor, quenching, GQDs, graphene, functionalization of GQDs, hetero-atom doping, fluorescent material

(Some figures may appear in colour only in the online journal)

1. Introduction

With recent advancements in materials sciences and advanced materials, research on the cost of the effective synthesis of materials has gained a lot of attention. Graphene is

one of the most celebrated and fascinating 'wonder materials' and is investigated by many branches of science. The graphene family includes graphene, graphene oxide (GO), reduced graphene oxide (rGO) and graphene quantum dots (GQDs). Graphene-based nanomaterials generally exist as





Perspectives of characterization and bioconjugation of gold nanoparticles and their application in lateral flow immunosensing

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Abstract

Gold nanoparticles (AuNPs) are an important component in the field of biomedical diagnostics. Because of its unique physico-chemical properties, AuNPs have been widely used in biomedical applications such as photothermal cancer therapy, drug delivery, optical imaging, labeling, and biosensing. In this review, we have described synthesis and characterization techniques for AuNPs with recent advancements. Characterization of AuNPs has played an important role in directing its application in various fields and elaborated understanding of its functioning. The characterization techniques used for the analysis of AuNPs utilize its intrinsic properties, such as surface plasmon resonance (SPR) and size-dependent shift in absorption. These properties of AuNPs are furthermore used for the characterization of bioconjugated AuNPs. Surface conjugation of the AuNPs with biomolecules is explored widely for its use in numerous biosensing applications. Biosensor-based diagnostic devices use AuNPs conjugated with a sensing probe for the detection of a specific analyte. AuNPs are also commonly used as a colorimetric sensor in various point-of-care diagnostic techniques. Lateral flow immunosensing (LFIS) technique utilizes AuNPs for the rapid and sensitive detection of various analytes. LFIS is a paper-based detection technique, where the sample containing the analyte flows through the membrane, interacts with immobilized counterparts, and produces results using a detection probe. AuNPs are used as color markers in LFIS, and the presence of an analyte is indicated by the appearance of colored lines on the membrane. The color is a result of the accumulation of AuNP complexes containing the analyte and probe. Effect of characterization parameters of AuNPs on the sensitivity of LFIS, advantages, and disadvantages of using AuNPs for LFIS are discussed concerning the recent reports. Recent applications of AuNPs in LFIS development for the detection of various biomarkers are summarized comprehensively in the table. The review may offer significant insight into the utility of AuNPs for application in the LFIS technique for future development.

Keywords Gold nanoparticles (AuNPs) · Characterization · Bioconjugation · Lateral flow immunosensing (LFIS) · Diagnostics

Introduction

Nanotechnology is a comparatively new field in research which has been emergent since its introduction as a separate but interdisciplinary subject. Nanomaterial has characteristic

properties, which are attributed to its small size and quantum effects. Special physical and chemical properties include high surface to volume ratio, different optical properties from their bulk counterparts, surface plasmon resonance, photothermal effects, fluorescence emission, etc. These unique physical and chemical properties of nanomaterial have enabled their use in a variety of applications such as optical imaging, cancer therapeutics, medical diagnostics, and drug delivery as shown in Fig. 1 [1–9]. The nanomaterial is fabricated using a variety of components, among which metal nanoparticles have gained much importance. Gold nanoparticles (AuNPs) have been proved to be useful for imaging, cancer therapy, and drug delivery [10, 11]. AuNPs have been used for the development of electrochemical immunosensors for detection of Zika virus proteins [12]. Iron nanoparticles, i.e., iron oxide nanoparticles, have been used as nanocarriers to encapsulate anti-HIV drugs

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Central composite design-based optimization of lopinavir vitamin E-TPGS micelle: *In vitro* characterization and *in vivo* pharmacokinetic study

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ABSTRACT

This study was aimed at formulating Lopinavir loaded Vitamin E-TPGS micelles to enhance its oral bioavailability. Lopinavir is an HIV-1 protease inhibitor with low aqueous solubility leading to poor oral bioavailability and thus frequent dosing. Drug loaded micelles were fabricated using thin film hydration technique and optimized by two-factor five-level central composite design. For this purpose independent variables selected were TPGS to drug ratio and rotational speed of rotary evaporator, whereas dependent variables chosen were particle size and % entrapment efficiency. The effect of an independent variable on the dependent variable was studied by generating a quadratic polynomial model. Results of *in vitro* characterization showed that prepared lopinavir micelles exhibited particle size 91.71 nm, polydispersity index 0.129, zeta potential -24.8 mV, entrapment efficiency $99.36 \pm 1.06\%$ and drug loading $20.83 \pm 1.23\%$. Results of DSC and P-XRD evaluation revealed that drugs were successfully encapsulated inside the Vitamin E-TPGS micelles. *In vitro* release studies displayed enhancement in drug dissolution as a result of its loading into micelles. TEM images showed that micelles were spherical. On oral administration of lopinavir micelles; the relative bioavailability was boosted by 3.17 folds compared to lopinavir suspensions. Thus, we can conclude that TPGS based micelles possess the prodigious potential to overcome the challenges of current HAART therapy.

1. Introduction

Based on statistics given by the Joint United Nations Programme on HIV and AIDS of the year 2018, nearly 3.79 crores individuals globally are surviving with HIV/AIDS. Out of these 18 lakhs were children of less than 15 years of age. With a rate of 5000 new infections per day about 17 lakhs people universally newly developed HIV infection [1]. Human immunodeficiency virus also abbreviated and commonly known as HIV is a lentivirus. It causes HIV infection which ultimately causes AIDS (Acquired Immunodeficiency Syndrome). AIDS is a condition where the human immune system progressively fails allowing life-threatening opportunistic infections and cancers to conquer the body. It is estimated that normal lifetime post-HIV infection is 9–11 years, based on the HIV subtype [2]. Therefore, an HIV patient needs constant antiretroviral therapy throughout life. This regimen of anti-HIV medication is commonly known as HAART (Highly Active Anti-Retroviral Therapy), which includes a combination of three or more different antiretroviral drugs. Although a complete cure for HIV does not exist, this treatment slows the progression of the virus in the body

by reducing the viral titer in body fluids [3]. Thereby conserving the immune system strength and averting opportunistic infections that may cause death [4].

Lopinavir (LPV) is chemically designated as (2S)-N-[(1S,3S,4S)-1-benzyl-4-[(2,6-dimethyl phenoxy)acetyl]amino)-3-hydroxy-5-phenylpentyl]-3-methyl-2-(2-oxotetrahydropyrimidin-1(2H)-yl) butanamide. It is an integral part of the HAART program. But LPV suffers a major drawback i.e., poor bioavailability due to its poor water solubility and cytochrome P450 as well as P-glycoprotein efflux mediated hepatic first-pass metabolism [5]. Thus it is used in combination with ritonavir with the trade names Kaletra[®] and Aluvia[®]. Therefore there is a need to develop antiretroviral drug formulation with enhanced bioavailability to improve HAART therapy. Lopinavir and ritonavir both are antiretroviral drugs that are used in combination. Ritonavir is just used as a booster dose for other protease inhibitors and does not have significant antiretroviral activity against HIV and hence it is not prescribed for treatment now a day. It just helps to enhance the bioavailability of Lopinavir. Since after loading into nanocarrier bioavailability of Lopinavir will get enhanced significantly therefore there is no need to use

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Silk industry waste protein: isolation, purification and fabrication of electrospun silk protein nanofibers as a possible nanocarrier for floating drug delivery

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Abstract

Amongst assorted regio-selective and targeted oral drug delivery strategies accepted for the gastro-retentive drug delivery system (GRDDS), the floating drug delivery system (FDDS) holds a major share as clinically accepted formulations. The major objective of the present investigation was to explore the silk industry waste protein, silk fibroin (SF) as a possible electrospun nanocarrier for the FDDS. In a nutshell, electrospinning (ES) is one of the flexible and astonishing strategies for the fabrication of porous electrospun nanofibers (NFs), which offers the potential to amend the floating profile, dissolution rate, solubility, and release patterns of the drug, etc as per compendial requirements. Looking at the prospects of floating SF-NFs preparation, we have isolated and lyophilized the SF from industrial waste cocoons and prepared drug-loaded SF single polymer nanofibers (SPN). Lafutidine (LF) being a good candidate for GRDDS selected as a model drug, which is an excellent proton pump inhibitor, mainly used in the treatment of gastric ulcers. Finally, the obtained LF loaded SF-NFs (LF-SF-NFs) were successfully analyzed for physicochemical characteristics, porosity, swelling index, antioxidant activity, mucoadhesion strength, floating properties, enzymatic degradation, and accelerated stability study, etc. Further, these LF-SF-NFs were evaluated for percent drug content, weight variation, *in-vitro* dissolution in 0.1 N hydrochloric acid (HCl, pH:1.2) and fasted state simulated gastric fluid (FSSGF), and accelerated stability study. It has shown significant floating time >18 h, about 99% \pm 0.58% floating buoyancy with sustained release up to 24 h. LF-SF-NFs showed good compatibility, entrapment efficiency, antioxidant activity, mucoadhesion strength, enzymatic degradation, and long term stability. Soon, the essential floating and drug release profiles can claim single polymer (SF) based electrospun protein NFs as a possible novel oral nanocarrier for FDDS.

Keywords: processing industrial waste cocoons, silk fibroin, electrospun nanofibers, lafutidine, floating drug delivery system

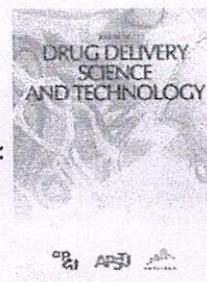
(Some figures may appear in colour only in the online journal)



Journal Pre-proof

One- Pot Development of Spray Dried Cationic Proliposomal Dry Powder Insufflation: Optimization, Characterization and Bio-interactions

Ajjappla Basavaraj Shreya, Abhijeet Pandey, Ajinkya Nitin Nikam, Pravin O. Patil, Raju Sonawane, Prashant Deshmukh, Srinivas Mutalik



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Review

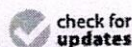
Black Phosphorus as Multifaceted Advanced Material Nanoplatfoms for Potential Biomedical Applications

Abhijeet Pandey¹, Ajinkya N. Nikam¹ , Gasper Fernandes¹, Sanjay Kulkarni¹, Bharath Singh Padya¹, Ruth Prassl² , Subham Das³, Alex Joseph³, Prashant K. Deshmukh⁴, Pravin O. Patil⁵ and Srinivas Mutalik^{1,*}

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Abstract: Black phosphorus is one of the emerging members of two-dimensional (2D) materials which has recently entered the biomedical field. Its anisotropic properties and infrared bandgap have enabled researchers to discover its applicability in several fields including optoelectronics, 3D printing, bioimaging, and others. Characterization techniques such as Raman spectroscopy have revealed the structural information of Black phosphorus (BP) along with its fundamental properties, such as the behavior of its photons and electrons. The present review provides an overview of synthetic approaches and properties of BP, in addition to a detailed discussion about various types of surface modifications available for overcoming the stability-related drawbacks and for imparting targeting ability to synthesized nanoplatfoms. The review further gives an overview of multiple characterization techniques such as spectroscopic, thermal, optical, and electron microscopic techniques for providing an insight into its fundamental properties. These characterization techniques are not only important for the analysis of the synthesized BP but also play a vital role in assessing the doping as well as the structural integrity of BP-based nanocomposites. The potential role of BP and BP-based nanocomposites for biomedical applications specifically, in the fields of drug delivery, 3D printing, and wound dressing, have been discussed in detail to provide an insight into the multifunctional role of BP-based nanoplatfoms for the management of various diseases, including cancer therapy. The review further sheds light on the role of BP-based 2D platfoms such as BP nanosheets along with BP-based 0D platfoms—i.e., BP quantum dots in the field of therapy and bioimaging of cancer using techniques such as photoacoustic imaging and fluorescence imaging. Although the review inculcates the multimodal therapeutic as well as imaging role of BP, there is still research going on in this field which will help in the development of BP-based theranostic platfoms not only for cancer therapy, but various other diseases.

Keywords: bioimaging; wound healing; 3D printing; surface modification; characterization



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1. Introduction

The discovery of Black Phosphorus (BP) dates back to a hundred years ago. It all began with Bridgman [1], who brought about the conversion of white phosphorus to black phosphorus under a high temperature and pressure. Later, Hultgren et al. [2] demonstrated



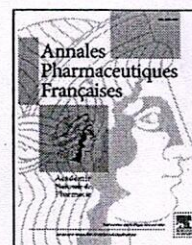


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GENERAL REVIEW

Carbon dots: A novel trend in pharmaceutical applications



Carbon dots : *une nouvelle tendance dans les applications pharmaceutiques*

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HIGHLIGHTS

- Presents basic concepts, advantages, synthesis approach of CDs.
- Numerous CDs based pharmaceutical applications of were reviewed.
- CDs were used in gene therapy and nanomedicine.
- CDs were used in bioimaging and biosensing.

KEYWORDS

Carbon dots;
Pharmaceutical applications;
Bioimaging;
Sustained drug delivery;
Targeted drug delivery

Summary Carbon quantum dots (CQDs, C-dots, or CDs), are generally small carbon nanoparticles having a size less than 10 nm. Carbon dots (CDs) were accidentally discovered during the purification of single-walled carbon nanotubes through preparative electrophoresis in 2004. Carbon is an organic material having poor water solubility that emits less fluorescence. However, CDs have good aqueous solubility and excellent fluorescent property, hence more attention has been given to the synthesis of CDs and their applications in chemistry and allied sciences. CDs being easily accessible for in-house synthesis, simpler fabrication as per compendial requirements are widely accepted. In addition, since CDs are biocompatible, of low toxicity, and of biodegradable nature, they appear as a promising tool for the health care sector. Furthermore, owing to their capabilities of expressing significant interaction with biological materials, and their excellent photoluminescence (PL), CDs have been emerging as novel pioneered nanoparticles useful for pharmaceutical and theranostic applications. Also, CDs are more eco-friendly in synthesis and therefore can be favorably consumed as alternatives in the further development

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REVIEW

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Pharmaceutical applications of citric acid



Sopan Nangare¹, Yogini Vispute², Rahul Tade¹, Shailesh Dugam³ and Pravin Patil^{1*}

Abstract

Background: Citric acid (CA) is a universal plant and animal-metabolism intermediate. It is a commodity chemical processed and widely used around the world as an excellent pharmaceutical excipient. Notably, CA is offering assorted significant properties viz. biodegradability, biocompatibility, hydrophilicity, safety, etc. Therefore, CA is broadly employed in many sectors including foodstuffs, beverages, pharmaceuticals, nutraceuticals, and cosmetics as a flavoring agent, sequestering agent, buffering agent, etc. From the beginning, CA is a regular ingredient for cosmetic pH-adjustment and as a metallic ion chelator in antioxidant systems. In addition, it is used to improve the taste of pharmaceuticals such as syrups, solutions, elixirs, etc. Furthermore, free CA is also employed as an acidulant in mild astringent preparations.

Main text: In essence, it is estimated that the functionality present in CA provides excellent assets in pharmaceutical applications such as cross-linking, release-modifying capacity, interaction with molecules, capping and coating agent, branched polymer nanoconjugates, gas generating agent, etc. Mainly, the center of attention of the review is to deliver an impression of the CA-based pharmaceutical applications.

Conclusion: In conclusion, CA is reconnoitered for multiple novels pharmaceutical and biomedical/applications including as a green crosslinker, release modifier, monomer/branched polymer, capping and coating agent, novel disintegrant, absorption enhancer, etc. In the future, CA can be utilized as an excellent substitute for pharmaceutical and biomedical applications.

Keywords: Citric acid, Pharmaceutical applications, green crosslinkers, Fluorescent materials, Absorption enhancer

Background

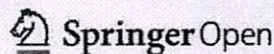
Citric acid (CA, 2-hydroxy-2, 3-propanetricarboxylic acid, tricarboxylic acid) is the largest organic acid contained in the tonnage. Generally, it is a universal plant-and animal-metabolism intermediate. CA is a commodity chemical processed and widely used around the world for plentiful pharmaceutical applications (Fig. 1) [1]. To begin with 1784, Carl Scheele (a Swedish chemist) isolated the CA (Molecular Weight: 210.14 Da) from the lemon juice. Whereas in 1893, at the first time Wehmer demonstrated the culture medium includes sugars and inorganic salts, *Penicillium glaucum* (*Citromyces*) accumulating CA. Amusingly, CA was first commercially manufactured in England from the imported Italian

lemons. In 1917, Currie discovered that some of the *Aspergillus niger* strain generated CA into adequate nutrient mediums that contain high levels of sugar plus mineral salts and along with that preliminary medium pH (2.5–3.5). Despite these notable findings, lemon juice was still a commercial source for the manufacturing of CA until 1919. This provided the foundation for industrial CA production with *Aspergillus niger* [2]. As per literature, CA has been unrevealed by Krebs in the late 1930s as a key ingredient in the metabolism of all aerobic species [3, 4]. The developmental stages of the discovery and manufacture of CA from 1784 to 2020 [4] are represented in Fig. 2.

From its inception, plenty of literature reported that CA is a major component in the processing of several products, mainly as an acidulant in the food, chemical, and pharmaceutical industries. Natural resources, such as fruit sugar, become more and more essential for CA

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Eco-friendly synthesis of surface grafted Carbon nanotubes from sugarcane cubes for the development of prolonged release drug delivery platform

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Abstract

Surface grafting of nanocarriers could modulate their properties and characteristics. As carbon nanotubes synthesis is a very tricky process and requires high-end methods, hence the present investigation was aimed to develop an eco-friendly method for synthesis carbon nanotubes (CNTs) and subsequent surface grafting for enhanced drug delivery application. The present study elaborates two-step chemical modifications, wherein the first step is catalytic cleavage of natural precursor in the presence of ferrocene and the second step involve chemical grafting of Acyclovir (ACV) as a model drug to understand the drug release behaviour. The catalytic cleavage of sugarcane cubes (natural precursor) was carried out in a closed copper tube, which prevents oxidation and results in a conversion of tubular nanostructures to amorphous carbon. The covalent attachment of ACV on purified CNTs (fCNTs) was done using carbodiimide chemistry. The preliminary UV-Vis absorbance spectra defined at 260 nm was arisen due to $\pi-\pi^*$ stacking of aromatic C-C bonds. The Fourier Transforms Infrared Spectroscopy (FTIR) indicates the hydroxyl stretch at 3300 cm^{-1} while amide I bond formation was observed at 1672 cm^{-1} . The XRD spectra confirmed successful synthesis of CNTs. The calculated average crystallite size (Scherer equation) of synthesized CNTs was found to be 42.84 and 44.45 nm; it was also in accordance with the morphological observation as confirmed simultaneously using SEM analysis. The covalently attached ACV was released up to 80% during 8h of *in vitro* drug release study. The surface grafting potential of CNTs was found to be promising compared to other nanomaterials.

Keywords: Acyclovir; Amorphous Carbon; Carbodiimide Chemistry; Natural Precursor; Purification.

How to cite this article

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INTRODUCTION

Even though the investigation on allotropic forms of carbon was begun before 1990, but the most intuitive form of carbon allotrope i.e. carbon

nanotubes (CNTs) were reported in 1991[1]. Numerous classical approaches for the synthesis of CNTs are reported by academic researchers and industry experts for their promising physicochemical properties. In case of CNTs, the

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Research Article

Fabrication of N-Doped Graphene@TiO₂ Nanocomposites for Its Adsorption and Absorbing Performance with Facile Recycling

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Abstract

The present work aims to synthesize nitrogen-doped reduced graphene oxide-titanium dioxide nanocomposite (N-rGO@TiO₂) using a simple, eco-friendly method and its applications in spectroscopic detection of heavy metal ions such as lead (Pb²⁺), mercury (Hg²⁺), and chromium-VI [Cr(VI)] in potable water. Initially, TiO₂ nanoparticles loaded N doped rGO sheets were fabricated by an ecological method using *Gossypium hirsutum* (cotton) seeds extract as a green reducing agent. Then, the N-rGO@TiO₂ nanocomposites were subjected for characterizations such as spectroscopic techniques, particle size analysis, zeta potential analysis, and spectroscopic sensing. Notably, the results of this study confirmed that N-rGO@TiO₂ exhibited countless stupendous features in terms of sensing of an analyte. Briefly, the UV-visible spectroscopy and Fourier transform infrared (FTIR) spectroscopy confirmed the successful synthesis of N-rGO@TiO₂. The SEM images showed the wrinkled, folded, and cross-linked network structures that confirmed the surface modification and nitrogen doping in the rGO sheet and synthesis of N-rGO@TiO₂. The EDAX study confirmed the elemental composition of the N-rGO@TiO₂ nanocomposite. Finally, due to the larger surface area, porous nature, high electron mobility, etc. the N-rGO@TiO₂ probe provides the lower detection limit for Pb²⁺, Hg²⁺, and Cr (VI) as low as 50 nM, 15 μM, and 25 nM, respectively. Concisely, our study affirms the admirable sensitivity of N-rGO@TiO₂ nanocomposite to the Pb²⁺, Hg²⁺ and Cr (VI) in potable water can provide better environmental remediation.

Keywords: Graphene oxide, N-rGO@TiO₂, Nanocomposite, Cotton-seed, Heavy metals, Biodegradable, Sensing

Introduction

Over the past two decades, graphene-based materials are gaining tremendous attention from a scientific fraternity in various fields [1-3]. It may

because of its astonishing properties and potential to revolutionize the scientific sector [3-5]. Graphene can be used to fabricate several dimension materials such as 1D nanostructure [6], 2D layer stacked films [7], 3D graphene hydrogel [7-9], and aerogel [10-13], etc. Out

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RESEARCH

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Purification and modification of neem gum for enhancement of its suspending property

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Abstract

Background: The present study aimed to purify and modify the neem gum (NG) to evaluate its dispersing ability in a pharmaceutical suspension formulation. The modification was carried out to cross-link the sugars as carbamate in the presence of calcium chloride to improve the suspending property. Physicochemical properties such as pH, solubility, swelling index and ash value were performed before investigating the dispersing potential. The suspending potential of neem gum was studied in its different forms such as purified and modified gum in paracetamol suspension and was compared with sodium carboxymethylcellulose (CMC) being used as standard at a concentration range of 0.25–1% (w/v). The test suspensions were evaluated for the redispersibility, flowability, sedimentation volume (%) and stability study for 3 months.

Result: The redispersibility of modified neem gum (MNG) was found equal to CMC at a higher concentration. The flowability and apparent sedimentation of test suspending agents and CMC were found in the order of NG > MNG > CMC. It showed a positive correlation with the viscosity of suspension formulations. All the test paracetamol suspension formulations were found stable in the stability study.

Conclusion: The findings of the present study showed that as an alternate suspending agent, modified cross-linked neem gum could be used.

Keywords: Neem gum, Sedimentation volume, Redispersibility, Flowability

Background

Pharmaceutical excipients are additives with unique physicochemical properties that help to transform the drug substances into an effective type of dosage suitable for patient administration. Demand for new and updated excipients for drug delivery systems has been growing in order to meet the needs of new, better formulations. To be used as pharmaceutical excipients, natural polymers are readily available, biodegradable, non-toxic and cost-

effective, to be used as an excipient for a range of pharmaceutical formulations [1].

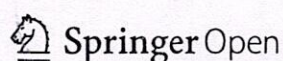
Gums are ideal natural polymer for pharmaceutical emulsion and suspension formulations by increasing the viscosity of the continuous phase. Furthermore, it increases the tensile strength, by hydrogen bonding and molecular interactions, of the hydration layer formed around the suspended particles without minimizing the surface and interfacial tension.

Neem gum (*Azadirachta indica*) is a large evergreen tree that may grow up to 20 m in height. It occurs in tropical and semitropical regions of the world. The plant oozes plenty of gum throughout the year. Chemically, it contains mannose, glucosamine, arabinose, galactose,

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007

RESEARCH ARTICLE



Electrostatic deposition assisted preparation, characterization and evaluation of chrysin liposomes for breast cancer treatment

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ABSTRACT

Chrysin (CHR), a flavone found in multiple vegetables, fruits and mushrooms has been explored so far as a neurotropic, anti-inflammatory and anti-cancer biomolecule. Despite the stated therapeutic potential, low solubility and bioavailability limit its therapeutic benefit. To circumvent these drawbacks, development of chrysin liposomes (CLPs) is reported in the present investigation. The CLPs were developed by electrostatic deposition assisted film hydration method using chitosan/lecithin to protect chrysin in the nano-lipoidal shell. Developed CLPs were extensively characterized by DSC, XPRD, FE-SEM, TEM, particle size, polydispersity index, zeta potential, percent drug loading and encapsulation efficiency. These CLPs were further characterized by *in vitro* dissolution, *in vivo* bioavailability, *in vitro* anticancer and stability study. Suitable particle size, PDI and ZP implying stabilization of developed CLPs. The % DL and % EE was found to be 3.56 ± 0.13 and 90.5 ± 1.49 respectively. DSC and PXRD study revealed amorphous transition of CHR, which may help to increase its solubility and dissolution profile. *In vivo* pharmacokinetic study demonstrated more than 5-fold increase in relative bioavailability of CLPs. The *in silico* molecular docking study results demonstrated the electrostatic interaction between two polymers. The present study suggests that chitosan could protect and encapsulate chrysin which eventually enhances its cytotoxicity as well as bioavailability.

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KEYWORDS

Electrostatic deposition; hydration; chrysin; liposomes; *in silico* molecular docking

Introduction

Encapsulation of bioactive drug using polymeric coating is beneficial due to its nontoxic, nonimmunogenic and biodegradable properties, along with protection of drug with improved biocompatibility [1–3]. In addition to this, issue of poor aqueous solubility and bioavailability of many bioactive compounds could be resolved using techniques like nanoencapsulation [4].

The electrostatic deposition method is based on the deposition of one polymer material on another in liquid form followed by evaporation of the solvent to form encapsulation of the subsequent polymer. This technique of encapsulation attracted researchers in recent years; herein it coats the active ingredient with the assistance of polymeric matrix [1]. The electrostatic deposition based microencapsulation approach has also been used for the preparation of hydrogels [5], microemulsion [6], liposomes [7] to name a few.


Out of the many approaches used for drug encapsulation, liposomes are widely used for both hydrophilic and hydrophobic drugs such as antioxidants, antimicrobials and other pharmacologically important compounds [8]. However, organic residual effect, leakages of active compounds and instability during storage of traditional liposomes may restrict their applications [9,10]. So as to conquer these limitations, polycationic polymer like chitosan could be used as a coating material which forms

polyelectrolyte complex with oppositely charged polymeric material by intermolecular electrostatic deposition [11,12].

Chrysin (CHR), a flavone found in multiple vegetables, and mushrooms, has been suggested as neurotropic for cells, anti-inflammatory, and anti-amyloidogenic [13]. The CHR has been known as an anti-cancer and wellbeing-promoting compound [14]. In several biological tests, it has demonstrated to be effective against many disorders. The CHR may most cancer-related pathways and inhibits cancer by fostering apoptosis and moderating cell death due to autophagy. Hence, extensive research in this direction should be focused on the coming years to validate its possible clinical use in cancer.

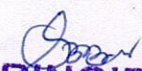
The main objective of the present study was to encapsulate CHR in liposomal form using the electrostatic deposition technique for protection and further enhancement in bioavailability. For the same, biocompatible and biodegradable biological macromolecules viz. chitosan (CHN) and soya lecithin (SOL) were used which form a polymeric nanoshell with the aim to shield against degradation and to enhance its biocompatibility [15]. Being a polycationic macromolecule, chitosan, through intermolecular electrostatic deposition, forms polyelectrolyte complex with oppositely charged macromolecules [17]. Developed chrysin liposomes (CLPs) were further characterized using different physicochemical parameters like particle size (PS), polydispersity index (PDI), zeta potential (ZP), entrapment efficiency (% EE), drug loading (% DL), differential scanning calorimetry (DSC), transmissi-

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 Supplemental data for this article can be accessed here.

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Cissus quadrangularis L.: A comprehensive multidisciplinary review

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Keywords:

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 Pharmacology
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 Patents

ABSTRACT

Ethnopharmacological relevance: *Cissus quadrangularis* L. is a perennial herb of the Vitaceae family and is utilized comprehensively as a medicinal herb in most tropical regions by various names. This herb is documented to possess a wide-ranging ethnomedicinal uses in malaria, fever, epilepsy, gout, piles, skin diseases, colic, etc.

Aim of the review: A organized summary of the botany, traditional uses, phytochemistry, pharmacology, toxicology, available marketed formulations and filed patents were presented to explore the future therapeutic potential and scientific potential of this herb.

Materials and methods: For a review of the literature, various databases were searched, including PubMed, EMBASE, and Scopus etc. From, total 408 records of this herb, we have screened 155 articles consist of desired information and available as full text. Present manuscript is structured from comprehensive information on this herb from screened 155 records. Plant taxonomy was confirmed to the database "The Plant List".

Results: Phytochemical assessment as a whole indicated the presence of flavonoids, triterpenoids, alkaloids, saponins, iridoids, stilbenes, vitamins, steroids, and glycosides. A toxicity study revealed that its LD₅₀ value is above 3000 mg/kg in animals indicating its safety. A variety of pharmacological studies of aerial parts of this herb by different extracts have demonstrated analgesic, anti-inflammatory, anticonvulsant, antimicrobial, anti-cancer, anti-osteoporotic activity and other bone-related disorders to justify its name as *Hadjod*. Still, the herb has been utilized in clinical practice and several patents were filed in India and US for its antiosteoporotic property.

Conclusion: The studies on *Cissus quadrangularis* Linn. are extensive, but gaps still remain. The molecular mechanism, structure-activity relationship, potential synergistic and antagonistic effects of these components needs to be further elucidated. These findings suggest the need for further research on this herb for the management of several other chronic ailments.

1. Introduction

Natural substances are being used as a principal source of medicines directly or indirectly, for many decades and have proven to be extremely beneficial to human health. These substances are being investigated for biological activities in nearly every part of the world. Despite the fact that a large number of plant-derived chemicals are widely available, rigorous initiatives have been undertaken to isolate, identify and test molecular leads and develop novel chemicals with enhanced biological potential and low toxicity.

Natural products, notably those extracted from plants, tend to provide valuable leads in the drug development process (Balunas and Kinghorn, 2005). The initial process in drug research is to gather data on

materials that have previously been used to cure a disease. Due to the custom of verbal transfer of the information regarding medicinal plants and their relevant techniques of use (Bhatia et al., 2014), there is concern that aboriginal herbal medicine knowledge is being endangered (Ssegawa and Kasenene, 2007). It is a need of time to conserve and document this traditional and advanced knowledge of plants proven through various experimentation and study protocols so that it will work as a lighthouse for the future researchers and give guideline with respect to safety, efficacy and specific uses (Bunalema et al., 2014).

Cissus is a genus of the Vitaceae family consisting of 800 species divided into 13 genera throughout the world, including Africa, Arabia, South Asia, Srilanka, India and other tropical regions. Out of these, 8 genera and 63 different species are found in India (Ansarali et al., 2016). *Cissus quadrangularis* L. (CQL), Vitaceae is a dicotyledonous flowering,

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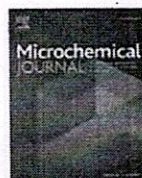
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Review Article

Surface architected metal organic frameworks-based biosensor for ultrasensitive detection of uric acid: Recent advancement and future perspectives

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Colorimetric biosensor

ABSTRACT

Gout is the world's most popular inflammatory arthritis and the prevalence of gout is rapidly rising worldwide. Typically, gout develops in a single joint as excessive swelling and intense pain wherein excessive deposition of uric acid (UA) crystals results in inflammation of the joint. Accordingly, UA is considered an effective biomarker to diagnose gout. Recently, the use of innovative sensors has attracted great attention, as it is effortless, responsive, quick, and powerful. While the traditional sensors for UA assessment are widely used, they pose many limitations and hurdles in terms of sensitivity, selectivity, and simplicity. In this vein, metal ions and organic ligand-based metal-organic framework (MOF) have gained much attention for the recognition of UA due to its larger surface area, porosity, high sensitivity, and defined selectivity. In this review, we provide details on the latest developments of MOF-centered biosensors for sensitive detection of UA. The status of gout, fundamentals of MOF, and MOF availed for detection of UA have been elaborated. Besides, we highlighted the nanoparticles and conjugates that rely on advanced strategies along with MOF that boost the sensitivity and selectivity towards the UA. Interestingly, different surface architected MOFs biosensors showed a lower detection limit for UA from μM to nM . Finally, the threats and potential opportunities for MOF-based UA biosensors have been summarized. Therefore, based on ongoing research, the commercialization of this advanced platform for the biosensing of diverse biomarkers will open a new door for the *in vitro* diagnosis of assorted diseases.

1. Introduction

From its inception, arthritis is a severe health issue of a joint in almost all developed and developing nations. Arthritis is a term that derives from the Greek word "disease of the joint." Commonly, it can be stated as acute inflammation or chronic inflammation of the joint that is

sometimes with the effect of pain and sometimes co-exists with structural damage [1]. As many as 100 classes of arthritis have been characterized according to the research. Generally, it can be classified into two type's namely non-inflammatory arthritis and inflammatory arthritis. In the first category, non-inflammatory arthritis is commonly known as osteoarthritis, while inflammatory arthritis is categorized

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Emerging Approaches to Overcome Acquired Drug Resistance Obstacles to Osimertinib in Non-Small-Cell Lung Cancer

Matin Shaikh, Yashodeep Shinde, Rahul Pawara, Malleshappa Noolvi, Sanjay Surana, Iqrar Ahmad,*
 and Harun Patel*

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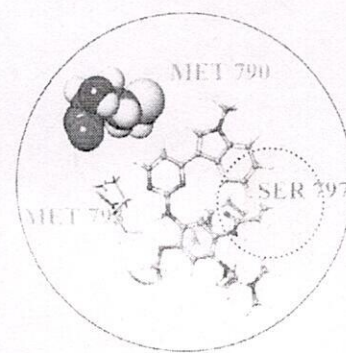
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ABSTRACT: The pyrimidine core-containing compound Osimertinib is the only epidermal growth factor receptor tyrosine kinase inhibitor (EGFR-TKI) from the third generation that has been approved by the U.S. Food and Drug Administration to target threonine 790 methionine (T790M) resistance while sparing the wild-type epidermal growth factor receptor (WT EGFR). It is nearly 200-fold more selective toward the mutant EGFR as compared to the WT EGFR. A tertiary cysteine 797 to serine 797 (C797S) mutation in the EGFR kinase domain has hampered Osimertinib treatment in patients with advanced EGFR-mutated non-small-cell lung cancer (NSCLC). This C797S mutation is presumed to induce a tertiary-acquired resistance to all current reversible and irreversible EGFR TKIs. This review summarizes the molecular mechanisms of resistance to Osimertinib as well as different strategies for overcoming the EGFR-dependent and EGFR-independent mechanisms of resistance, new challenges, and a future direction.



1. INTRODUCTION

On March 30, 2017, the US Food and Drug Administration (FDA) conceded regular approval to Osimertinib (AZD9291) for the management of patients with metastatic “EGFR-T790M Non-Small Cell Lung Cancer (NSCLC)”.^{1,2} The FDA-approved drug Osimertinib is at the forefront for the treatment of NSCLC patients (Figure 1).^{3–5} However, a significant proportion of Osimertinib-treated patients developed the EGFR kinase tertiary cysteine 797 to serine 797 (C797S) mutation by the loss of covalent binding with the Cys797 residue, which renders a resistance to all the existing drugs.^{6,7} Additional studies with mutant cell lines have shown that the allelic context of the activating gatekeeper and C797S mutations affects the sensitivity of three generations of EGFR inhibitors, with no epidermal growth factor receptor tyrosine kinase inhibitor (EGFR-TKIs) alone or in combination able to suppress activity when the mutation is in the *cis*-form.^{8–10} These data suggest that there is a pressing need for drugs that can overcome the ternary mutation (L858R/T790M/C797S EGFR) obstacle in NSCLC.¹¹ The crystallographic structure of C797S-EGFR revealed that the C797S mutation has no effect on the EGFR kinase’s structure or function but does increase the degree of local hydrophilicity around residue 797 (Figure 2).^{12–14}

The EGFR-independent pathway also contributes to the resistance to Osimertinib in addition to the acquired C797S mutation.^{15,16} The EGFR-independent pathway (bypass pathway) is ascribed to the modification of other signaling molecules, such as MET amplification, MEK activation, ALK

activation, EGFR amplification, HER2 amplification, AKT activation, BRAF activation, and AXL activation.^{17,18} The tertiary undruggable C797S mutation in the EGFR kinase domain, which causes more than 20% of the incidence rate in clinical results, is the most difficult to deal with of all these potential mechanisms.^{19–21} The focus of this review is to provide an exhaustive overview of Osimertinib resistance mechanisms and use the available information to develop potential strategies to overcome the associated resistance problem.

2. EGFR-MEDIATED SIGNALING PATHWAYS IN NSCLC

Different growth factors, cytokines, and hormones bind to the receptor tyrosine kinases (RTKs). Structurally, RTKs consist of the ligand-binding extracellular domain, the hydrophobic transmembrane domain, and the intracellular protein tyrosine kinase region.²² Therefore, intracellular pathways that signal EGFR play a major role in various cancers, specifically NSCLC. The binding of a ligand (growth factor) to the EGFR extracellular domain causes dimerization, which subsequently activates the cytoplasmic tyrosine kinase domain

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Green synthesis of Fe-doped Ag-loaded reduced graphene oxide ternary nanocomposite for efficient photocatalytic degradation of toxic dyes

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Abstract

The green synthesis of iron nanoparticles (FeNPs) doped and silver nanoparticles (AgNPs) loaded reduced graphene oxide (rGO) (Fe-Ag@rGO) nanocomposite and its applications in methylene blue (MB), malachite green (MG), rhodamine B (RB) degradation were reported. Initially, AgNPs loaded rGO (Ag@rGO) nanocomposites were synthesised simultaneously by an ecological method using *Tamarindus indica* shell extract as a green reducing agent. Then, the doping of FeNPs into rGO@Ag nanocomposites afforded Fe-Ag@rGO nanocomposite. Interestingly, the finding of this study confirmed that the Fe-Ag@rGO nanocomposites exhibited countless stupendous features in terms of dye degradation. Briefly, the UV-visible spectroscopy and Fourier-transform infrared spectroscopy (FTIR) study confirmed the synthesis of Fe-Ag@rGO nanocomposite. The scanning electron microscopy (SEM) images showed the spherical shape with cross-linked network structures that confirmed the surface modification and synthesis of Fe-Ag@rGO nanocomposite. Finally, the dye degradation potential of the photocatalyst was found to be 97.20%, 98.43%, and 97.33%, for MB, MG, RB, respectively. Herein, the improved photocatalytic performance of the Fe-Ag@rGO was found due to the larger surface area, porous nature, high electron mobility, and synergistic effect of the Fe-Ag@rGO nanocomposite. Additionally, the effective interfacial hybridisation of 'Ag', and doping of 'Fe' on the rGO sheet extended the duration of the photogenerated electron (e⁻) hole pairs that can also be contributing to dye degradation. Conclusively, the present experiment provides the new Fe-Ag@rGO nanocomposite to the dye degradation, which could be improved environmental remediation.

Keywords: dye degradation, nanocomposite, Fe-Ag@rGO, *Tamarindus indica* shells, graphene oxide, Green synthesis
Classification numbers, 2.00, 5.00, 5.11


1. Introduction

Today is the era of accelerated industrialisation, which has seen rapid developments and has played an essential role in

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Crystallinity modulated silk fibroin electrospun nanofibers based floating scaffold as a candidate for controlled release of felodipine

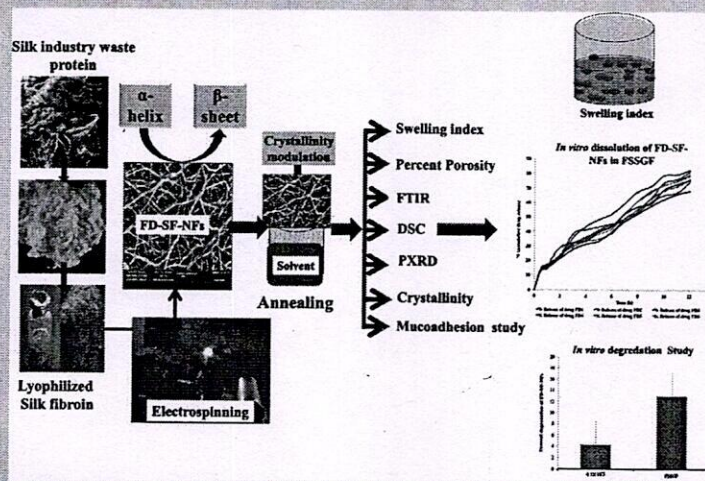
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ABSTRACT

Floating gastro-retentive delivery approach provides a significant pathway for controlled release of drug with increase gastric residence. In this study, we report crystallinity modulated electrospun silk fibroin nanofibers (SF-NFs) floating scaffolds for the controlled release of felodipine (FD). The alteration in the crystallinity behavior due to changes in the structural conformation of SF helps to customize the release kinetics of FD-loaded SF-NFs scaffolds. Additionally, FD-loaded SF scaffolds system having a density less than the acidic gastric fluid explore as a new tactic for floating drug delivery system. The prepared FD-loaded SF nanofibers (FD-loaded SF-NFs) were characterized by spectral, thermal, and diffractometric techniques, scanning electron microscopy; floating profile, *in-vitro* degradation, mucoadhesion, and *in-vitro* dissolution studies, etc. The optimized batch had the least porosity and swelling, was annealed with ethanol and water for crystallinity modulation of SF-NFs to get controlled release of FD. Spectral, thermal, and diffractometric analyses could unveil the molecular dispersion of FD, coupled with amorphous form stabilization in NF. Excellent floating profile and satisfactory mucoadhesion of FD-SF-NFs also endorsed the formation of a novel floating drug delivery system. Temporal control over FD release was elucidated by *in-vitro* dissolution, demonstrating controlled release due to crystallinity modulation of SF-NFs. In conclusion, crystallinity-modulated electrospun NFs fabricated from SF waste could be used as a customizable carrier for drug delivery to the gastric region.

GRAPHICAL ABSTRACT



Crystallinity modulated silk fibroin electrospun nanofibers based floating scaffold as a candidate for controlled release of felodipine

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KEYWORDS

Silk fibroin; electrospun nanofibers; crystallinity modulation; felodipine; floating drug delivery; controlled release

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Structural design of nanosize-metal–organic framework-based sensors for detection of organophosphorus pesticides in food and water samples: current challenges and future prospects

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Abstract

Organophosphorus pesticide (OPP) is regarded as an important food-chain and environmental contaminant that causes primary acute toxicity and numerous severe health issues. Therefore, the minute concentration of OPP present in food materials and environments needs to be identified before it causes any brutal harm to lives. Despite the plenty of merits of qualitative and quantitative sensing methods, the lower sensitivity, poor selectivity, detection speed, etc. towards the interest OPP are major drawbacks. Nanoparticles have attracted a lot of attention because of their unique and intriguing features, which have a variety of applications including sensor development as compared to their bulk counterparts. Recently, the structural design of nanosize-metal–organic framework (MOF) is gaining huge consideration from researchers for sensing applications owing to their versatile and tunable properties. Additionally, MOF-based sensors offer the rapid, simplistic, selective, and sensitive sensing of interest analyte. The present review provides brief information about OPPs and their toxicities. The emerging trends of structural design of nanosize-MOF including their properties have been summarized. Finally, nanosize-MOF-based fluorescent sensors, electrochemical sensors, and colorimetric sensors have been discussed with central focus on sensitivity and selectivity to OPPs. Due to the higher surface area, rich topology, ease of structural tunability and functionalization, tunable pore size, plenty of binding sites, good adsorption potential, excellent charge conductivity, and chemical stability, etc., MOF based sensors are endowed with the ability of OPPs detection upto μM . Hence, MOF as nanoporous sensors can be preferred as an excellent alternative for highly sensitive and selective recognition of OPPs in food and water samples.

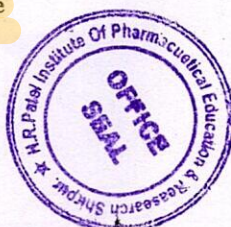
Sopan N. Nangare and Sayali R. Patil contributed equally as a first author.

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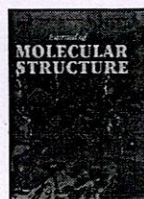


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Synthesis, molecular modelling study of the methaqualone analogues as anti-convulsant agent with improved cognition activity and minimized neurotoxicity

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ABSTRACT

In the current research, methaqualone derivatives were synthesized and assessed for their anti-convulsant activity. Among them, compounds **3**, **4**, **6**, **7** and **11** exhibited significant anti-convulsant activities with ED₅₀ values of 132.23 mg/kg, 120.34 mg/kg, 100.78 mg/kg, 145.89 mg/kg, and 148.46 mg/kg, respectively. The toxicity profiling (TD₅₀) of these compounds (**3**, **4**, **6**, **7** and **11**) demonstrated that these drugs caused only a minor neurological impairment. The PI scores of these compounds (**3**, **4**, **6**, **7** and **11**) were higher than the reference drug (methaqualone PI: 1.99). The acetylcholinesterase enzyme level is significantly reduced in these compounds, indicating the enhancement of cognition activity. Pharmacophoric modelling and molecular docking studies against the human GABA-A receptor are in close agreement with each other. Molecular dynamic simulation of compound **6** indicates that it remains stable with the human GABA-A receptor for a 100 ns time span.

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Introduction

Epilepsy is among the oldest medical disorders recorded in history [1]. Despite the wide and expanding range of antiepileptic drugs (AEDs) available for treatment, around 30% of epileptic patients have suboptimal seizure control, and another 25% have serious side effects [2]. Epilepsy is linked to a higher incidence of neuropsychological disorders, including emotional disturbance, cognitive deficits, and psychiatric disorders, all of which have a severe impact on quality of life [3–7]. Therefore, there is an immense need to develop new AEDs that are both effective and have a better safety profile. Methaqualone has a tumultuous past as both medicinal and a recreational substance [8,9]. In the early 1960s, methaqualone was sold under the trade names Parest, Quaalude, Somnafac, and Mandrax, as a non-barbiturate hypnotic with a broad safety margin and limited abuse potential [1]. In recent years, methaqualone became one of the world's best-selling sedative-hypnotic agents with other structural analogues (collec-

tively known as "quaaludes") [1]. Although the clinical characteristics of methaqualone are quite typical for a sedative-hypnotic medication, some of its *in vivo* effects differ from those produced by conventional central nervous system (CNS) depressants. [10,11]. As compared to benzodiazepines and barbiturates, methaqualone, purportedly facilitates a rapid induction of a more natural deep sleep, resulting in less severe dizziness/dullness, and headaches in insomnia patients [10,11].

Several quinazoline derivatives have been identified and reported to stimulate GABA-A receptors [12]. The GABA-A receptor is an ionotropic ligand-gated ion channel receptor, and γ -aminobutyric acid (GABA) is an endogenous ligand that is the primary inhibitory neurotransmitter in the CNS. Upon activation, the GABA-A receptor primarily flows Cl⁻ via its pore, causing the neuron to hyperpolarize. This inhibits neurotransmission by inhibiting the action potential [13–15]. Many quinazolinones with structural similarities to methaqualone have been discovered and investigated for anti-convulsant action (Fig. 1) [12]. A continuous issue faced with these compounds emanates from the fact that nearly every analogue evaluated in combined neurotoxicity and anti-convulsant testing revealed neurotoxicity values (TD₅₀) that were less than or only slightly higher than the effective doses

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Scientific paper

Development and Evaluation of Lyophilized Methotrexate Nanosuspension using Quality by Design Approach

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Abstract

With the application of the quality by design (QbD) approach, a high-pressure homogenizer (HPH) methodology was employed to develop methotrexate nanosuspension (MTX-NS) to boost bioavailability. The Ishikawa diagram was used to analyze potential risk factors in formulation development. To screen and study the impact of various formulation and process factors on the critical quality attributes (CQA), the Plackett–Burman design and central composite design were utilized. The number of HPH cycles, poloxamer 188 concentration, and tween 80 concentration were shown to be significant parameters ($P < 0.05$), that were further optimized using Central Composite Design. The zeta potential of optimized lyophilized MTX-NS was determined to be -11.6 ± 7.52 mV and the average particle size was 260 ± 0.25 nm. In vitro cytotoxicity experiments revealed a greater than 80% inhibition, with apoptotic cells shrinking, fragmentation, and cell death. Furthermore, the C_{max} and AUC_{0-t} were increased by 2.53 and 8.83 folds, respectively. The relative bioavailability of MTX-NS was found to be 8.83 times higher than that of MTX-aqueous dispersion. As a result, the QbD method resulted in the development of a lyophilized MTX-NS with process understanding and control based on quality risk management.

Keywords: Nanosuspension; Lyophilized, QbD approach; Central Composite Design; Plackett–Burman Design; *In-vivo* study.

1. Introduction

Pharmaceutical experts have long struggled with the formulation and development of poorly water-soluble drugs, and these challenges are projected to worsen since more than 40% of new chemical entities discovered by drug discovery are poorly aqueous soluble.¹ Whereas, it is more problematic in the case of poorly soluble drugs with poor absorption profile, and bioavailability because it is dissolution rate-limited and can be affected by patient fed or fasted state condition². Traditional approaches including solubilization by surfactant, surfactant dispersion, micronization, use of the oily solution, permeation enhancers, which evolved too earlier, that address the challenges of formulation and have limited use.^{2,3} The major mile-

stone has been achieved in the development of poorly water-soluble drugs using various newer technology, but to date, there is no universal thumb approach applicable to all active pharmaceutical ingredients.³ Consequently, a new approach has been progressively required to deal with formulation issues that are associated with the delivery of poorly soluble drugs, to enhance their therapeutic efficacy and maximize their pharmacodynamics therapy.²

A drug delivery aims to deliver a sufficient amount of drug to a proper side in the body such that, the optimal concentration of the drug is reached rapidly and then sustained. The development of a proper dosage form is an essential element to achieve this objective.⁴ From its inception, oral drug delivery is the most commonly used route of administering the drug in various dosage forms due to



Design of "Turn-Off" Fluorescent Nanoprobe for Highly Sensitive Detection of Uric Acid using Green Synthesized Nitrogen-Doped Graphene Quantum Dots

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Abstract

Green synthesized graphene quantum dots (GQD) have been doped with nitrogen in an attempt to boost their optical characteristics and application sectors. In the present investigation, the blue luminescent nitrogen-doped GQDs (N-GQDs) were synthesized by single-step hydrothermal synthesis using tamarind shell powder as a precursor. The particle size and zeta potential of N-GQDs were found to be 11.40 nm and be -35.53 mV, respectively. A quantum yield as high as 23.78 % was accomplished at an excitation wavelength of 330 nm at neutral pH. It gets quenched sensitively in the existence of uric acid (UA) combining static quenching, electron transfer, and an inner filter effect mechanism. A linear range was obtained for UA from 10 μM to 100 μM, with a limit of detection (LOD) of 401.72 ± 0.04 pM. Additionally, the N-GQDs were selective toward UA in presence of metal ions and biomolecules that indicated its impending use to monitor UA in clinical samples. In conclusion, this work demonstrates that the N-GQDs as a sensing probe for UA recognition with notable advantages including socioeconomic, simple, and less time-consuming methods as compared to other methods. In the future, it can be potentially explored as a biosensor for UA detection in clinical samples.

Keywords: Graphene Quantum Dots; N-GQDs; Uric acid; Biosensor; Tamarind Shell Powder

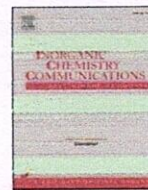
1. Introduction

Principally, UA (2,6,8-trihydroxypurine) is the primary product of purine synthesis.¹ As per literature, in the general population, UA is referred to between 0.13 mM to 0.46 mM and 2.49 mM to 4.46 mM in serum and urine, respectively.² As we know, the abnormal levels of such metabolites in body fluids can cause several diseases.³ Plentiful literature revealed that the increased UA levels in body samples are indicative of hypertension, gout, cardiovascular disease, kidney disease, high cholesterol, and many more.⁴ In comparison, low concentrations of UA are also connected with multiple sclerosis and oxidative stress.^{5,6} In diagnosis and healthcare, it is crucial to quantify me-

tabolites in blood or other biological samples. Therefore, a rapid, responsive, precise, and cheap method of assessment must be developed to track such metabolites in body fluids including serum and urine.⁵

Literature survey reported that electrochemical sensing,⁷ a colorimetric method,⁸ a chromatographic method,⁹ etc. are currently engaged detection techniques for UA in different body fluid samples. However, some in-conveniences such as complicated synthesis or challenging extraction, advanced equipment, expensive and tedious limiting their practical uses, are present in these approaches.⁵ There are no exceptions for benefit of fluorescence. It is highly sensitive, and it shows a fast reaction, and operative simplicity in contrast to the oth-





Short communication

Design of graphene quantum dots decorated MnO₂ nanosheet based fluorescence turn “On-Off-On” nanoprobe for highly sensitive detection of lactoferrin

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ABSTRACT

Lactoferrin estimation is increasingly acquiring prominence as a novel biomarker for the diagnosis of periodontal disease. To date, diverse lactoferrin detection methods which include electrochemical, surface-enhanced Raman scattering, colorimetric, and others have been extensively portrayed. Unfortunately, these systems have significant shortcomings including low sensitivity, selectivity, high cost, arduous and time-consuming technique, and so forth. Recently, the fluorescence-based method shows remarkable uniqueness that overcomes the demerits of traditionally reported techniques. Therefore, graphene quantum dots (GQDs) and manganese dioxide nanosheets (MnO₂-NS) based simplistic, highly sensitive, and selective fluorescence turn ‘Off-On’ mediated GQDs@MnO₂-NS nanoprobe was designed. Herein, MnO₂-NS addition demonstrated the quenching of GQDs containing fluorescence through inner filter effects (IFE) and strong interaction between GQDs and MnO₂-NS. The lactoferrin addition destroyed the MnO₂-NS and fluorescence emission of GQDs reappeared which may be because of redox reaction between lactoferrin and prepared MnO₂-NS. Herein, nanoprobe offers a wide concentration range and low limit of detection of 5 to 1600 ng/mL and 1.69 ng/mL, respectively. As fabricated GQDs@MnO₂-NS nanoprobe sensor demonstrated high selectivity, good stability, and reproducibility towards lactoferrin that assuring applicability of biosensor. Therefore, the GQDs@MnO₂-NS nanoprobe will offer a simplistic sensor with adequate sensitivity to achieve highly responsive and selective detection of lactoferrin.

1. Introduction

Periodontal disease is common in many countries [1], and is frequently produced by microbial infection. It stimulates the adherence of connective tissue and the prevention of bone surrounding the teeth at the onset of illness [2,3]. Despite this, its following inflammatory response adds to the loss of periodontal tissues in a patient. As a result, it is a prolonged inflammatory illness in people that causes not only regional mouth diseases but also systemic organ abnormalities [3]. Importantly, periodontal disease if remain untreated, the illness progresses to gradual bone damage, resulting in tooth movement and eventual tooth loss. As per literature, periodontal disease affects more than half of the grownup people in the United States, with around 10% suffering from serious disease those results in earlier tooth loss [4]. To prevent additional severances of periodontal disease, it is critical to

accurately diagnose it. In this regard, biomarker detection is essential in the prediction of health difficulties, and scientists are presently investigating novel biomarkers for sickness diagnosis. In latest days, advances in the science of diagnosing oral as well as periodontal illness have evolved into ways for measuring periodontal threats employing quantifiable evidence kind of as biomarkers [5].

Lactoferrin (family: transferrin) is an iron-binding glycoprotein found in secondary neutrophil granulocytes [6]. As per literature, it demonstrates responsiveness to acute inflammation [3]. In addition, lactoferrin is observed in tears and saliva [6]. Lactoferrin estimation has received a lot of attention during the last two decades as a new biomarker [7] for the diagnosis of periodontal disease. Furthermore, it may be recommended for the diagnosis of various inflammatory illnesses [8]. Several identification studies have proposed various approaches for lactoferrin detection. Mainly, single radial

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Preparation And Characterization Of Dapsone Hydrogel Using Quality By Design

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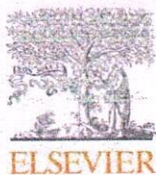
ABSTRACT:

The present study work undertaken with the intend to develop a topical hydrogel formulation of dapsone 7.5% which would attenuate the first pass metabolism associated with an oral administration. Dapsone has low solubility and low permeability and classified as BCS class II drug as per biopharmaceutics classification system. The dapsone is formulated as hydrogel which premeditated to application by topical route for the treatment of skin disease acne vulgaris. The QTPP was define considering the product quality and efficacy. CQAs are drug product quality metrics and identified for process validation. The hydrogel formulation containing dapsone was optimized by using central composed design (CCD). Concentration of polymer's and concentration of pH modifier were identified as independent variables and drug release, pH measurement, viscosity and extrudability were dependent variables. Hydroxypropyl methyl cellulose (HPMC) with concentration of 5 – 10 %, Sodium Carboxymethyl Cellulose (Sod. CMC) with 5 – 10 % as pH modifier Triethanolamine (TEA) with 2.5 – 7.5 %. The optimization study confirms with 20 runs which designate a high level of prognostic skill of response surface methodology. The formulations characterized by drug content, pH, extrudability, residence time, drug release and viscosity. From the obtained results of drug release it was concluded that an optimized formulation shows a complete drug release. An accelerated stability study analysis showed acceptable results for an optimized trial formulation.

Keywords: Hydrogel, CCD, dapsone, extrudability, etc

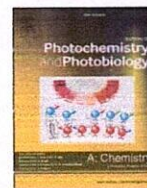
Introduction:

The administrations of topically applied drugs are considered as local drug delivery method everywhere on body such as skin, vaginal, rectal, ocular and topical route. Dermal layer is the major way of drug delivery system for topical administration because skin is one of the largest and most easily available organ on the human body. Skin plays a major obstruction for access of many substances and this is mostly because of stratum corneum of the skin, it allows only small molecules to penetrate over a period of time into a systemic circulation.



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Bovine serum albumin-derived poly-L-glutamic acid-functionalized graphene quantum dots embedded UiO-66-NH₂ MOFs as a fluorescence 'On-Off-On' magic gate for *para*-aminohippuric acid sensing

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Para-amino hippuric acid
Poly-L-glutamic acid
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ABSTRACT

Evaluating *para*-aminohippuric acid (PAH) is emerging as a promising biomarker for the diagnostics of renal disease and other kidney-related illnesses. The present study aims to develop novel bovine serum albumin-derived poly-L-glutamic acid (PLGA) functionalized graphene quantum dots (PLGA-fGQDs) embedded in UiO-66-NH₂ metal-organic frameworks (PLGA-fGQDs@UiO-66-NH₂ MOFs) for monitoring of PAH. Initially, GQDs were achieved from bovine serum albumin (green precursor) via the single-step hydrothermal method. Here, functionalization with PLGA offers a tremendous increment in optical properties of GQDs. Then, highly luminescent UiO-66-NH₂ MOFs were achieved using zirconium tetrachloride (ZrCl₄) and 2-Aminoterephthalic acid (2-ATA) as a metal ion source and organic linker. Here, surface modification of GQDs with PLGA offered high quantum yield (QY), and responsiveness. Also, luminous UiO-66-NH₂ MOFs afford a wide surface area for decorating of PLGA-fGQDs. The addition of gallium ions (Ga³⁺) into the probe solution resulted in fluorescence quenching (Turn-Off) whereas the incorporation of PAH resulted in fluorescence recovery (Turn-On). It is because of interaction with carboxylic functionality of PAH to Ga³⁺ followed by Ga-PAH complex formation. Herein, the wide concentration range and lowest limit of detection (LOD) were found to be 10 ng/mL to 900 ng/mL and 15.88 ng/mL, respectively. The specificity and real-time analysis in artificial urine validated the real-time adoption of a sensor for PAH detection. As well, it demonstrated good intraday/interday precision, stability analysis, and repeatability. In near future, the bundled illuminating PLGA-fGQDs@UiO-66-NH₂ MOFs nanoprobe will be an attractive preference for tracking PAH in clinical specimens.

1. Introduction

Renal diseases have already been considered a major public health concern around the globe. In this shade, the scientific community constantly committed to the advancement of screening methods [1]. In this ray, *para*-amino hippuric acid (PAH, 4-amino derivative of hippuric acid) is utilized in the assessment of renal plasma flow (RPF) as a diagnostic agent [2]. Hence, PAH is a valuable agent for accurately measuring effective renal plasma flow (ERPF) in clinical and laboratory research to evaluate renal functioning [3,4]. Basically, PAH is an amide derivative of glycine and *para*-aminobenzoic acid. It doesn't naturally

occur in humans. As a result, it must be injected via intravenous (IV) prior to diagnosis. As an outcome, at low plasma concentrations (1 mg to 2 mg/100 mL), the kidneys can remove 90 % of aminohippurate from the renal circulating blood in a single circulation. As a function, PAH can be exploited to examine renal function as an essential indicator [5]. The renal extraction ratio of PAH in a normal individual is between 0.92 and 1.65 mL/min/kg [6]. Traditionally acknowledged indications of renal dysfunction encompass high uric acid levels and an imbalance in PAH levels [7]. In this regard, numerous analytical techniques, such as HPLC with UV detection [6], colorimetric detection [8], tandem mass spectrometry [9], and electrochemical detection [10], have been proposed

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Mucoadhesive Tablets of Atenolol: Design, Formulation by using Thiomers Matrix and In-Vitro Evaluation

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Abstract

The major goal of this study was to develop and evaluate gastric retentive mucoadhesive tablets of atenolol and synthesized a xyloglucan- or thiomers of tamarind seed polysaccharide-were used. The oral sustained release formulations with low risk of dosage clearance are particularly well suited for the mucoadhesive drug delivery systems. Amounts of synthesised and oxidised Xyloglucan-Cysteine conjugates (Thiomers), HPMC K100M, PVP K 30, Mg-Stearate, talc, and lactose were used to create the seven formulations F1 to F7, which were used to create mucoadhesive tablets using the direct compression technique. Weight variation, friability, hardness, thickness, drug content, swelling index, drug release profiles, and mucoadhesion studies were all assessed for the produced tablets. Characterization was carried out. The formulation (F3) shown highest drug release i.e., 94% because of highest percentage of lactose and F2 shown highest mucoadhesive force comparatively. It was observed that Thiomers tablet remains in stomach for 7h, while Xyloglucan tablet disappears within 3h. The developed tablets shown drug release time T50 between 4.5-9hrs, had release after 12hrs between 42-94%, had Mucoadhesive force between 6.8-18.4g and sustained the drug release beyond 12h. The bioavailability of Atenolol was seen to have increased by use of Thiomers. The use of drug delivery carrier can be further explored for increasing bioavailability of limited permeability drugs.

KEYWORDS: Mucoadhesion, bioavailability, Atenolol, Xyloglucan, Thiomers.

INTRODUCTION

In order to deliver medications to a specific area of the body for extended periods of time, mucoadhesive drug delivery systems make use of the bioadhesion of specific polymers, which acquire adhesive following hydration. Two materials are kept together by interfacial forces in the case of bioadhesion, an interfacial phenomenon, where at least one of the components is biologically active. The bonding could occur between an artificial substance and a biological substrate, for as when a polymer adheres to a biological membrane [1]. The term "mucoadhesion" refers to the attachment of a polymer to a mucin layer of a mucosal membrane. [2] Mucoadhesive drug delivery methods include buccal, oral, nasal, ocular, vaginal, and rectal delivery drug delivery system. The most prominent drug delivery system is oral Drug delivery system for many medications. There are three types of drug delivery through the mucous membranes (1) Sublingual Drug Delivery and (2) Buccal Drug Delivery. (3) Local distribution of drugs. An appealing route of administration for precise and controlled systemic medication distribution is the buccal area of the oral mucosa. Buccal delivery refers to the distribution of medication through the mucosal lining of the cheeks. Although buccal mucosa is preferred for systemic transmucosal medication administration, sublingual mucosa is generally acknowledged to be more permeable. This is because the buccal mucosa has a larger span of smooth muscle and is comparatively immobile, making it a more desirable area for retentive systems. The buccal mucosa is a more suitable site for retentive systems due to the fact that it contains a broader span of smooth muscles and is relatively stationary. Therefore, the buccal mucosa is more suited for sustained medication administration [3].



A Review Article: Formulation of Topical Gel by QbD Approach

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Abstract Application of drug by topical route is an alternate route for the treatment of skin diseases for systemic route. The skin diseases can be treated by administration of drug by local application and may avoid first pass metabolism. It minimizes systemic side effects and when applied locally can be removed easily if any side effects occur like, irritation, skin rash, redness at the application site. The topical drug delivery has been beneficial for longer period of time because of availability of large surface area of skin which exposed to circulatory routes. Because of this route, one can be directly applied to any external body surface and it is only for local application. Amongst many types of topical dosage form delivery, gel is most likely to be used and is a patient-friendly dosage form. Due to the lack of insoluble excipients and oily bases, the gel represents better release of drug as compared to other topical drug delivery system. Nowadays, many industries follow QbD (Quality by Design) approach for the formulation of Gel to prepare a quality medicine delivery to patients. The QbD approach describes the CQA, CMA and CPP of the formulation which ensures the quality of dosage form. This review article focuses on the different dosage forms, types of gel, evaluation by taking parameters such as drug content, pH, spreadability, extrudability, viscosity, swelling index and in-vitro drug diffusion and application of QbD approach to gel formulation.

Keywords Gel, QbD Approach, Topical Drug Delivery

Delivery

1. Introduction

1.1. Drug Delivery System (DDS) by Topical Route

The administrations of topically applied drugs are considered as local drug delivery system anywhere on the body such as skin, vaginal, rectal and ophthalmic topical routes. Skin is the major way of drug delivery system for topical administration because skin is one of the largest and most easily available organs on the human body. Skin plays a major obstruction for access of many substances kept on the body and this is mostly due to stratum corneum which is outer layer of the skin, it allows only small molecules to penetrate over a period of time into a systemic circulation. Avoidance of the risk and inconveniences of injectable delivery and varied physiological condition like gastric emptying time, pH change, absorption, presence of enzyme are advantages of drug delivery by topical route. The topical drug delivery systems generally used where the other systems of drug administration fail or it is mainly used in pain management, contraception and acne. Topical drug delivery system is well-defined as an application of drug comprising preparation onto the skin which directly deliver cutaneous maladies (e.g. acne) or the cutaneous





Development of amino acid salt-based curcumin@lysine acetate co-amorphous system using liquid-assisted grinding for improved solubility and dissolution

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ABSTRACT

Curcumin, multivalued phytochemical, exhibits appreciable safety. However, its therapeutic utility is significantly compromised due to low aqueous solubility, and thus, poor absorption and low bioavailability become apparent. To surpass this limitation, the present work aims to develop amino acid salt-based curcumin@lysine acetate co-amorphous system for improved solubility and dissolution. Initially, screening of curcumin-amino acid mixtures was performed for saturation solubility assessment. Considering the outcome, lysine acetate was formulated to generate a co-amorphous mixture (COAM) by liquid-assisted grinding and evaluated for saturation solubility and different spectroscopical characterizations. Curcumin-lysine acetate COAM tablet formulation was developed by direct compression method and evaluated for appearance, thickness, hardness, weight variation, friability, drug content, disintegration, and *in vitro* dissolution studies. Further, curcumin-lysine acetate COAM and tablet formulation were screened for the accelerated stability study. Resultantly, curcumin-lysine acetate binary mixture demonstrated the highest saturation solubility among screened curcumin-amino acid binary mixtures that might be ascribed to the hydrotropic properties of lysine acetate. Moreover, 476-fold solubility enhancement in water was observed by curcumin-lysine acetate COAM. Later, the amorphization of the curcumin-lysine acetate COAM was confirmed using Fourier-transform infrared spectroscopy, differential scanning calorimetry, and powder X-ray diffraction. COAM tablet formulation showed optimum evaluation characteristics with improved drug dissolution. Therefore, the amino acid salt-based co-amorphous system can be used for solubility and dissolution improvement of curcumin and other multivalued phytochemical.

Keywords: Amino acid, co-amorphism, curcumin, dissolution, lysine acetate, solubility

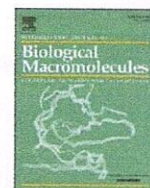
Graphical Abstract

Development of lysine acetate-based curcumin co-amorphous system using liquid-assisted grinding for improved solubility and dissolution.

INTRODUCTION

Co-amorphism has been widely attempted for improving the physicochemical and technological properties of actives.^[1,2] The co-amorphous mixture (COAM)





Design of polyacrylamide grafted sesbania gum-mediated pH-responsive IPN-based microbeads for delivery of diclofenac sodium: *In-vitro-in-vivo* characterizations

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Acrylamide grafting
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pH-sensitive microbeads, diclofenac sodium

ABSTRACT

Microwave-assisted grafting of polyacrylamide on sesbania gum (PAAM-g-SG) was implemented employing a 3² full factorial experimental design and was hydrolyzed using sodium hydroxide (NaOH) to form H-PAAM-g-SG. Further, the diclofenac sodium-loaded novel pH-sensitive interpenetrating polymeric network (IPN) microbeads were designed using an optimized H-PAAM-g-SG and sodium alginate (SA). Different spectroscopic analysis including FTIR spectroscopy, ¹H NMR spectroscopy, elemental analysis, thermal analysis, etc. was performed to confirm the synthesis of PAAM-g-SG and diclofenac-loaded pH-sensitive IPN H-PAAM-g-SG-SA microbeads. Here, Ca⁺² ions combine with two strands of SA and form a round-shape structure that encloses uncross-linked H-PAAM-g-SG polymer and diclofenac sodium. As well, glutaraldehyde (GL) addition improved the mechanical strength due to acetal structure between hydroxyl of H-PAAM-g-SG and aldehyde of GL. The drug entrapment was confirmed proportional relationship to the Ca⁺² ions concentration whereas an increase in GL concentration resulted in a reduced drug entrapment. The pH pulsatile study assured the reversible swelling-shrinkage behavior of IPN microbeads due to the carboxyl group of PAAM-g-SG. The drug release from H-PAAM-g-SG-SA microbeads (batch: S9) was found to be 84.21 % (12h) which was non-significant ($p > 0.05$; $f_2 = 79 \sim 90$) over marketed formulation (83.31 %). Moreover, it follows the Korsmeyer Peppas ($R^2 = 0.996$) as the best-fit release kinetic model. The pH-sensitive release of diclofenac sodium from IPN H-PAAM-g-SG-SA microbeads was assured based on *in vivo* anti-inflammatory activity ($p < 0.05$). Therefore, developed novel pH-sensitive IPN microbeads based on H-PAAM-g-SG are a promising polymeric carrier substitute for delivery of drugs actuated by a pH stimulus.

1. Introduction

Sesbania gum is a natural polysaccharide obtained from the annual legume seeds (biological source: *Sesbania grandiflora*; family: Leguminosae). Importantly, it contains a synthetic framework similar to guar gum. The constituent of SG is α (1–6) glycosidic bond to galactose as well as β (1–4) glycosidic bond to mannose. Hence, it is composed of mannose and galactose with a proportion of 2:1. In pharmaceutical dosage form, it has been reported as a thickening agent, floating agent, cosmetics, etc. [1,2]. Literature reported that SG can be a suitable alternative for the

development of advanced pharmaceutical dosage forms [3,4] such as hydrogels, beads, etc. It ensured that limited consideration was given to the utilization of SG as a potential replacement for excipients in pharmaceutical applications. Regardless of these benefits, there are issues with natural polysaccharides like uncontrolled hydration, lower shelf life, pH-dependent solubility, change in viscosity during storage, and terrific swellability. For the development of pharmaceutical dosage, there is a design to overcome the demerits of natural polysaccharides [5]. A wide variety of chemically modified/grafted polysaccharides has become an essential element in various biomedical applications [6].

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Medicinal Benefits of Black Rice (*Oryza Sativa L. Indica*): A Review

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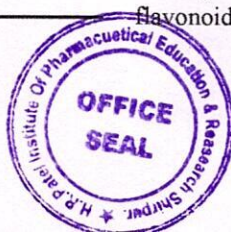
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Abstract Black rice (*Oryza sativa L. indica*) is also called purple rice (gluten free rice), emperor's rice (tribute food) and king's rice. It is abundantly grown worldwide, specifically in Asian countries such as Bangladesh, China, Japan, Sri Lanka, Indonesia, and Thailand. In India, it is majorly found in north-eastern states, including Meghalaya, Assam, and Manipur, which are the cultivators of black rice. It is also considered a superfood owing to its potent antioxidant activity which mediates numerous health-beneficial effects with anticancer, anti-inflammatory, immunomodulatory and anti-allergic characteristics. Black rice has a high nutritional value due to its rich source of various vitamins (A, B, E), amino acids and lipids, dietary fibre. The presence of the flavonoid plant pigment anthocyanin contributes to its purple-black colour and strong antioxidant properties. Other components like manganese and calcium support a healthy metabolism and stronger bones. Black rice is getting popularized in recent times because of its very low toxicity and higher nutritional qualities. This review focuses on the nutritional composition, toxicity, pharmacological uses and future opportunities of black rice for better health and well-being.

Keywords Black Rice, Health, Antioxidant, Nutrition, Pharmacology, Toxicology

1. Introduction

Rice is one of the most common key regular meal food components universally engross, specifically in South Asia. Most of the population of the countries, including India, China, Japan and other southeast countries, prefer rice over wheat as their primary food source. In ancient times in China, due to its big nutritional value, black rice was restricted only to emperors and was called "Imperial Rice" [1]. In India, people have a basic predisposition for white rice, due to the percipience of the cleaner mien of the shining and cleaner grain. Black rice is aboriginal to the North-Eastern states in India, like Assam, Manipur, and Meghalaya. Other states like Odisha, West Bengal, and some parts of Jharkhand also cultivate it [2]. In the native language of Manipur, it is commonly pronounced as 'chak-hao', where chak means rice and ahaoba means delicious, which is majorly consumed during the traditional feasts. It comes in various forms, such as short grain and long grain. The presence of the flavonoid plant pigment anthocyanin contributes to its purple-black color and is also a potent antioxidant. Black rice is growing in popularity because it is gluten- and cholesterol-free and low in sugar, salt and fat. Black rice contains more nutrients like vitamins, minerals, and proteins. Black rice contains 18 amino acids, carotene, vitamin E, iron, zinc, and copper [1]. Apart from the anthocyanins, black rice also contains many types of flavonoids and carotenoids and more than 23 other plant



Fabrication and Characterization of Curcumin-loaded Gelatin Nanoparticle Using A Two-Step Desolvation Protocol

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Abstract Recently gelatin nanoparticles (G-NPs) have been gaining substantial consideration because they offer excellent properties like low cost, biocompatibility, and biodegradability. One of the protein materials that can be utilized to make nanoparticles is gelatin. The emphasis is constructed on the datum that gelatin is non-toxic, easy to crosslink, and chemically changeable, and hence consumes a gigantic potential for colloidal drug delivery system synthesis. The surface of G-NPs can be easily cat-ionized with a variety of amine derivatives to provide targeted and sustained drug delivery. Curcumin-loaded gelatin G-NPs were manufactured using a two-step desolvation progression in this study. A glutaraldehyde cross-linker was also employed to provide G-NP with good stability. Inclusive, the ordinary size of the curcumin-loaded gelatin (CGNPs) was 112 nm, with a zeta potential of +31.80 mV. An *In-vitro* dissolution study confirmed 88 % of the drug was released from the CGNP within 24 h. In comparison, drug release showed a lower release rate, at about 66 % after 24 h. In the present work, we fabricated a curcumin-loaded gelatin nanoparticle to improve the solubility and thereby enhance the stability of a formulation, which will further encourage the progress of curcumin based on nanoformulation. Curcumin-loaded

gelatin nanoparticles have a higher stability in biological fluids than colloidal carriers, allowing for the desired delimited and unrelenting release of encapsulated drug molecules. In all, the fabricated curcumin-loaded gelatin nanoparticle proved to be a sustained-release drug delivery system.

Keywords Gelatin Nanoparticle, Gelatin, Curcumin-loaded Gelatin Nanoparticles, Glutaraldehyde, Anti-Cancer, Desolvation Method

1. Background

Because of their excellent biocompatibility and biodegradability, gelatin nanoparticles (G-NPs) have been widely used as drug and gene carriers for diseased tissues such as HIV infection [1], tuberculosis, and cancer [2]. Coating with gelatin, for example, reduces cytotoxicity while also allowing G-NPs to traverse the blood-brain barrier, allowing them to better target brain problems [3]. Recently, nanoparticles (NPs) have provided enormous benefits in terms of improving drug delivery systems by



Neuroprotective Effect of Barbaloin on Streptozotocin-Induced Cognitive Dysfunction in Rats via Inhibiting Cholinergic and Neuroinflammatory Cytokines Pathway—TNF- α /IL-1 β /IL-6/NF- κ B

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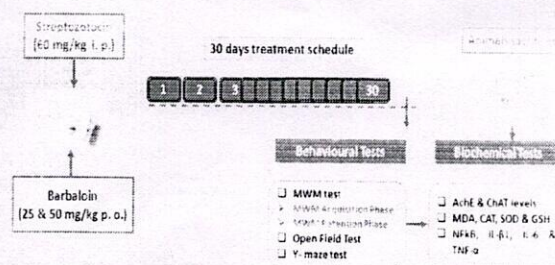
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ABSTRACT: Streptozotocin (STZ) impairs memory in rats through altering the central nervous systems (CNS) as a result of impaired cholinergic dysfunction, oxidative stress, persistent hyperglycemia, and alterations in the glucagon-like peptide (GLP). In this model cholinergic agonist, antioxidant and antihyperglycemic treatment has been shown to have positive effects. Barbaloin has a variety of pharmacological effects. However, there is no evidence on how barbaloin improves memory dysfunction caused by STZ. Thus, we examined its effectiveness against cognitive damage caused by STZ at a dose of 60 mg/kg i.p. in Wistar rats. Blood glucose levels (BGL) and body weight (BW) were assessed. To assess learning and memory skills, the Y-maze test and Morris water maze (MWM) test were utilized. Superoxide dismutase (SOD), malondialdehyde (MDA), catalase (CAT), and glutathione (GSH) as oxidative stress markers were regulated to reverse the cognitive deterioration, and choline-acetyltransferase (ChAT) and acetyl-cholinesterase (AChE) as indicators of cholinergic dysfunction, nuclear factor kappa-B (NF- κ B), IL-1 β (interleukin-1 β), IL-6, and tumor necrosis factor- α (TNF- α) contents were used. Barbaloin treatment thereby significantly decreased the BW and learning and memory capacities, resulting in substantial behavioral improvement in the Y-maze and MWM test. BGL, SOD, CAT, MDA, GSH, AChE, ChAT, NF- κ B, IL-6, TNF- α , and IL-1 β levels were also altered. In conclusion, the findings revealed that barbaloin had a protective impact against cognitive dysfunction caused by STZ.



1. INTRODUCTION

Diabetes mellitus (DM), which has been around for a while, is regarded as a prevalent metabolic illness that has a negative influence on people's quality of life. Brain atrophy and cognitive decline are two neurological problems that are recurrently seen in the CNS and peripheral system.^{1–3} Multiple organs, including the brain, eyes, heart, lower limb blood vessels, and lungs, may have complications as a result of DM. There is growing evidence that DM causes memory loss and cognitive dysfunction in diabetic (DM) animal models. Although the precise mechanism is unknown, a major risk factor for cognitive decline is DM. The hippocampus is a crucial part of the brain that regulates learning and memory, and it has been shown that chronic hyperglycemia can cause ultrastructural destruction of the hippocampus.^{4,5}

There are a number of things that seem to contribute to cognitive decline in diabetics.⁶ Many investigations have shown that hyperlipidemia and persistent hyperglycemia are important initiating and developing factors for diabetes-related cognitive impairments.^{7–9} Additionally, deposition of amyloid- β (A β), aberrant insulin signaling, and a strong inflammatory reaction

can all result from a disruption of protein, carbohydrate, and lipid metabolism under diabetic conditions, which also contributes to diabetes-related neuronal injury and cognitive deficiencies.^{9–11}

The cerebrovascular changes,^{12–14} oxidative stress,^{15–17} enhanced advanced-glycation end products,^{17,18} and underlying causes of diabetic dementias are assumed to be dysfunctions in brain insulin signaling systems.¹⁹ Additionally, it has been suggested that antioxidants,^{20,21} hypoglycemics, and insulin sensitizing medications²² can decreased DM-related cognitive decline. However, no specific medications are offered at this time to address or prevent cognitive impairment in DM.

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Graphene Quantum Dots Incorporated UiO-66-NH₂ Based Fluorescent Nanocomposite for Highly Sensitive Detection of Quercetin

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Abstract

Quercetin can help with a variety of health problems. Most methods for measuring quercetin in biological fluids are characterized by low sensitivity and selectivity. The employment of metal-organic frameworks in sensor applications with carbon-based materials ushers in a new era. In this study, blue fluorescent graphene quantum dots (GQDs) embedded in a UiO-66-NH₂ metal-organic framework-based nanoprobe (GQDs@UiO-66-NH₂) were constructed for quercetin sensing. Initially, maize husk was used to produce blue fluorescent GQDs, whereas zirconium tetrachloride and 2-aminoterephthalic acid were used to synthesize extremely luminous UiO-66-NH₂. The addition of quercetin to GQDs@UiO-66-NH₂ leads to fluorescence dampening due to the adsorption potential of UiO-66-NH₂. The complexation of zirconium ions with the 3-OH and 4-C=O functionalities of quercetin resulted in fluorescence quenching. The sensor has a linear concentration range and limit of detection for quercetin of 50–500 and 2.82 ng/mL, respectively. The nanoprobe's usefulness for quercetin detection was then validated by a selectivity investigation in the presence of interfering chemicals. Furthermore, the percentage relative standard deviations were 4.20% and 2.90%, respectively, indicating great stability and repeatability. Fluorescence "Turn-On-Off" nanoprobe provides a simple, quick, sensitive, and selective method for monitoring quercetin.

Keywords: quercetin; graphene quantum dots (GQDs); fluorescence; nanoprobe; metal-organic framework; GQDs@UiO-66 NH₂; sensitivity

Introduction

Quercetin is the most important flavonoid in fruits and vegetables [1]. It does not produce in human bodies [2]. Quercetin is widely reported for antioxidant, antiviral, immunomodulation, antitumor [3], and anti-inflammatory [4] applications. The literature claimed that 945 mg/m² is the safe dose for quercetin. A high dose of quercetin can produce

different several health issues including hypertension, a decline in potassium levels in serum, and emesis [2]. Therefore, accurate measurement of the concentration of quercetin is essential in the biomedical field [3]. Moreover, to measure the bioavailability of quercetin, it is essential for pharmacological response [1]. In general, analysis of quercetin with a simplistic, speedy, highly selective, and sensitive method is a prime necessity [4].





Chemopreventive aspects, investigational anticancer applications and current perspectives on allyl isothiocyanate (AITC): a review

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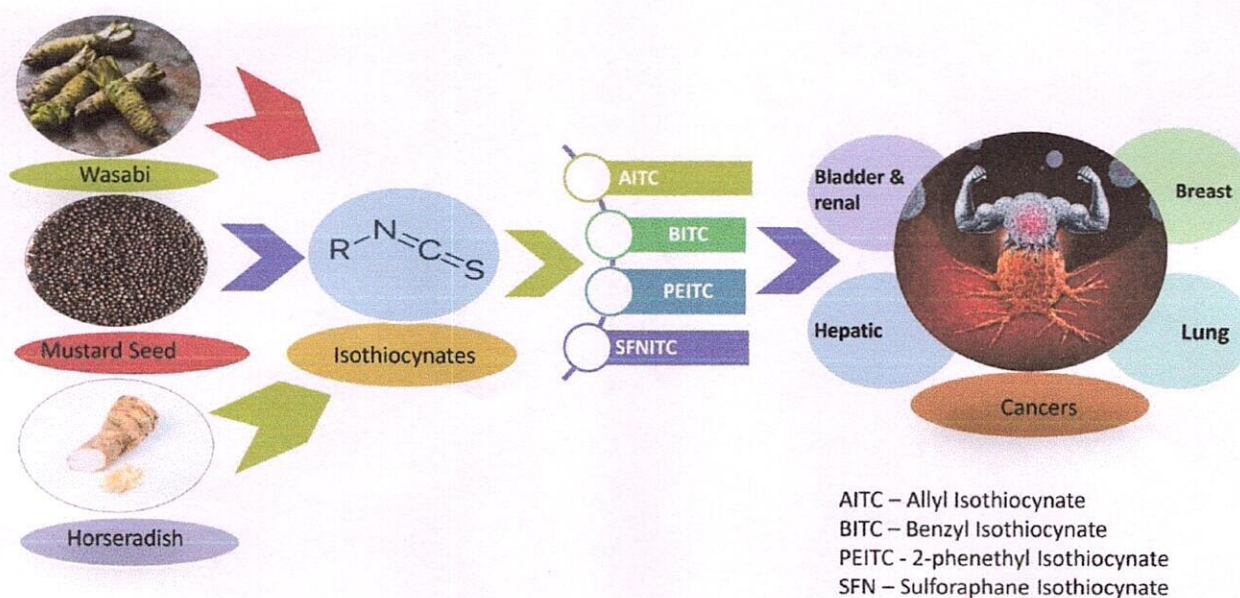
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Abstract

Allyl isothiocyanates (AITC) have gained recognition in recent years as effective chemotherapeutic and epigenetic modulators. The chemopreventive properties and toxicological perspectives of AITCs from the last few decades were taken into account by a number of investigations. Their active therapeutic relevance was hindered by a number of factors, including instability under typical physiological conditions and low bioavailability due to low aqueous solubility. In this review, we highlighted the chemopreventive attributes of AITC in relation to its molecular mechanisms and metabolic fate for cancer. Moreover, we emphasized on investigational anticancer activities and various strategies for delivery of AITC in different types of cancer. Considering cellular interactions, we shed light on the toxicological properties of AITCs to address further issues regarding their assessment in therapeutic development. This review identifies knowledge gaps with various contemporary approaches involving most recent studies and may pave the way for a better understanding for the development of novel AITC therapeutics.

Graphical abstract



Keywords Allyl isothiocyanate · Molecular mechanisms · Anticancer-activity · Drug delivery · Toxicity

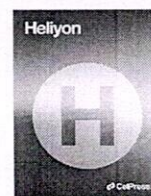
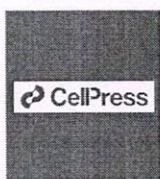
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Research article

Phytochemical profile, antioxidant, cytotoxic and anti-inflammatory activities of stem bark extract and fractions of *Ailanthus excelsa* Roxb.: *In vitro*, *in vivo* and *in silico* approachesPriyanka R. Sapkal^a, Anilkumar U. Tatiya^a, Sandip D. Firke^a, Vivek K. Redasani^b, Shailendra S. Gurav^c, Muniappan Ayyanar^d, Prasad G. Jamkhande^e, Sanjay J. Surana^a, Rakesh E. Mutha^f, Mohan G. Kalaskar^{a, *}^a R. C. Patel Institute of Pharmaceutical Education & Research, Shirpur, Maharashtra 425405, India^b Yashoda Technical Campus, Faculty of Pharmacy, Satara, Maharashtra 412 802, India^c Department of Pharmacognosy, Goa College of Pharmacy, Goa University, Panaji, Goa 403 001, India^d Department of Botany, A.V.V.M. Sri Pushpam College (Affiliated to Bharathidasan University), Poondi, Thanjavur, Tamil Nadu 613 503, India^e Centre for Research in Pharmaceutical Sciences, Sharda Bhavan Education Society's Nanded Pharmacy College, Nanded, Maharashtra, 431605, India^f H. R. Patel Institute of Pharmaceutical Education & Research, Shirpur, Maharashtra 425405, India

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ABSTRACT

This study aimed to assess the phytochemical composition, *in vitro* antioxidant, cytotoxicity, and *in vivo* anti-inflammatory activities of the methanolic extract of *Ailanthus excelsa* (Simaroubaceae) stem bark and its fractions. Quantitative phytochemical analysis revealed that methanolic extract and all fractions contained a high level of flavonoids (20.40–22.91 mg/g QE), phenolics (1.72–7.41 mg/g GAE), saponins (33.28–51.87 mg/g DE), and alkaloids (0.21–0.33 mg/g AE). The antioxidant potential was evaluated *in vitro* using a range of assays, i.e., DPPH•, ABTS radical scavenging ability, and total antioxidant capacity. The chloroform and ethyl acetate fractions showed stronger antioxidant activity than the methanol extract. *In vitro* cytotoxic activity was investigated in three human tumor cell lines (A-549, MCF7 and HepG2) using the SRB assay. In addition, the *in vivo* anti-inflammatory effect was assessed by carrageenan-induced paw edema in rats. The chloroform fraction showed a more pronounced effect by effectively controlling the growth with the lowest GI50 and TGI concentrations. The human lung cancer cell line (A-549) was found to be more sensitive to the chloroform fraction. Furthermore, the chloroform fraction exhibited significant anti-inflammatory activity at a dose of 200 mg/kg in the latter phase of inflammation. Besides, methanol extract and ethyl acetate fraction revealed a significant cytotoxic and anti-inflammatory effects. The chloroform fraction of stem bark showed a strong anti-inflammatory effect in experimental animals and significant COX-2 inhibitory potential in the *in vitro* experiments. GC-MS analysis of chloroform fraction identified the phytochemicals like caftaric acid, 3,4-dihydroxy phenylacetic acid, arachidonic acid, cinnamic acid, 3-hydroxyphenylvaleric acid, caffeic acid, hexadecanoic acid, and oleanolic acid. The *in-silico* results suggest that identified compounds have better affinity towards the selected targets, viz. the BAX protein (PDB ID: 1F16), p53-binding protein Mdm-2 (PDB ID: 1YCR), and topoisomerase II (PDB ID: 1QZR). Amongst all, caftaric acid exhibited the best binding affinity for all three targets. Thus, it can be

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Antifungal Nail Lacquer For Enhanced Transungual Delivery Of Ciclopirox Olamine

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Abstract:

Onychomycosis of the nails, onychomycosis is the most common nail disease. It is characterized by discoloration, brittleness and thickening of the nail infection and is usually caused by dermatophytes but can also be caused by non-dermatophyte molds and yeasts. Besides the negative effects of the nails, it can be painful and sometimes serious in some severe cases of the disease. There is also a link between onychomycosis and other fungal diseases (athlete's foot, hand, etc.) and the spread of hand infection to other parts of the body, etc. believed to spread. There is also a link between onychomycosis and HIV, which may indicate that patients are immune to the virus. It can also cause diabetes and uncontrolled diabetes, which is important for the disease. Other conditions that can increase the risk of onychomycosis are trauma, age, and peripheral vascular disease, although genetics also play a role. In addition, studies have shown that nail mold can affect patients' mental and health, affect their self-confidence and quality of life, and affect their ability to work. Because of its increasing global prevalence and greater prevalence in elderly patients or people with comorbidities, this is an important disease that needs to be addressed.

Keywords: Transungual, Onychomycosis, Antifungal.

Introduction

Current treatment recommendations for onychomycosis include treatment with oral or topical antibiotics. Oral treatment preference of the patient and the doctor is low due to its known side effects, especially pain. Cosmetics are unsatisfactory in terms of performance and are limited by the impermeability of the nail plate to hydrophobic antifungal agents. Cosmetic treatments often need to be combined with oral antibiotics to achieve the desired results. But researchers are working to develop antibiotics that can be applied topically to the infected area, and some show promise.¹⁻²

Recent methods for effective delivery of antibiotics include the use of modified materials such as colloidal or chemical substances or improved penetration methods of cosmetic use. Chemical methods that improve access have some advantages over physical methods, such as being cheaper, attached to or used with models, and can be easily used without expert practice.³

Deck's structure is essentially a composite of keratin fibers with a low lipid content (0.1% - 1%) and water (10 - 25%). Many researchers refer to nail files as hydrogels and have found that better hydrated nails are more permeable due to loose structure and increased porosity.

This is thought to be due to changes in van der Waals forces, hydrogen bonding, and ionic interactions between the matrix and proteins, which lead to the elasticity and breakdown of the keratin matrix during hydration.

By design, solutions and varnishes are the most popular, but creams and gels have also been tried as drug delivery vehicles. Lacquers are a promising distribution as they are based on the idea that after the solvent has evaporated, they form a polymeric drug-laden film on the tissue that contains a lot of chemicals and has



RESEARCH ARTICLE

Development and Evaluation of Vasoactive Intestinal Peptide Freeze-Dried Injection

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ABSTRACT

Introduction: Vasoactive intestinal peptide (VIP), a ubiquitous, naturally synthesized human peptide is extensively documented to have diverse physiological effects like anti-inflammatory, immune-modulatory, anti-hypertensive, stimulation of contractility in the heart, vasodilation, and promoting neuroendocrine-immune communication. The synthetic form of VIP is called aviptadil (AVP). The main objective of this research was to develop a novel stable lyophilized dosage of VIP (Aviptadil) using sucrose as a bulking agent.

AVP is a peptide with known concern for aqueous stability, which seems to be challenging for storing finished drug products and supply chain management. The VIP injection was developed using the lyophilization technique in the presence of bulking agent and some other pH-adjusting agent. The bulking agent and solvent system selection depends upon the solubility, stability of the drug substance, and feasibility during manufacturing. During product formulation development, the bulk solution was evaluated for processing time and temperature impact. The lyophilization cycle was developed using the most advanced freeze-drying technology.

Result and discussion: With the usage of bulking agent (sucrose) as may act as a cryoprotectant for peptide, the formulated bulk solution was freeze-dried, and primary drying was done at -25°C (below than critical product temperature) followed by secondary drying at 25°C. The critical quality attributes of lyophilized drug products like the description of lyophilized cake/powder, moisture content, reconstitution time, active drug content and color of the solution were evaluated. The developed formulation bulk solution was stable and compatible with contact materials like SS vessels when hold up to 24 hours at 2 to 8°C. The optimized freeze-dried product meets the predefined acceptance criteria as part of the quality target product profile.

Conclusions: It can be concluded from the research work carried out that a stable lyophilized parenteral formulation containing VIP (AVP) was developed using sucrose as a bulking agent. These findings show that the freeze-dried formulation is an appropriate technological remedy for stabilizing VIP in lyophilized injectable dosage form.

Keywords: Vasoactive intestinal peptide, Aviptadil, sucrose, quality by design, Freeze dried microscope, lyophilization.

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Source of support: Nil.

Conflict of interest: None

INTRODUCTION

Vasoactive intestinal peptide (VIP), a ubiquitous, naturally synthesized human peptide, is extensively documented to have diverse physiological effects like anti-inflammatory, immune-modulatory, anti-hypertensive, stimulation of contractility in the heart, vasodilation, and promoting neuroendocrine-immune communication.¹ VIP is the synthetic form of VIP that increases adenosine cyclase activity with consequent smooth muscle relaxation. Relief Therapeutics has been granted investigational new drug (IND) status in the US and Europe, along with orphan drug designation for the use of VIP in acute respiratory distress syndrome (ARDS), acute lung injury (ALI), pulmonary fibrosis, and sarcoidosis.²

The male genital tract naturally contains the 28-amino acid neurotransmitter known as the VIP (VIP: International non-proprietary name, Aviptadil), which is thought to play a part in the local neurological control of smooth muscle activity and penile erection.³ VIP appears to play a specialized role in smooth muscle relaxation, which results in systemic vasodilation, enhanced cardiac output, and bronchodilation.

VIP has a variety of physiological effects, including smooth muscle relaxation that causes systemic vasodilation, increased cardiac output, bronchodilation, some variations in the effects on gastric motility and secretory processes, hyperglycemia, inhibition of smooth muscle cell proliferation, hormonal regulation, analgesia, hyperthermia, neurotropic effects,

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RESEARCH ARTICLE

Design, Development and Characterization of Ropinirole Mouth Dissolving Film by using Spin Coating Technique

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ABSTRACT

The aim of the research was to develop a ropinirole mouth-dissolving film employing solvent casting and spin coating methods with sesbenia gum acting as a film-forming agent. Parkinson's disease is treated with ropinirole. Sesbenia gum was designed as a film-forming ingredient in the 25 to 600 mg concentration range for solvent casting and 50 to 250 mg for spin coating. For both procedures, the concentration of the plasticizer propylene glycol was optimized between (0.3 and 1.0 mL). Film-forming agent and plasticizer effects at various concentrations were examined. For the solvent casting and spin coating processes, the plasticizer concentration was 0.3 mL for each, while the optimal film-forming agent concentrations were 50 and 150 mg, respectively. Ropinirole MDFs were made employing an enhanced concentration and more excipients. In comparison to the solvent casting approach, the spin coating process produced films with better surface morphology, a 24 seconds shorter disintegration time, good tensile strength of 3.2 (N/mm²), a thinner thickness of 0.2 mm, and a maximum drug content of 93.14%. Sesbenia gum has been discovered to have greater potential for the spin-coating method of developing a ropinirole mouth-dissolving film.

Keywords: Sesbenia gum, Ropinirole, Mouth dissolving film, Solvent casting and spin coating method.

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Conflict of interest: None

INTRODUCTION

For most therapeutic agents, administration through the mouth has been considered the most convenient and well-liked delivery method. Over the past few decades, researchers have been working on developing intraoral delivery systems (IODS) that can provide the ideal drug exposure for the optimum therapeutic benefit. In order to provide those who had trouble in swallowing tablets, capsules and syrup, with an alternative to these traditional solid dosage forms, in the late 1970s, the first fast-dissolving drug delivery system was developed. The problem of swallowing solid dosage forms can be resolved with new and innovative oral drug delivery system, which swiftly dissolves in the mouth in a few seconds without water. Tablets, granules, pills, caplets, films, wafers and powders are part of fast and quick dissolving system. The tongue's top or bottom is where the film is placed. It maintains the application site while rapidly releasing the active ingredient for local and/or systemic absorption.¹

A novel oral fast-dissolving dose form combines the convenience of dosing without water or beverage with the

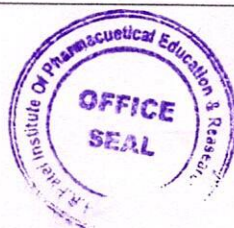
simplicity of administration. Despite their quick disintegration/dissolution times, some patient groups still worry about swallowing solid pills and run the danger of choking. Fast-dissolving film eliminated The possibility of choking.² Oral films can be divided into the following three categories.³

- Mucoadhesive sustained release wafers,
- Mucoadhesive melt away wafers and
- Flash release

Fast-dissolving film criteria: A good oral film should melt or disintegrate in mouth in few seconds without being swallowed, and it should work effectively for flavor masking. There should be no little residue left in the mouth on oral intake. Environmental variables, including humidity and temperature, have minimal effects on oral fast-dissolving film.

Ropinirole is used to treat Parkinson's disease and the symptoms of restless legs syndrome. The production of oral films involves the rolling method, hot melt extrusion, solid dispersion, semisolid casting, and solvent casting. The current investigation used spin coating and solvent casting to produce the oral film for the drug ropinirole.³

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RESEARCH ARTICLE

Synthesis and Characterization of Hydroxypropyl *Sesbania* Galactamannan Seed Gum for Pharmaceutical Application

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ABSTRACT

The core focus of current research is chemical polysaccharide modification in pharmaceutical applications. The gum is made from the endosperm of *Sesbania grandiflora* Plant seeds that belongs to family Leguminosae. Both water-soluble and water-insoluble gum were present in the *Sesbania* seed powder; the water-soluble gum was removed during purification, yielding a 30% purification yield. In order to increase the applications of partially hydroxypropyl *Sesbania* gum, the modifications indicated here entail adding hydroxypropyl groups to the molecule under a variety of different conditions. Among the factors that were looked at were the etherifying agent concentration, alkaline volume, and preparation medium parameters, including the reaction time and temperature. The degree of substitution (DS) was raised, which boosted the unaltered gum's solubility, stability, and viscosity. Increases in an etherifying agent and alkali concentration, volume, reaction duration, and temperature increase DS from 0.4 to 0.7. The finished product was characterized using IR spectroscopy, differential scanning calorimetry, X-ray diffraction, scanning electron microscopy, rheologic property, solubility, swelling index, and gel fraction analysis of batch F1 as an improved batch. The alternate method for developing drug-loaded nanoparticles for controlled release dosages form by using hydroxypropyl *Sesbania* gum.

Keywords: *Sesbania* gum, Hydroxypropylation, Chemical modification, Degree of substitution, Viscosity, Solubility.

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Source of support: Nil.

Conflict of interest: None

INTRODUCTION

Polysaccharide gums are among the most popular industry components and have become the subject of much research regarding their long-term sustainability, biodegradability and biological safety.¹ A few drawbacks, however accompany the use of gums. They include the potential of microbial contamination, changing rates of hydration, influenced by pH soluble content, thickening up, and viscosity loss on storage are a few of these. Gums can be chemically altered to reduce these limitations while simultaneously increasing their solubility and viscosity.²

According to Duke *et al.*, the endosperm, or outermost layer, of a seed of the species *Sesbania grandiflora* (Leguminosae) is used to make *Sesbania* gum. According to Farooqi *et al.*, *Sesbania* seeds are composed of a coat 6.9 to 18.9%, endosperm 40 to 42% and germ about 51.1%.

The outermost layer of seed is made up of galactose side chain residues linked by -(1-6) and a mannan backbone connected by -(1-4) glycosidic connections, which is known as

galactomannan. According to one study, the ratio of galactose to mannose produced by the acid hydrolysis of *Sesbania* galactamannan gum was 1.2:2.2 as opposed to 1:3.9 for locust bean (carob), and for tara gum 1:2, and 1:3. It is believed that the varying degrees of branching are what produce the variances in the characteristics of galactamannan gums. More side groups reduce the amount of molecular bonding and improve the cold-water dispersion of gum, as reported as.^{3,4}

Galactamannan, sometimes referred to as galactose side chain residues and a mannan backbone coupled by -(1-4) glycosidic linkages, make up the endosperm. In contrast to the ratios of 1:3.9 for locust bean (carob), 1:2, and 1:3 for Tara gum, one study found that the ratio of galactose to mannose generated by the acid hydrolysis of *Sesbania* galactamannan gum was 1.2:2.2. The differences in properties of galactamannan gums are assumed to be caused by the varied degree of branching.⁵

The reagents utilized and the reaction conditions have a significant impact on how effective the hydroxy propylation reaction is. Due to its accessible structure, the amorphous area

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Clotrimazole-loaded Silver Nano - cellulose fibre preparation and characterization

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ABSTRACT:

In this study, a brand-new, simple procedure for environmentally friendly silver nanoparticle and Clotrimazole production on wheat fibre was reported. The Polyethylene glycol-400 (PEG 400) was used in the liquid phase chemical technique to produce silver nanoparticles. PEG 400 was used in the manufacture of silver nanoparticles as a stabilizer and reducing agent. The typical silver nanoparticle is 150 nm in size. The produced silver nanoparticles may be distributed in water, ethanol, and other polar solvents, and they have promising uses in the electrical and biological sciences. Silver nanoparticle aggregation was reduced by using ethanol as a solvent. Clotrimazole was physically loaded onto cellulose fibre using a physical loading technique. The Wheat fibre received an effective antifungal property from the combination of Clotrimazole and silver nanoparticles. After washing, there was hardly any loss in the antifungal effectiveness of the cotton fabrics treated with nano silver and clotrimazole. As more silver nanoparticles were loaded onto the outer layers of the white Wheat fabrics, their colour altered to a yellowish brown. Additionally, the antifungal effectiveness of wheat fibre loaded with drugs and AgNP was assessed against the common fungus *Candida albicans*. The presence of Clotrimazole and silver

