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MEDICINAL CHEMISTRY RESEARCH

VIEW ARTICLE

n insight into prodrug strategy for the treatment of Alzheimer's isease

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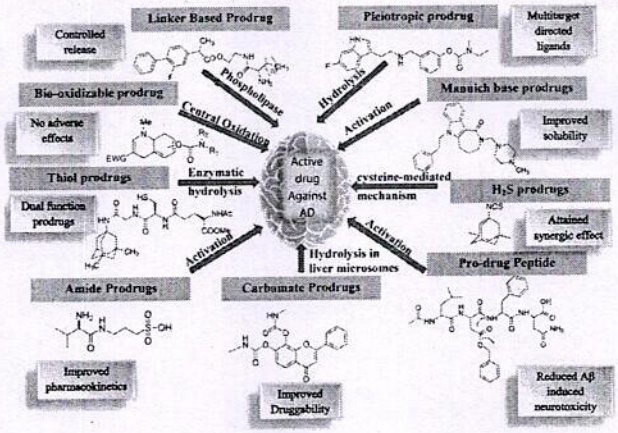
bstract

lzheimer's disease (AD) is the leading cause of dementia worldwide. With 35 million people over 60 suffering from ementia, new treatments for AD are immediately needed. In order to streamline this process, it is critical to use insights and ssons learned from previous failures to future drug development efforts. Prodrugs have turned into a well-established elivery for increasing the physicochemical, pharmacokinetic or biological properties of pharmacologically potent ndidates and overcoming hurdles to a drug's usefulness in both drug research and development. In the present work, we cus on how prodrug strategy can leverage drug discovery to address drug development issues in AD. This review ghlights the application of prodrug approach in treatment of AD by categorizing them into bio-oxidizable prodrugs, ester/ mide prodrugs, pleiotropic prodrugs, linker-based prodrugs, Mannich base prodrugs, peptide-based and thiol-based rodrugs and gives an elaborate account of the research reported in the last two decades, i.e., from the year 2000 to 2021.

raphical abstract



ywords Alzheimer's disease · Prodrugs · Blood–brain barrier · Dementia · CNS delivery

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VIEW

nostructured metal–organic framework-based luminescent sensor r chemical sensing: current challenges and future prospects

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stract

m its inception, an astonishing movement has been made in the architecture and fabrication of a fresh category of nano-ctured material acknowledged as luminescent metal–organic frameworks (MOFs). Luminescent MOFs are self-assembled nostructure by coordinating suitable metal cations or clusters and ideal organic linkers, which exhibited an abundance of tis for sensing of interest of analytes, such as chemicals, metal ions, biomarkers, etc. Herein, tunable surface morphology d diverse functionality of luminescent MOFs offer high sensitivity, high selectivity, good stability, recyclability, real-time plicability, etc. Additionally, the accessible porosity and luminescence property of nanostructured MOFs provides the nsducing potential from host–guest chemistry to recognizable improvement in nanosize MOFs luminescence. Therefore, this review article, we have summarized the nanostructured design of MOFs-based luminescent sensors for chemical d metal ions sensing. At first, the requirement of monitoring of chemical residues and metal ions exposure has been dis-sed that demonstrates the topical necessity for the chemical and metal ions recognition. Afterward, the current trends of OFs-centered sensors, synthesis types, and their properties have been elaborated in brief. It revealed that several theoreti-l sensing mechanisms, such as electron transfer, energy transfer, ligand interaction, overlapping effect, oscillation effect, er filter effect, decomposition, etc., are accountable for sensing of metal ions and chemical residues. The applications of no-architectured MOFs-based luminescent sensors for chemical as well as metal ions sensing have been illustrated, which ibit the lowest detection limit (μM–nM) for both metal ions and chemicals. Interestingly, the nanostructured MOFs relied luminescent sensors that exhibited high sensitivity and selectivity for the chemical and metal ions in presence of diverse erfering substances. Surface functionality presented on the surface of nano-size MOFs, types of ligands, and selected metal s provides precise recognition of real-time samples containing metal ions and chemicals. On the whole, the nanostructured sign of a MOFs-based luminescent sensor will release a fresh preference for sensing of a target analyte.

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Formulation of Silk Fibroin-based Single Polymeric Floating Microspheres for Sustained Release of Lafutidine

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ABSTRACT

Purpose: The present study was aimed at the formulation of lafutidine-loaded silk fibroin-based floating microspheres (LAFU-SF-Microspheres) for the site-specific sustained release of the drug. **Materials and Methods:** Briefly, the single polymeric system comprising SF was selected to prepare LAFU-SF-Microspheres by employing the emulsion solvent evaporation method. Subsequently, the obtained LAFU-SF-Microspheres were assessed for particle size, zeta potential, percent entrapment efficiency (%EE), percentage drug content (%DC), micromeritics, floating profile, *in-vitro* drug release, spectroscopical analysis, and accelerated stability study. **Results:** The particle size and zeta potential of the LAFU-SF-Microsphere were found to be 2.3-6.8μm and -21.93mV respectively whilst % EE and % DC of LAFU-SF-Microspheres were found to be 86.83 ± 3.46% and 93.89 ± 3.98% respectively. Moreover, it demonstrated the adequate angle of repose (26.50 ± 1.06°) and Carr's Compressibility Index (CI) confirming the excellent flow properties. In view of the floating profile, LAFU-SF-Microspheres showed floating lag time (FLT) between 9-13sec and total floating time (TFT) more than 12hr. Moreover, the % buoyancy was found to be 97.62 ± 4.78%. LAFU-SF-Microspheres showed *in-vitro* % drug release up to 92.41 ± 4.29% adopting the first-order model. The FTIR indicated successful incorporation of LAFU in LAFU-SF-Microspheres. The DSC and PXRD indicated the disrupted crystallinity of LAFU in LAFU-SF-Microspheres. The SEM images of microspheres displayed spherical shapes with smooth textures. **Conclusion:** SF microspheres can be fruitfully applied for customized floating and release patterns of drugs with distinct solubility classes.

Key words: Lafutidine, Silk fibroin, Microsphere, Floating drug delivery, Sustained release.

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INTRODUCTION

Despite tremendous advancements in drug delivery approaches, the oral drug delivery system still contributes the major share owing to its versatility, convenience, patient compliance, and cost-effectiveness. Considering recent developments, modified oral dosage forms can prominently offer targeted drug delivery.[1] In this context, the gastroretentive drug delivery system has gained much attention from researchers specifically for actives that act locally and exhibit absorption windows in the upper part of the gastrointestinal tract (GIT).[2,3] Interestingly, various approaches have been developed to achieve gastro retention which includes swelling and expanding system, floating system, bio(muco) adhesive system, etc. by incorporation of excipient that can modify density, shape, size, and adhesion ability of dosage form.[4] Amongst them, the floating drug delivery system has been widely explored by researchers due to the simplicity and feasibility of formulation design.[5,6]

Lafutidine (LAFU); a recent H2- receptor antagonist (second generation) is widely advised for the treatment of gastric ulcers.[7] LAFU demonstrates high receptor binding affinity (2-80 folds) compared to the

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NEUROPROTECTIVE PROPERTIES OF MEDICINAL PLANTS: A COMPREHENSIVE REVIEW

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Abstract
This result of uplifted metabolic rate and weak antioxidant system, the central nervous system (CNS) is exposed to oxidative stress. Reactive oxygen species (ROS) are increasingly implicated in neurodegenerative disorders, according to growing experimental data. The preservation of neuron structures and functionality despite assaults occurring from cellular damages caused by a number of substances or neurological diseases is termed as neuroprotection. Schizophrenia, depression, alzheimer's disease, dementia, cerebrovascular impairment, seizure disorders, head injury, and parkinsonism are examples of neurodegenerative illnesses that can be substantially functionally disabling. Antioxidants work by inactivating and reducing or avoiding these diseases. Ayurveda, an ancient Indian medical system, has identified a variety of botanicals with therapeutic effects for neurological illness and antioxidant properties. Ayurveda, an indigenous Medical system, has identified a variety of herbs with therapeutic effects for neurological illness and antioxidant potential. Human cognitive performance has been demonstrated to be improved by *Bacopa monniera* extracts.Antioxidant properties are reported for bacopa extract. Ginkgo biloba has been shown to lower levels of free oxygen radicals. In oxidative stress-induced neurodegeneration, extracts of *Withania somnifera* enhance antioxidant state. There are still a lot more plants that need to be looked at and see whether they want any neuroprotective characteristics. A variety of medicinal herbs utilised in Ayurveda practises, as well as Chinese medicines, were found to include diverse components and phytochemicals that may have a neuroprotective impact, which might be advantageous in various neurodegenerative and neuropsychiatric problems, and per the review.
Keywords: Neuroprotection; Antioxidant; Neurodegenerative disease; Medicinal herbs.

Introduction

Neuroprotection refers to the techniques and their significance mechanisms that can protect the Central Nervous System (CNS) from neuronal loss caused by different neuropsychiatric and alzheimer's disease disorders such as Alzheimer's disease, anxiety, cerebrovascular impairment, seizures, Parkinson's disease, and so on. Neurodegenerative diseases are estimated to be the second the most frequent primary cause of death throughout elderly by the 2040s [1]. Phytochemicals may be a beneficial therapy in hopes of preventing neurodegenerative illnesses, as one of the neuroprotection techniques. There have been several observations of both natural and synthetic neuroprotective agents; nevertheless, synthetic neuroprotective agents are thought to produce adverse effects such as dry mouth, weariness, drowsiness, sleepiness, worry or uneasiness, issue with balance, and so on. Herb based medicated products have drawn considerable awareness from research bases and industries in recent years at the national and international levels. As a result, There has been a considerable measure of research on the potential of phytochemicals to alter neuronal activity and protect against neurodegeneration. Herbal medicine, also characterized as phytotherapy, is a complementary and alternative medication that involves the medicinal use of plant components (leaves, stems, roots, flowers, fruits, and seeds) for their medicinal

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REVIEW

Surface nanoarchitectured metal–organic frameworks-based sensor for reduced glutathione sensing: a review

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Abstract
Reduced glutathione (GSH) is a major biomarker related to a variety of diseases including cancers, cardiovascular disease, liver damage, autism in children, and others. Although the human body can synthesize GSH, it falls well short of meeting the needs of all of the body's functions. Consuming GSH-containing meals may help in solving the problem of low GSH levels. As a result, the development of an effective probe for measuring GSH in foods, agricultural products, nutritional supplements, and other products is critical for food safety and disease diagnostic. This, in turn, leads to the creation of metal–organic frameworks (MOFs) as nanoporous sensors for sensing of GSH in complicated samples such as urine, human serum samples, various foods, and vegetables, etc. Unfortunately, widely utilized sensors have numerous drawbacks such as selectivity, sensitivity, detection speed, simplicity, and so on. As a result, there is a great demand for the upgrading of extremely sensitive, selective, fast, and robust biosensors for GSH measurement. Presently, the structural design of MOFs has piqued the interest of researchers for detection of GSH owing to its remarkable and adaptable qualities such as high sensitivity, excellent selectivity in clinical samples, food components, agriculture goods, nutritional supplements, and so on. The methods and tactics for measuring GSH utilizing MOFs-based sensors, such as fluorescent, colorimetric, electrochemical, and ratiometric sensors, are summarized. In addition, detail explanation regarding synthesis of MOFs, fabrication of DNA conjugated MOFs, and enzyme-functionalized MOFs for specific sensing of GSH has been explored. Development of novel strategies for selective sensing of GSH with respect to all categories has been summarized. Remarkably, the low detection limit for GSH in the M to nM range was demonstrated by surface nanoarchitectured MOFs-centered biosensors. Finally, current challenges and future prospects for advanced applications of MOFs-based biosensors are highlighted. Eventually, this review may aid both academic and industrial researchers in the rational development of MOFs-based biosensors for GSH sensing.

Minal Patil has contributed to this work.

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Opinion paper

Formulation, optimization, and *in vitro* evaluation of anastrozole-loaded nanostructured lipid carriers for improved anticancer activity

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ABSTRACT

The present study aims to develop and optimize anastrozole (ANZ)-nanostructured lipid carriers (ANZ-NLCs) for improved anticancer efficacy. In a nutshell, ANZ-NLCs were prepared by a 3^2 factorial design approach through the solvent evaporation method. In this study, key formulation factors impacting particle size, % drug encapsulation, and zeta potential were optimized in ANZ-NLCs. The physicochemical characterization and *in vitro* cytotoxicity, cell apoptosis, cell cycle analysis, cell uptake, and investigation of apoptotic nuclei by DAPI study was performed on MCF 7 to assess the potential of ANZ-NLCs. The optimized batch exhibited the spherical and smooth surface morphology that was confirmed by AFM and HR-TEM. In addition, the optimized batch showed 164.4 nm particle size, 62.95% entrapment efficiency, and −26.3 mV zeta potential. Elucidation of FTIR and H NMR studies revealed compatibility of ANZ with the carrier lipids and DSC and XRD confirmed amorphous ANZ-NLCs (which was the type of NLC formed). The *in vitro* ANZ release study revealed the significance of compritol in release modulation from ANZ-NLCs. Herein, the optimized batch demonstrated extended-release in different release media (upto 48 h), following the fickian type. *In vitro* anticancer efficacy was assessed by cytotoxicity, cell apoptosis, cell cycle analysis, cell uptake, and apoptotic nuclei, which confirmed the significant anticancer efficacy of ANZ-NLCs compared to free ANZ. Consequently, ANZ-NLCs made from compritol 888 ATO and capryol could be a prospective formulation exhibiting significant anticancer potential in the oral delivery of ANZ for the effective dealing of breast cancer (BC).

1. Introduction

From its inception, the mortality of female breast cancer (BC) remains one of the prime leading causes of mortality, across the globe [1]. In this line, numerous drugs including aromatase inhibitors, have been prescribed as a potential adjuvant in postmenopausal women for hormone-sensitive advanced metastatic BC. Anastrozole (ANZ), a third-generation non-steroidal aromatase inhibitor (type-II), has displayed a considerable advantage in lessening BC-related and global mortalities. It primarily suppresses oestrogen production by reversibly binding to and inhibiting the enzyme aromatase [2,3]. Literature survey reported that the ANZ has been widely prescribed as a tablet formulation for the management of BC. In high-risk women, it has been endorsed in the United Kingdom for the treatment of BC. Principally, its prospective role can be ascribed to selectivity and potent nature [4]. It is commonly prescribed as a 1 mg tablet per day for the treatment lasting up to 2.5 years. Literature reveals that the ANZ is moderately soluble, poorly permeable (BCS III), and associated with many severe adverse effects viz: gastrointestinal disturbances including hemorrhage, vaginal bleeding, thrombocytosis, osteoporosis, etc. [5]. As a consequence, there is a tremendous desire for solutions to ANZ's aforementioned difficulties.

For two decades, lipidic systems have substantiated the potential for the effective delivery of various anticancer drugs. Lipidic soluble drugs are ideal candidates for lipidic nanosystems. Hence, the selection of lipids having high solubility of drug leads to high encapsulation potent transfection abilities, and lesser toxicity compared to other polymeric nanosystems [6]. Besides this, the orally administered NLCs can also adhere to the gut wall prolonging the residence time, and consequently the absorption [7]. Additionally, lipidic nanosystems may also shield the loaded active from chemical degradation as well as enzymatic degradation, and gradually release them from the prepared lipid matrix at the

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Original Article

A 3^2 Factorial Design Approach for Formulation and Optimization of Azilsartan Medoxomil Nanosuspension for Solubility Enhancement

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ABSTRACT

Background: Azilsartan medoxomil (AZL) is an orally active nonpeptide angiotensin II receptor antagonist with less water solubility and oral bioavailability. **Objectives:** Increase the solubility and dissolving rate of AZL. **Materials and Methods:** For formulation we used a probe sonication approach to create nanocrystals. The impacts of independent factors such as % polymer concentration (X_1) and sonication duration (X_2 min) on dependent variables such as particle size (Y_1 nm) and % drug release (DR) were optimised using a 3^2 response surface methodology (Y_2). **Results:** The prepared batches were examined for size, polydispersity index (PDI), zeta potential, solubility study and dissolution study. AZL nanocrystal (PS2 batch) particle size and zeta potential was found to be 168 ± 10 nm, 0.314 ± 0.02 and - 22.72 ± 2.6 mV respectively. The batch (PS2) with the best results was chosen and subjected to additional testing. *In vitro* dissolution of all 13 batches and pure drug was in ranges of 51.98-81.99% and 11.23 %, respectively. **Conclusion:** The FTIR analysis indicated that AZL and soluplus have no physical interaction. DSC, XRD, and SEM investigations revealed that the crystalline form of the medication was converted to an amorphous form, resulting in an improve water solubility and dissolution rate. Thus the studies exhibited nanocrystals prepared by probe sonication method showed significant enhancement in solubility and dissolution rate.

Key words: Azilsartan medoxomil (AZL), Nanocrystal, Sonication, Solubility, Drug release.

INTRODUCTION

In whatever mode of administration, solubility is a critical element for medication therapy. Up to 40% of new medications developed by the researchers in recent years have been predicted to be poorly water soluble or lipophilic substances.[1] Unfortunately, due to solubility issues, many of these prospective medications are abandoned in the early phases of development. Poor solubility medications in gastrointestinal fluids are common causes of insufficient bioavailability. According to the BCS, increasing the drug's solubility and dissolution rate in gastrointestinal fluids can improve bioavailability, especially for class II (they are low solubility and high permeability) drugs. Because the drug release and solubility in the gastric fluid is rate limiting step for BCS class II drugs, rather than absorption, increasing solubility increases bioavailability.[2] As a result, it's critical to understand these medications' solubility issues and techniques for overcoming them so that the active compounds' potential therapeutic effects can be realised.[3] As a result, numerous efforts have been made to improve medication solubility.[4]

A number of approaches have been developed throughout the years to increase the solubility of medications that are poorly water soluble. Physical adjustments to the drug substance, chemical modifications to the drug substance, and other procedures are all examples of solubility improvement technique. These strategies can increase the aqueous solubility of poorly soluble medications. Nanosuspension is most favorable techniques for enhancing the solubility and dissolution rate of poorly water soluble drugs.[5]

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Scientific paper

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 metabolites 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-

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Chitosan mediated layer-by-layer assembly based graphene oxide decorated surface plasmon resonance biosensor for highly sensitive detection of β-amyloid

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ARTICLE INFO

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Graphene oxide, silver nanoparticles

ABSTRACT

Alzheimer's disease (AD), and its consequent effect primarily clinical dementia, Parkinson's disease dementia, etc. currently bring potential avenues for diagnosis centered on identification of beta-amyloid$_{1-42}$ ($A\beta_{1-42}$). Unfortunately, techniques engaged in AD core biomarker ($A\beta_{1-42}$) detection are majorly suffering from poor sensitivity and selectivity. Thus, we fabricated graphene oxide (GO) surface decorated chitosan (CS) mediated layer-by-layer (LbL) assembly based surface plasmon resonance (SPR) biosensor for highly sensitive and selective recognition of $A\beta_{1-42}$. Briefly, silver nanoparticles (AgNPs) and GO synthesis were achieved through a greener approach. LbL assembly was designed using CS and polystyrene sulphonate (PSS) on surface of AgNPs (AgNPs-CS-PSS-CS) and then antibodies of Aβ (anti-Aβ) were fixed on LbL assembly (AgNPs-CS-PSS-CS@anti-Aβ). Herein, amine functionality of CS offers a plethora of sites for anti-Aβ antibody immobilization that gives specific direction, high selectivity, and an adequate amount of antibody immobilization. For fabrication, synthesized GO was immobilized on an amine-modified gold-coated sensor chip via carbodiimide chemistry followed by AgNPs-CS-PSS-CS@anti-Aβ immobilization on an activated GO surface. Inimitable features of LbL assembly showed improved selectivity towards Aβ peptide whereas utilization of affinity biotransducer with a combination of plasmonic and non-plasmonic nanomaterial improved sensitivity and selectivity. Consequently, linearity range and limit of detection (LOD) of $A\beta_{1-42}$ antigens were found to be 2 fg/mL to 400 ng/mL and 1.21 fg/mL, respectively. Moreover, analysis of $A\beta_{1-42}$ in AD-induced rats confirmed the real-time-applicability of the designed SPR biosensor. Hence, GO surface decorated AgNPs-CS-PSS-CS@anti-Aβ mediated SPR biosensor would provide a novel approach for exceptionally sensitive and selective Aβ detection.

1. Introduction

Alzheimer's disease (AD) is a progressive, and irreversible neurodegenerative disease [1]. Subsequently, continuous progress in AD results in clinical dementia [2]. Importantly, AD is defined biologically by the presence of β -amyloid (Aβ) plaques and tau-containing neurofibrillary tangles in the brain [3]. It causes amnestic cognitive impairment in the prototypical form and non-amnestic cognitive impairment in the less common variants [3,4]. Literature divulged that AD is perhaps the leading prevalent form of dementia among individuals over the age of 65. It affects approximately 5 million individuals in the United States (US). As the population ages, the number of AD cases in the US is expected to climb to 16 million by 2050 [5]. Conventional diagnostic methods including imaging, laboratory analysis, examination, and initial history of the patient have been preferred to diagnose AD [5,6]. Such methods are suffering from plenteous demerits including less detection accuracy, extremely expensive, time-consuming, etc. Moreover, there is no promising treatment existed for the management of AD whereas symptomatic treatment can endow with a short period of relief. As a result, there is necessary to establish a newish solution to diagnose AD and clinical dementia at an early stage, which can contribute to the improvement of individual life [6,7].

Merely on AD phenotype, it is complicated to determine the fundamental disease process concerned in AD. Herein, assorted biomarkers might be of considerable assistance in expediting the early recognition of AD [8]. As per literature, biomarkers are quantitative signals that are expressed within a certain stage of the ailment. It renders them essential for both diagnosis and tracking therapy response [9]. In the case of AD,

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Short communication

Design of graphene quantum dots decorated MnO_2 nanosheet based fluorescence turn "On-Off-On" nanoprobe for highly sensitive detection of lactoferrin

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Sensitivity

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 (MnO_2-NS) based simplistic, highly sensitive, and selective fluorescent turn 'Off-On' mediated GQDs@MnO_2-NS nanoprobe was designed. Herein, MnO_2-NS addition demonstrated the quenching of GQDs containing fluorescence through inner filter effects (IFE) and strong interaction between GQDs and MnO_2-NS. The lactoferrin addition destroyed the MnO_2-NS and fluorescence emission of GQDs reappeared which may be because of redox reaction between lactoferrin and prepared MnO_2-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@MnO_2-NS nanoprobe sensor demonstrated high selectivity, good stability, and reproducibility towards lactoferrin that assuring applicability of biosensor. Therefore, the GQDs@MnO_2-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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Biomedical Materials

PAPER

Biofabricated functionalized graphene quantum dots (fGQDs): unraveling its fluorescence sensing mechanism of human telomerase reverse transcriptase (hTERT) antigen and *in vitro* bioimaging application

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Keywords: functionalized graphene quantum dots, hTERT, fluorescence quenching, turn 'On-off-On' biosensing, bioimaging

Supplementary material for this article is available online

Abstract

Lung cancer (LC) is a deadly malignancy that is posing a serious threat to human health. Therefore, early detection of LC biomarkers is the key to reducing LC-related fatalities. Herein, we present the first fluorescent-based selective detection of LC biomarker human telomerase reverse transcriptase (hTERT) using polyethyleneimine (PEI) functionalized graphene quantum dots (fGQDs). One-pot *in situ* synthesis of amine-functionalized GQDs was accomplished by hydrothermal carbonization of biowaste-derived cellulose and PEI. Synthesized fGQDs were characterized by various analytical techniques. Synthesized fGQDs not only exhibited enhanced fluorescence life-time but also excellent stability in the different solvents compared to bare GQDs. The surface activation of hTERT-Ab by carbodiimide chemistry (EDC-NHS) resulted in stacking interactions with fGQDs, involving adsorption-desorption as well as competitive mechanisms. The higher inherent affinity of hTERT-Ag (hTERT antigen) for hTERT-Ab (hTERT antibody) resulted in complex formation and recovery of fGQD fluorescence. As a result, this fluorescence sensing demonstrated a greater linear detection range (0.01 ng ml^{-1}–100 μg ml^{-1}) as well as a notable low detection limit (36.3 pg ml^{-1}). Furthermore, the fabricated immunosensor (Ab@fGQDs) has excellent stability and performance in real samples, with an average recovery of 97.32%. The results of cytotoxicity and cellular bioimaging study in A549 cells show that fGQDs can be used for additional nanotherapeutics and biological applications.

1. Introduction

Among all cancer-related deaths worldwide, lung cancer (LC) is accounted for the highest mortality rate on a global scale [1]. The global pattern of LC incidence and mortality rates is changing every day, with experts predicting that the general population will be at a higher risk of developing LC [2]. According to recent reports, LC is the most commonly diagnosed cancer (11.4%) and has the highest death rate (18%) of all cancers [3]. The literature revealed that a variety of LC biomarkers have been studied independently viz. cancer antigen 125 (CA125) [4], cytokeratin fragment (CYFRA21-1) [5], neuron-specific enolase (NSE) [6, 7], melanoma-associated antigens (MAGE A2, MAGE A11) [8], carcinoembryonic antigen (CEA) [9], heterogeneous nuclear ribonucleoprotein (hnRNP A2-B1) [10] and fibrin degradation product (D-dimers) [11], including human telomerase reverse transcriptase (hTERT) [12–14].

The hTERT is a ribonucleoprotein polymerase (RNP), which adds the TTAGGG repeating units to the telomere by which it performs its characteristic functions [15]. Telomerase is mostly found in fetal tissues, mature germ cells, and tumor cells about 70%–90%. Telomerase expression is critical for cellular immortalization and cellular senescence. The ectopic expression of hTERT plays an important role in the

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Design of zero-dimensional graphene quantum dots based nanostructures for the detection of organophosphorus pesticides in food and water: A review

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ARTICLE INFO

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ABSTRACT

From its inception, traditional analytical approaches have been the primary strategies for sensing organophosphorus pesticides (OPPs). Unfortunately, traditionally reported methods are suffering from plentiful limitations that include their cost factor, poor responsiveness, low specificity, tedious, etc. Recently, graphene quantum dots (GQDs) have been widely applied to researchers' recognition of OPPs sensing in water and food samples, due to their outstanding and versatile attributes. Moreover, the combination of other nanomaterials like inorganic and organic materials, along with surface tuning of GQDs such as doping and functionalization, shows the potential to boost the performance of the sensing system. Despite this indubitable development, there is no detailed report on the design of zero-dimensional GQD-based nanostructures for the detection of OPPs in food and water. Therefore, we have addressed the GQDs-centered nanostructures for the recognition of OPPs in water and food. Importantly, it covers the consumption of OPPs and their impact on human health, while the synthesis and properties of nanosized GQDs have been reviewed. Besides, GQDs based on fluorescent, electrochemical, and colorimetric nanoprobe for monitoring OPPs have been illustrated. Moreover, sensing mechanisms, anti-interference potential, current challenges, and future research have been described. Fascinatingly, modification of GQDs enabled sensors exhibits supreme responsiveness and specificity for recognition of OPPs in provided samples. Accordingly, existing architectured GQDs mediated nanoprobes furnish the lower detection limit for OPPs up to a picogram. In near future, the nano-design of GQD-centered sensors will open up a new door for sensing OPPs in real-time samples.

1. Introduction

Pesticides are increasingly being utilized in crop management and pest control in advanced agricultural practices. Surprisingly, the world food demand rises, leading to increased pesticide utilization [1]. Pesticides have been categorized into rodenticides, insecticides, fungicides, and herbicides [2]. As well, pesticides such as organochlorines, organophosphorus, carbamates, pyrethrin, and pyrethroids are often chemically categorized [3]. Among reported pesticides, organophosphorus pesticides (OPPs) are most widely employed in agriculture due to the relatively long half-life, low persistence, cheaper price, high insecticidal efficacy, and high effectiveness [4,5]. Principally, OPPs are phosphoric acid ester, thiol, or amides derivatives with a diverse range of carbon, oxygen, sulfur, and nitrogen bonded compositions [6]. There are hundreds of OPPs in use due to the enormous number of chemical combinations. Moreover, most extensively OPPs used in agriculture are malathion, parathion, methyl parathion, azamethiphos azinphos-methyl, chlorpyrifos, diazinon, dichlorvos, disulfoton, fenitrothion, fonofos, phosmet, tetrachlorvinphos, terbufos, etc [7]. Owning to lethal effect on the target pests and easy accessibility, OPPs are extensively utilized over the globe [8]. Likewise, organochlorine pesticides such as dichlorodiphenyltrichloroethane (DDT), aldrin, and dieldrin have been phased out due to lack of effectiveness and environmental persistence. OPPs are usually soluble in water and rapidly degrade via hydrolysis once introduced into the air, sunlight, and soil [9]. Moreover, the extensive use and non-persistent nature of OPPs remain for a longer period in the environment. It leads to environmental contamination and has gradually evolved into the food supply chain via water, air, and soil [10]. Surprisingly, OPPs residues accumulate in the body even at very low concentrations, triggering serious health issues [11].

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Fabrication of poly (aspartic) acid functionalized graphene quantum dots based FRET sensor for selective and sensitive detection of MAGE-A11 antigen

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MAGE-A11
Fluorescence resonance energy transfer
Turn "on–off-on" sensing
Bioimaging

ABSTRACT

In the present work, we investigated a label-free fluorescence resonance energy transfer (FRET) based poly (aspartic) acid (PAsP) functionalized graphene quantum dot (PAsP-GQDs) immunosensor for the selective and sensitive sensing of MAGE-A11 antigen.

Synthesis of GQDs was accomplished with hydrothermal carbonization of Onion hull (ONI-GQDs). Synthesized PAsP-GQDs were characterized for fluorescence performance, functional compositions and morphological analysis. To form a typical FRET system, functionalized GQDs conjugated with anti-MAGE-A11 (antibody) using EDC/NHS chemistry served as an energy donor, while graphene nanosheets served as energy acceptors (quenchers). The fabricated PAsP-GQDs@M−A11−Ab immunosensor demonstrated high selectivity to MAGE-A11 with a broader detection range about of 0.05 ng mL^{-1} – 5 μg mL^{-1} (R^2 = 0.9906) and a detection limit of about of 5.6 pg mL^{-1}, with a rapid response time of 12 min. The performance of the developed immunosensor was established using real sample analysis, which showed an average recovery of 96.8 % with % RSD 0.71 indicating the high precision and reproducibility of the method. Furthermore, to implicate the post-functionalization modifications, cellular bioimaging potential and cytotoxicity studies were conducted as a comparative assessment. The present immunosensing strategies can be utilized as an analytical tool for detecting MAGE-A11 in various cancers.

1. Introduction:

The global cancer risk is growing steadily, with a high fatality rate per year. The most recent epidemiological survey statistics raised concerns about the possibility of imposing cancer cases [1]. Among the various types of cancer, lung cancer (LC) is the most frequently diagnosed cancer worldwide next to breast cancer [2]. With precise early detection testing, the stages of LC can be identified. In that, identification of different tumor markers could be the key finding to arrest at the proper stage with desirable treatment. Different types of tumor marker (protein) were identified as an indication of the LC such as carcinoembryonic antigen (CEA), cancer antigen-125, pro-gastrin-releasing peptide (proGRP), cytokeratin fragment (CYFRA 21–1), Melanoma-associated antigen family proteins (MAGE's) and neuron-specific enolase (NSE) etc. [3,4]. Amongst these, MAGEs are often observed in the fetal keratinocytes, placenta, and male germ cells as well as different human malignancies. Melanoma-associated antigen-A11 (MAGE-A11) is an X-linked gene that is expressed at a lower rate specifically in the placenta, testis, endometrium and ovary of humans [5]. The MAGEs family protein plays a vital role in physiology as well as pathology of germ cell development embryogenesis, neurogenetic, cell cycle progression, apoptosis, etc. MAGE-A11 antigen expression is also found at differential levels in lung cancer, breast cancer and prostate cancer [6]. Surprisingly, it was found at higher levels in adenocarcinoma than in squamous cell carcinoma of lungs. Hence, MAGE family antigens are considered ideal target markers for immunotherapy as well as early diagnosis and management [7,8].

Accordingly, the use of different methods such as Southern blotting with reproductive tract fluid (RTF), polymerase chain reaction-based (PCR) based methods, high-resolution telomere length analysis (STELA), DNA-Microarrays, enzyme-linked immunosorbent assay (ELISA), etc. being investigated as supportive methods [9]. Though the systematic estimation methodology of MAGEs is limited, there is growing interest in researchers for the assessment of their interactions

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Formulation, optimization, and *in-vitro-ex-vivo* evaluation of dual-crosslinked zinc pectinate-neem gum-interpenetrating polymer network mediated lansoprazole loaded floating microbeads

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ABSTRACT

Low methoxy pectin (LM pectin) suffers from burst release owing to its high swellability and solubility in water. Consequently, in ways to design an ideal drug delivery system, these obstacles must be surmounted. Therefore, the work aimed to design dual crosslinked LM pectin -neem gum (NG) mediated interpenetrating polymer network (IPN) floating mucoadhesive microbeads for lansoprazole (LNZ) gastro-retentive delivery. In short, LNZ-loaded floating microbeads were achieved by using the ionic gelation method wherein zinc acetate was preferred as a crosslinking agent. The optimization of IPN microbeads was performed employing a 3^2factorial design wherein concentration of pectin and NG was considered as independent factors whereas dependant factors are entrapment efficiency and drug release. Importantly, carboxylic functionality of low methoxy (LM) pectin and hydroxylic functionality NG cross-linked with Zn^{+2} forms a 3D network. Diffractogram and thermogram revealed that conversion of drug from crystalline to amorphous form because of entrapment of drug within polymeric network. Anticipated floating microbeads showed that polymer concentration had considerable effect on drug encapsulation efficiency and drug release. Briefly, optimizing floating microbeads (Batch B:5) showed maximum drug entrapment (87.47 %) with a delayed drug release (69.20 %, at 8 h) due to formation of strong IPN. Moreover, it showed good mucoadhesive aptitude with goat stomach mucosa because of entanglement between gum and mucus layer. In addition, use of calcium silicate assists to modulate floating profile of IPN microbeads. Therefore, designing dual crosslinked zinc-pectinate-NG mediated IPN floating mucoadhesive microbeads will offer a new substitute for floating delivery.

1. Introduction

Gastro-retentive drug delivery system (GRDDS) one of the oral drug delivery systems gained popularity due to various qualities, such as decreased therapy costs, easy administration, self-medication, greater patient compliance, and acceptability [1]. It is an approach that overcomes the problems in drug absorption due to the short residence time in the stomach faced by conventional drug delivery. It can markedly extend the residence time of drugs in the stomach, increasing bioavailability and decreasing drug waste. Therefore, it is possible to achieve site-specific drug delivery specifically to the stomach and upper small intestine [2,3]. Floating drug delivery is one of the major approaches of GRDDS to achieving prolonged gastric retention to attain appropriate drug bioavailability and drug targeting [2]. These devices release the medicine gradually at a predetermined and controlled rate without influencing the gastric emptying rate [4,5]. At the moment, dual-functioning systems that combine floating and mucoadhesive processes are getting a lot of interest since they can greatly boost the performance of traditional GRDDS [6,7]. Additionally, the multiple-unit GRDDS demonstrates its advantage over the single-unit forms by ensuring uniform dispersion across the gastrointestinal tract [8].

Nowadays, Recent trends incline toward the use of natural products derived from plant materials [9,10] to minimize and restrict the use of synthetic additives because the former is biodegradable, found in abundance in nature, non-toxic, and provides ease in working and at low cost [11,12]. In the current scenario, due to their outstanding

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REVIEW ARTICLE

Nanosuspension: A New Horizon in the Drug Delivery System

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ABSTRACT

Solubility is one of the major concerns in various drug formulations. Since the majority of new drug molecules belong to the BCS II (Biopharmaceutical Classification of Drug) they often lead to poor bioavailability and ultimately affect the drug's effectiveness. The majority of new drug molecules are insoluble and hence poorly bioavailable. Because of these limitations, the proportion of newly discovered drugs reaching the market is decreasing. Nano-suspension emerges as one of the novel solutions for these problems. As it helps in delivering poorly water-soluble drugs, due to their all-around features and unique advantages. The distinctive features of nanosuspensions allow them to be used in a variety of dosage forms, including mucoadhesive hydrogels, nanogels, etc. The present review article provides information regarding the introduction to nanosuspensions, the advantages, and disadvantages of nanosuspensions, different methods of their preparations, and numerous practical applications in drug delivery.

Keywords

Nanosupension, Dissolution, Surfactant, Solubility, Bioavailability.

Introduction

Nanosuspension is a biphasic dispersion of superficially stabilized micron-sized drug particles. Therapeutic nanosuspensions seem to be very tiny solid particles of a drug suspended in an aqueous carrier for administration via oral, local, parenteral, or pulmonary routes. Dispersed particles in nanosuspensions are in the size range of 200 to 600 nm (Èller et al., n.d.). The drug maintains the ideal crystalline state with smaller particles in nanosuspension technology, enhancing the rate of dissolving and penetration and improving bioavailability. Higher solubility and micronized particle penetration (particle size <10 μm) is associated with increased surface area and thus dissolution rate. Nano-sized particles can increase the dissolution rate and solubility. Except; as the diffusion distance on the drug nanoparticle surface decreases, the concentration gradient increases (Mü & Peters, 1998). The stability of nanosuspension is affected by the size of the particles produced by the various manufacturing processes. Crystal development and consequent fine particle production are caused by Ostwald ripening. The difference in dissolution rate between fine and coarse particles is due to the availability of surface area. Molecules diffuse from a zone of greater concentration to a region of lower drug concentration. As a result, a supersaturated solution forms surrounding the large particles, causing the medication to crystallize and huge particles to proliferate. Sedimentation, high-pressure homogenization, emulsification, and milling processes can all be used to make nanosuspensions. Nanosuspensions can be made in one of two ways.

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ORIGINAL ARTICLE

Fabrication of polyaspartic acid surface-modified highly fluorescent carbon quantum dot nanoprobe for sensing of reduced glutathione in real sample

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Abstract
The goal of this study was to create a polyaspartic acid (PAA) surface-modified blue luminescent carbon quantum dots (CDs)-based biosensor (PAA-CDs) that could detect calcium (II) ions and glutathione (GSH) with excellent sensitivity and selectivity. Herein, the hydrothermal approach was adopted to produce blue luminescent CDs from mint plant stalks. To improve surface irregularities, quantum confinement effects, and to impart recognition sites for the analyte sensing, the CDs were surface-functionalized with PAA. Spectroscopic techniques like UV, FT-IR, XPS, and other techniques were used to sanction the synthesis and surface functionalization of PAA-CDs. The probe PAA-CDs was utilized for the detection of Ca (II) ions via a quenching process (turn-off) and subsequently, restoration in fluorescence intensity (turn-on) was accomplished by incorporation of GSH, forming a novel probe for sensing of biothiol. For a linearity range of 0–45 µM concentration of Ca (II), the LOD was obtained as 25 nM in phosphate-buffered saline solutions (PBS, pH 7.4). Similarly, for a linearity range of 0–40 µM concentration of GSH, LOD was obtained as 64 nM. The surface-modified PAA-CDs exhibited stronger affinity towards Ca (II) ions via the FRET mechanism, which formed the Ca (II)@PAA-CDs complex that was unable to emit photons when excited. Thereafter, thiol (-SH) group of GSH offered selective attraction with Ca (II) ions among the various biomolecules; this caused the breaking of Ca (II) from Ca(II)@PAA-CDs complex. So, the detachment of Ca (II) from the complex re-established the fluorescence intensity of PAA-CDs in linear fashion. In addition, the cytotoxicity study of the PAA-CDs revealed their biocompatible nature, and the methodology was effectively practical to estimate the GSH concentration in human serum samples.

Keywords Carbon quantum dots · Polyaspartic acid · Functionalized carbon quantum dots · Calcium (II) ions sensing · Glutathione sensing · Fluorescent probe

Introduction

The reduced glutathione (GSH), homocysteine (Hcys), and cysteine (Cys) are major biothiols playing noteworthy functions in the conservation of pathological and physiological processes (Ballatori et al. 2009). The distinguished biothiol, GSH, is an important biological stuff that could be monitored to diagnose a number of diseases (Staal and Ela 1992).

The GSH is a putative antioxidant that performs a variety of important biological tasks such as maintaining biological redox status, modulating cell growth, gene regulation, decontamination, and metabolic activity (Yoo et al. 2019). GSH is reportedly found in normal cells (1–10 mM) and plasma (1–6 µM) (Khan and Patil 2020). Abnormal levels of GSH are linked to numerous diseases and disorders. According to the study, increasing GSH levels boosted antioxidant levels and oxidative stress resistance in cancer cells (Lucero and Chan 2021). Reduced GSH levels, on the other hand, indicate the loss of immune system functions as well as the possibility of an aging problem. Similarly, its shortage may lead to enhanced levels of oxidative stress, causing cancer (Bottino et al. 2021).

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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-NH_2 MOFs as a fluorescence 'On-Off-On' magic gate for *para*-aminohippuric acid sensing

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Graphene quantum dots

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-NH_2 metal–organic frameworks (PLGA-fGQDs@UiO-66-NH_2 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-NH_2 MOFs were achieved using zirconium tetrachloride ($ZrCl_4$) 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-NH_2 MOFs afford a wide surface area for decorating of PLGA-fGQDs. The addition of gallium ions (Ga^{3+}) 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 Ga^{3+} 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-NH_2 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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Original Article

Mucoadhesive Tablets of Atenolol: Design, Formulation by using Thiomer 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 thiomer 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 (Thiomer), 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 Thiomer 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 Thiomer. The use of drug delivery carrier can be further explored for increasing bioavailability of limited permeability drugs.

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

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].

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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

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 keen 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 delight cutaneous maladies (e.g. acne) or the cutaneous