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3.3.2 Number of research papers published per teacher in the Journals notified on

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UGC website during calendar year 2023

| Sr. No. | Calendar Year | Number of Research Papers Published |
|---------|---------------|-------------------------------------|
| 1 | 2023 | 31 |
| | Total | 31 |



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Research publications in the Journals notified on UGC website during calendar year 2023

| Title of paper | Name of the author/s | Publication date | Name of journal | Calendar Year of Publication | ISSN number | Link to website of the Journal | Link to article / paper / abstract of the article | Scopus/Web of Science/UGC Care Link |
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Development of amino acid saltbased curcumin@lysine acetate co-amorphous system using liquidassisted grinding for improved solubility and dissolution

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ABSTRACT

Curcumin, multivalued phytoceutical, 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 curcuminlysine 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 phytoceutical.

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

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

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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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Keywords: Sesbania gum Acrylamide grafting Interpenetrating polymer network 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; f2 = 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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(b): Sakshi Bhardwaj, Dhanashree Javere, Pradnya Bagad, Likhit Akotkar, Vivekanad Chatap, Urmila Aswar (2023). Medicinal Benefits of Black Rice (Oryza Sativa L. Indica): A Review. Advances in Pharmacology and Pharmacy, 11(3), 199 - 207. DOI: 10.13189/app.2023.110303.

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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. 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 chakhao ', 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

Research Article



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" nanoprobes provide 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].

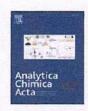


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Poly(allylamine) coated layer-by-layer assembly decorated 2D carbon backbone for highly sensitive and selective detection of Tau-441 using surface plasmon resonance biosensor

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HIGHLIGHTS

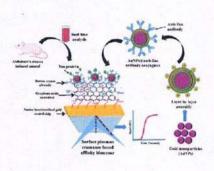
- The first-time layer-by-layer (LbL) approach was preferred for selective and sensitive recognition of Tau-441 antigen.
- Antibody immobilization on poly(allylamine) coated gold nanoparticles (AuNPs) LbL assembly gives affinity biotransducer.
- Graphene oxide (GO) layered surface plasmon resonance (SPR) biosensor provides detection limit up to femtogram level.
- Spiked sample and preclinical studies assured the feasibility of GO@LbL-Au NPs-Anti-Tau SPR biosensor for Tau-441 sensing.
- Report on label-free, highly sensitive, and selective detection of Tau-441 using GO@LbL-AuNPs-Anti-Tau SPR biosensor.

ARTICLEINFO

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Keywords:
Tau protein
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2D carbon backbone
Surface plasmon resonance
Lbl. assembly
Gold nanoparticles

GRAPHICAL ABSTRACT



ABSTRACT

The determination of clinically significant amounts of tau protein in bodily fluids is a major problem in Alzheimer's disease (AD) diagnosis. As a result, the present work aims to develop a simple, label-free, fast, highly sensitive, and selective 2D carbon backbone graphene oxide (GO) patterned surface plasmon resonance (SPR) mediated affinity biosensor for Tau-441 monitoring. Initially, non-plasmonic nanosized GO was made using a modified Hummers' method, whereas green synthesized gold nanoparticles (AuNPs) were subjected to a layer-by-layer (LbL) design employing anionic and cationic polyelectrolytes. Several spectroscopical evaluations were carried out to ensure the synthesis of GO, AuNPs, and LbL assembly. Following that, the Anti-Tau rabbit antibody was immobilized on the designed LbL assembly using carbodiimide chemistry, and various studies such as sensitivity, selectivity, stability, repeatability, spiked sample analysis, etc., were conducted using the constructed affinity GO@LbL-AuNPs-Anti-Tau SPR biosensor. As an output, it shows a broad concentration range and a very low detection limit of 150 ng/mL to 5 fg/mL and 13.25 fg/mL, respectively. The remarkable sensitivity of this SPR biosensor represents the merits of a combination of plasmonic AuNPs and a non-plasmonic GO.

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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. International Journal of Drug Delivery Technology (2023); DOI: 10.25258/ijddt.13.2.21

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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. 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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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.

International Journal of Drug Delivery Technology (2023); DOI: 10.25258/ijddt.13.2.10

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Source of support: Nil.

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

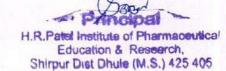
A novel oral fast-dissolving dose form combines the convenience of dosing without water or beverage with the simplicity of administration. Despite their quick disintegration/dissolution times, some patient groups still worry about swallowing solid pills and run the danger of choking. Fast-dissolving 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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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 waterinsoluble 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 suing hydroxypropyl Sesbania gum.

Keywords: Sesbania gum, Hydroxypropylation, Chemical modification, Degree of substitution, Viscosity, Solubility. International Journal of Pharmaceutical Quality Assurance (2023); DOI: 10.25258/ijpqa.14.2.11

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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. 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 Faroogi 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 coldwater 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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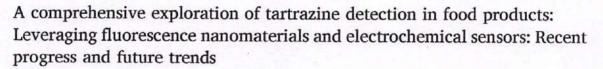


Food Chemistry

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Review





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ARTICLEINFO

Keywords: Fluorescence nanomaterial Carbon dot Tartrazine Quenching Sensing Food safety

ABSTRACT

Azo dyes are widely used as food coloring agents because of their affordability and stability. Examples include brilliant blue, carmoisine, sunset yellow, allura red, and tartrazine (Tar), etc. Notably, Tar is often utilized in hazardous food goods. They are frequently flavoured and combined with food items, raising the likelihood and danger of exposure. Therefore, detecting Tar in food is crucial to prevent health risks. Fluorescence nanomaterials and electrochemical sensors, known for their high sensitivity, affordability, simplicity, and speed, have been widely adopted by researchers for Tar detection. This comprehensive paper delves into the detection of Tar in food products. It extensively covers the utilization of advanced carbon-based nanomaterials, including CDs, doped CDs, and functionalized CDs, for sensitive Tar detection. Additionally, the paper explores the application of electrochemical sensors. The paper concludes by addressing current challenges and prospects, emphasizing efforts to enhance sensitivity, and selectivity for improved food safety.

1. Introduction

Tartrazine (Tar) (E 102) is an artificial orange-colored powdered azo dye (S. Chen, Yu, & Wang, 2018). This pigment was initially found in 1884 (Scientific Opinion on the Re-evaluation Tartrazine, 2009). This water-soluble azo food pigment has high stability, vivid color, high color strength, and low cost (Vidotti, Costa, & Oliveira, 2006). It is frequently found in food products, drugs, cosmetics, and pharmaceuticals (Tanaka, 2006). Tar is commonly used in a variety of foods, including soft drinks, sweets, juices, jellies, jams, flavor-infused chips, cakes, ice cream, and cereals (Demirkol, Zhang, & Ercal, 2012; Dey & Nagababu, 2022) and dairy products (Gan, Sun, Cao, Gao, Zhang, & Yang, 2012; State, van Staden, State, & Papa, 2022) to give them a yellow tint for easy identification, it is used in so many pharmaceutical products, including antacids, vitamins, prescription drugs (Mehmandoust, Erk, Karaman, Karimi, Bijad, & Karaman, 2021), and cold medications (Amin, Hameid II, & Abd Elsttar, 2010). However, Tar may have harmful health consequences such as altered hepatic and renal parameters, reproductive toxicity (Monisha, Sridharan, Kumar, Rangasamy, Krishnaswamy, &

Subhashree, 2022), neuro-behavioral poisoning (Amin et al., 2010; Tanaka, 2006), eczema, allergic migraines (Jafari-Arvari, Saei-Dehkordi, & Farhadian, 2021), anxiety, oxidative stress (Dorraii & Jalali, 2017; Sakthivel, Sivakumar, Chen,& Pandi, 2018), and DNA damage (Mazlan, Lee, & Hanifah, 2017; Visweswaran, 2012) especially when it is ingested in excess quantity. The maximum level of Tar that has been approved for use with various food items falls was set at 7.5 mg/kg body weight per day and within the range of 50-500 mg/kg by the World Health Organization and European Parliament and Council Directive 94/36/EC respectively (Tanaka (2006)). Therefore, the detection of Tar in food products has become a pressing concern, sparking significant interest among researchers in recent times. Over the years, various widespread techniques like high-performance liquid chromatography (de Matos et al., 2021), enzyme-linked immune-sorbent assay (L. Xu, Yang, Dias, & Zhang, 2022), and capillary electrophoresis (Wang, Mu, Hu, Zhuang, & Ni, 2019) etc are frequently used to measure Tar. Nevertheless, these methods are time-consuming processes, expensive tools, pricey reagents, or hostile environmental practises, which will restrict their usefulness. Thus, it is becoming more

Abbreviations: QD, Quantum Dot; CDs, carbon Dots; Tar, Tartrazine; IFE, Inner Filter Effect; LOD, Limit of Detection; LOQ, Limit of Qualification; ADHD, Attention-Deficit/Hyperactivity Disorder.

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ORIGINAL ARTICLE



Preparation, characterization, and in vitro cytotoxicity activity of allyl-isothiocyanate-embedded polymeric nanoparticles for potential breast cancer targeting

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Abstract

Background Allyl isothiocyanate (AITC) is an excellent active phytoconstituent recently revealed for cancer treatment. The strategic prominence of this study was to synthesize and characterize AITC-embedded tripolyphosphate-modified chitosan nanoparticles (AITC@CS-TPP-NPs) by ionic gelation.

Method Chitosan is recycled as a polymer to fabricate AITC@CS-TPP-NPs; the fabricated nanoparticles (NPs) are then characterized using FT-IR spectroscopy, DSC, XRD, zeta potential, size analysis, SEM, EDX, entrapment efficiency, in vitro drug release study, and in vitro cytotoxicity activity against MCF-7 to explore the effectiveness and strength.

Results As a result, developed AITC@CS-TPP-NPs demonstrates good stability with a zeta potential of 35.83 mV and 90.14% of drug release. The anticancer potential of AITC@CS-TPP-NPs shows the improved cytotoxicity activity of AITC due to the surface modification of CS using TPP. Hence, the cytotoxicity of AITC@CS-TPP-NPs was tested in vitro against a human breast cancer cell line (MCF-7) and found to be considerable.

Conclusion The AITC@CS-TPP-NPs were effectively synthesized and have significant benefits, including being easy to prepare, stable, and affordable with wide use in human breast cancer against cell line (MCF-7).

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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



Formulation Development and Evaluation of Freeze-dried Aviptadil Injection using Mannitol as Cryoprotectant

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ABSTRACT

Introduction: The naturally occurring human polypeptide known as vasoactive intestinal polypeptide (VIP) has a variety of physiological effects that have been well-documented, including anti-inflammatory, immune-modulatory, anti-hypertensive, enhancement of cardiac contractility, vasodilation, and fostering immune-neuroendocrine connection. Aviptadil (AVP) is the name of the vasoactive intestinal polypeptide's synthetic version.

Aims and Objectives: The main goal of this work was to create a novel, stable, lyophilized version of aviptadil injection. The stability of aviptadil is of utmost importance due to its classification as a polypeptide, recommended storage condition of -20°C, and susceptibility to degradation in aqueous solutions. To achieve this, the aviptadil injection was processed using freeze-drying technology with the addition of mannitol, serving as a bulking and cryoprotectant agent, within an aqueous solvent system. The choice of cryoprotectant and solvent system was based on factors such as the drug substance's solubility, stability, and feasibility in the manufacturing process. During the development of the formulation, the bulk solution underwent evaluation to assess the effects of process time, temperature, and compatibility with the materials it came into contact with.

Results and Discussion: The incorporation of mannitol, a sugar alcohol, led to the stability of the bulk solution for up to 24 hours before lyophilization when stored at temperatures between 2 and 8°C. Moreover, enhanced stability was observed post freeze-drying. The lyophilization process was meticulously optimized, taking into account critical quality attributes such as description, active drug content, pH of the reconstituted solution, reconstitution time, moisture content, and color absorption percentage.

The bulk solution demonstrated compatibility with various materials employed in manufacturing the drug product, such as stainless-steel vessels, polyethersulfone (PES) and polyvinylidene difluoride (PVDF) membrane filters. Notably, when the drug product bulk solution was kept refrigerated for up to 24 hours, there were no appreciable changes in the critical quality features found. The optimized freeze-dried product successfully meets the quality target product profile (QTPP)'s preset acceptance criteria.

Conclusions: The stabilization of AVP injection was successfully achieved through the implementation of the lyophilization process with mannitol as the cryoprotectant. The envisaged injectable formulation proves to be safe and showcases its economic viability, convenience, and overall safety in the preparation methods. These findings strongly support the viability of the freeze-dried formulation as a technically sound solution for ensuring the stability of aviptadil as a drug substance within the freeze-dried injectable dosage form. This formulation warrants more research due to its potential to treat patients with conditions such acute respiratory distress syndrome, acute lung injury, pulmonary fibrosis, and sarcoidosis.

Keywords: Aviptadil, Critical quality attributes Freeze dried, Cryoprotectant, Injectable, Mannitol, Vasoactive intestinal polypeptide, Lyophilization.

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Conflict of interest: None

INTRODUCTION

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Vasoactive intestinal polypeptide (VIP), a frequently occurring, naturally occurring polypeptide in people, has a variety of physiological effects that have been well-

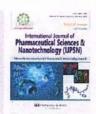
documented, including anti-inflammatory, immune-modulator, anti-hypertensive, augmentation of cardiac contractility, vasodilation, and fostering immune-neuroendocrine connection. VIP's synthetic equivalent, aviptadil (AVP),

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RESEARCH ARTICLE

Preparation and Characterization of Pitavastatin Calcium Loaded Biodegradable Porous Starch as Carrier Platform for Drug Delivery

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ABSTRACT

Introduction: Poor solubility and low oral bioavailability are major obstacles to the development of efficient drug delivery approaches. Numerous chemical entities fall into the biopharmaceutics classification system II (BCS II) class, categorized by low solubility and high permeability. Consequently, finding alternative solutions for improving drug efficacy becomes crucial. Hence, this study aims to formulate biodegradable porous acetostarch (BPSa) and biodegradable porous ethostarch (BPSe) carriers to augment the solubility profile of the poorly soluble drug candidate pitavastatin calcium (PTC).

Method: The biodegradable carriers (BPSa and BPSe) were prepared using the solvent exchange method. Then the PTC was loaded into the prepared carriers (PTC@BPSa and PTC@BPSe) using the passive drug loading procedure. Moreover, the obtained drug-carrier conjugates were evaluated using physiochemical evaluation techniques such as Fourier transform infrared spectroscopy (FTIR), x-ray powder diffraction (XRPD), and differential scanning calorimetry (DSC). Additionally, the surface morphology and drug release characteristics are determined.

Result: The experimental findings exhibited high drug content with 75.45% and 71.81% for PTC@BPSa and PTC@BPSe, respectively. The SEM analysis of the prepared conjugates demonstrates asymmetrical morphology with cracks between particles, indicating porous nature of the carriers. As a result of this, PTC@BPSa and PTC@BPSe exhibited modified drug release patterns, with cumulative releases of 78.63% and 78.50%, respectively.

Conclusion: The biodegradable porous carriers (BPSa and BPSe) effectively improve the dissolution pattern of PTC, by addressing the challenges associated with poor solubility. This study offers valuable insights into the potential of these biodegradable porous carriers as effective drug delivery platforms for increasing the efficacy of limited soluble medications.

Keywords:

Poorly solubility, Biodegradable porous starch, Carrier, Solvent exchange method, Pitavastatin calcium.

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SHORT COMMUNICATION

CUSTARD APPLE PEELS CONTAINING SAPONIN: ISOLATION AND FORMULATION OF HERBAL SHAMPOO

ABSTRACT

Presently, the cosmetics sector is among the fastest-expanding sectors of the economy. Plenty of researchers have reported that natural surfactants could prominently replace synthetic surfactants considering the superiority in safety and effectiveness. This research aimed to isolate surfactants from custard apple peel and formulate an herbal shampoo. Initially, isolation of the saponin was accomplished followed by the formulation of herbal shampoo. Interestingly, optimized batch A demonstrated the optimum synthetic pH and high foaming capacity of shampoo for upto 4 mins. Moreover, herbal shampoo showed good cleansing properties and detergency. Additionally, it exhibited superior smoothing, no skin irritation, and a shining effect with the respect to the marketed formulation. Hence, it can be prominently used as a substitute for chemical surfactants in designing shampoo and other cosmetics.

Keywords: Herbal shampoo, saponin, natural surfactant, foaming ability

INTRODUCTION

Out of the plenty of cosmetics products, shampoo is a widely used cosmetic intended for hair applications including cleaning, shining and smoothing1. One of its principal components is the surfactant, which is incorporated in an appropriate concentration and form. A naturally obtained surfactant has low toxicity to humans. Moreover, they are biodegradable and biocompatible. It demonstrates excellent stability at different temperatures2. Reportedly, saponin demonstrates the ability to absorb excess sebum without any adverse reactions. Moreover, it also acts as an antifungal and antibacterial, which are important pro-perties in cosmetic formulation3. Annona squamosal belongs to the Annonaceae family4. Recently published literature divulged that the agro-waste A. squamosal fruit peel extract contains a higher concentration of saponin5 that can be used as a substitute in the formulation of herbal shampoo. Hence, the main goal of the present research was to isolate saponin from custard apple (sitaphal) peel and to prepare herbal hair shampoo that can replace the chemical surfactant.

Formulation and evaluation of the herbal shampoo

At first, the cleaned custard apple fruit peels were converted into powder by grinding. After this, 100 g of powdered peels were defatted at 60 °C for 6 h using petroleum ether (solvent). Afterward, methanol was used to extract the saponin from defatted dried plant

powder at 60 °C for 6 h yielding, a dark brown colored crude extract. Subsequently, the methanolic extract was dissolved in 50 mL of double distilled water (decanted three times with n-butanol). In this process, diethyl ether was used to precipitate the total saponin present inside the butanolic extract followed by filtration using a Whatman filter paper (Fig. 1A). Based on initial trials, the 3 different concentrations (0.5 g, 1 g, and 1.5 g) of isolated saponin were selected for the preparation of herbal shampoo. Simultaneously, an aqueous system was prepared using a mixture of double-distilled water (upto 100 mL), vitamin E oil (5 mL), glycerin (10 mL), Aloe vera juice (15 mL), and lemon juice (5 mL). Herein, A. vera juice acts as a conditioning agent whereas lemon juice was selected as a preservative. After that, these selected concentrations were added into 70 mL of aqueous solution in three separate beakers followed by continuous stirring in a water bath at 50 °C. Finally, the volume of the formulation was adjusted using double distilled water. Several evaluation parameters were performed such as dry residue, dirt dispersion, moisture content, wetting time, foam stability, foaming ability, surface tension, detergency tests, in vitro skin irritation test7 and stability study.

RESULTS AND DISCUSSION

Fourier Transform Infrared (FTIR) spectra of saponin (Fig. 1B) showed hydroxyl stretching vibration (3100-3500 cm⁻¹), carbonyl stretching vibration (1606 cm⁻¹), antisymmetric deformation peak of -CH- (1444.73 cm⁻¹), bending vibration peak within the C-O-H plane (284.63 cm⁻¹) and C-O-C stretching vibration (1110.23 cm⁻¹). Importantly, the color of shampoo varies with the

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PREPARATION OF CRYSTALLINITY TAILORED SILK FIBROIN-SODIUM ALGINATE BASED FLOATING MICROBEADS FOR NEVIRAPINE DELIVERY

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The present work anticipated crystallinity-tuned silk fibroin (SFIB)-sodium alginate floating microbeads (MB) as a candidate for nevirapine (NEV) sustained release. Briefly, crystallinity tuning was accomplished using solvent annealing. The changes in structural conformation of SFIB were validated using FTIR spectroscopy. Here, the tangent baseline method revealed changes in crystallinity of floating NEV-loaded SFIB-MB. Importantly, solvent annealing offers conversion of amorphous ' α -helix' to crystalline ' β -sheet' of SFIB, helping to modify drug release from the matrix of SFIB-sodium alginate. As well, NEV-loaded SFIB-MB demonstrated good floating profile. The NEV-loaded SFIB-MB with ethanol (ETH-6) annealing for 6 hours shows 25.853% drug release at 12 hours (pH = 1.2), compared to untreated NEV-loaded SFIB-MB (65.132%, 12 hours, log p < 0.0001). The release kinetics of batch ETH-6 revealed first-order release kinetics and Fickian diffusion (n = 0.468) was found to be the drug diffusion mechanism. Therefore, crystallinity-modified floating NEV-loaded SFIB-based MB will open a new door for modified drug delivery.

Keywords: silk fibroin, nevirapine, floating drug delivery, microbeads, crystallinity modulation, solvent annealing

INTRODUCTION

Since its inception, oral dosing has been the most common route for administration of a therapeutically active agent. It is crystal clear that the goal of oral dose formulation is to achieve drug absorption through the gastrointestinal tract (GIT). However, quick gastrointestinal movement may result in the partial release of the active agent to the targeted area. Hence, due to the rapid gastric emptying issue, it is difficult to retain the dosage from the stomach site, resulting in reduced dosage potency.1 In light of current discoveries, modified oral dosage forms can effectively enable tailored drug incorporation.2 Efforts are taken to establish a novel drug delivery system that can maintain active concentration in plasma within therapeutic ranges for extended Moreover, it helps to diminish variability in plasma drug concentration at a fixed state by distributing the drug in a regulated and repeatable way.3 Out of several types of dosage forms, researchers are particularly interested in the gastro

retentive drug delivery system (GRDDS) for a specific drug that acts regionally and has absorption openings in the upper GIT. 4,5 For that purpose, swelling and expansion-mediated systems, floating systems, bio(muco)adhesive dosage forms, etc. have been developed. Principally, it has been achieved using different types of excipients selected based on the density of the material, shape, and size. Also, their adhesive behavior and swelling index (SI) need to be considered for intended pharmaceutical Particularly, formulations.6 in researchers have been focused on floating drug delivery systems (FDDS). It is due to their simple process and high effectiveness in formulation development.7,8 Moreover, it has been reported that the FDDS can extend the duration a dosage form spends in the stomach, hence increasing the drug's oral bioavailability.9,10 The use of effervescent agents produces carbon dioxide gas that can result in disturbances in the microbial



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Chitosan-Sesbania Gum Mediated pH-Responsive Polyelectrolyte Complexes for Targeted Delivery of Diclofenac Sodium: Preparation and Spectroscopical Evaluation

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ABSTRACT

Background: The implementation of chitosan as an enhanced vehicle for drug delivery is an interesting domain in the pharmaceutical dosage form. The combination of commonly accessible natural polysaccharides like gum may provide a new arrangement of dosage forms such as polyelectrolyte complex. Such modern improvements facilitate the modulated release of active, which can be beneficial in avoiding adverse consequences. There have been no reports on chitosan and sesbania gum-based polyelectrolyte complexes for drug delivery applications to date. Objectives: The chitosan-sesbania gum polyelectrolyte complex was developed for modified drug delivery of diclofenac sodium. Materials and Methods: pH-responsive polyelectrolyte complexes were accomplished utilizing the coacervation technique. It forms complex due to the capability of chitosan amine groups and sesbania gum carboxylic functionality. Results: The SEM analysis assured the aggregated polyhedral shape particles with a smooth surface of the final polyelectrolyte complex. The Diffractogram of the polyelectrolyte complex resulted in an amorphous form of diclofenac. The polyelectrolyte complex batch (B:3) showed satisfactory drug entrapment capabilities. It showed 88.96% of the drug release in 8 hr (pH 6.8). Importantly, it is because of the unprotonated condition of sesbania gum containing hydrophilic functionality that offers boosted hydrogen bonding via interaction with dissolution medium containing water molecules. Therefore, it offers the insertion of water molecules into a complex followed by the swelling of a matrix. Conclusion: The developed chitosan-sesbania gum polyelectrolyte complex offers a pH-responsive sustained release of diclofenac sodium. In the future, chitosan and sesbania gum-based polyelectrolyte complex can be preferred as an innovative drug carrier for diclofenac sodium delivery.

Keywords: Chitosan, Sesbania gum, Diclofenac sodium, Polyelectrolyte complex, Drug delivery.

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INTRODUCTION

Presently, the use of polymeric-based systems for the delivery of active is opening a new era that may be because of their prospective applications. These methods control drug delivery rates, maintain therapeutic action, and/or target drugs to tissues. In addition, they enhance and modify physicochemical properties such as stability and solubility, which provide the therapeutic effects of drugs with greater benefits. Due to their bioadhesive nature, they have been utilized as matrices for drug administration via oral, buccal, transdermal, and nasal routes.

However, they function as carrier systems for drugs, enzymes, or DNA because charged species may be conveniently incorporated into complex particles. These can be used as membranes, coatings on films and fibers, targeted nucleic acid delivery, nucleic acid isolation and fractionation, pharmaceutical product binding, preparation of microcapsules for drug delivery membranes for dialysis, contact lenses, enzyme mimics, medical applications, nanoparticles for targeted tissue delivery, and the development of biosensors.

Out of several kinds of polymeric systems, polyelectrolytes-based systems are recently reported that solely relied on charged-based components. Interestingly, two oppositely charged polyelectrolytes are simultaneously combined in solution without using any chemical covalent cross-linker leading to the formation of a polyelectrolyte complex.⁵ The polyelectrolyte complex has attracted attention due to its nontoxicity and well-tolerated



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Application of surface nitrogen-doped graphene quantum dots in the sensing of ferric ions and glutathione: Spectroscopic investigations and DFT calculations

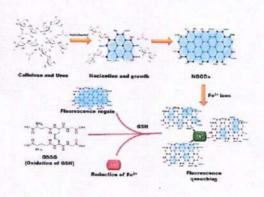
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HIGHLIGHTS

- NGQDs were synthesized using bamboo fiber powder and urea as green precursors.
- The reliability of the fabricated NGQDs was demonstrated to sense Fe³⁺ and GSH.
- DFT calculations were used to understand the mechanism involved.
- The NGQD/Fe³⁺ system fabricated has the potential to detect GSH in real samples.

GRAPHICAL ABSTRACT



ARTICLEINFO

Keywords: Graphene quantum dots Glutathione Green synthesis Fluorescence biosensing Bamboo fibre

ABSTRACT

Developing a sensing platform that can quickly and accurately measure glutathione (GSH) is crucial for the early detection of various human diseases. GQDs have shown great potential in many technological and biological applications. This study focused on synthesizing nitrogen-doped GQDs (NGQDs) with stable blue fluorescence using a simple and easy hydrothermal method in one step. The bamboo fiber was used as the green source for this synthesis. The NGQDs had a tiny particle size of 4.7 nm and emitted light at 405 nm when excited. They displayed a remarkable quantum yield of 40.36 % and were effectively used as fluorescent probe to specifically detect Fe³⁺. The energy transfer mechanism led to the NGQDs' fluorescence being deactivated by Fe³⁺ ions (turn-"off"). However, with the addition of GSH to the system, the fluorescence intensity of NGQDs was reactivated (turn- "on"). Thus, a fluorescence turn "off-on" system was developed for the sensitive detection of Fe³⁺ and GSH. Using density functional theory (DFT), it was theoretically calculated that the surface of the fabricated NGQDs possess lone pairs of electrons on oxygens and doped nitrogen causing a photo-induced electron transfer (PET) process to occur. This PET process was suppressed previously owing to complex formation between oxygen atoms of modeled structure and ferric ions. The sensing platform displayed a sensitive response to Fe³⁺ in the 1-1000 μM range with LOD of 34 nM and GSH in the range of 1-50 μM, with a detection limit of 45 nM. Furthermore, the NGQDs exhibited high selectivity towards Fe³⁺ and GSH over other electrolytes and

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Recent progress in targeting KRAS mutant cancers with covalent G12C-specific inhibitors

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KRAS^{G12C} has been identified as a potential target in the treatment of solid tumors. One of the most often transformed proteins in human cancers is the small Kirsten rat sarcoma homolog (KRAS) subunit of GTPase, which is typically the oncogene driver. KRASG12C is altered to keep the protein in an active GTP-binding form. KRAS has long been considered an 'undrugable' target, but sustained research efforts focusing on the KRAS^{G12C} mutant cysteine have achieved promising results. For example, the US Food and Drug Administration (FDA) has passed emergency approval for sotorasib and adagrasib for the treatment of metastatic lung cancer. Such achievements have sparked several original approaches to KRAS^{G12C}. In this review, we focus on the design, development, and history of KRAS^{G12C} inhibitors.

Keywords: KRAS^{G12C}; covalent inhibitors; drug design; lung cancer; KRAS mutation

Introduction

Activation of RAS guanosine triphosphatases (GTPases) regulates many signaling pathways that drive cell growth, division, proliferation, and survival.1 RAS family members KRAS, HRAS, and NRAS are involved in the transition between active GTP-bound and non-active GDP-bound states.2 RAS mutations are constitutively active and always 'activated' as a result of GTP-linked RAS and downstream activation signaling pathways (e.g., RAS-Raf-Mek-Erk), ultimately leading to cancer (Figure 1a).3 Small KRAS GTPase mutants are some of the most common and have a significant role in the etiology of the most aggressive carcinomas in humans. Among all KRAS mutations, the KRASG12C single-nucleotide variation, with a glycine residue substituted by a cysteine residue at codon 12, is the most frequent variant, with a prevalence of ~13% in nonsmall cell lung cancer (NSCLC), colorectal cancer (CRC), and pancreatic cancer.5 KRAS mutations are common in many patients with cancer and a new FDA-approved therapy that targets KRAS mutations is now available in the clinic.6 Nevertheless, KRAS has long been considered an 'undrugable' target owing to its high micromolar concentration of GTP inside cells and its high picomolar binding affinity

for GDP and GTP inside cells, which raises the possibility that the drug molecule would competitively bind to the KRAS-GTP site.2 Furthermore, the lack of deep, hydrophobic binding pockets in oncogenic KRAS impedes the search for effective inhibitor compounds. Moreover, KRAS activation and signaling is achieved through protein-protein interactions (PPIs) with guanine nucleotide exchange factors (GEFs), GTPase activating proteins (GAPs), and various KRAS effector proteins. PPIs are also challenging to target because of the relatively featureless topologies of the surfaces involved. Despite these issues, many efforts have been made to target aberrant KRAS signaling at different levels. For example, Shokat and colleagues reported the novel identification of the first selected cysteine 12 (Cys12) KRASG12C covalent inhibitors in 2013, suggesting that KRASG12C covalent inhibitors of Cys12 interfere with the KRAS signaling process via covalent bonding.8

Further research resulted in enhanced covalent KRASG12C inhibitors, which reached clinical trials, including adagrasib and ARS-1620. Direct targeting of KRASG12C might be one of the most effective ways to overcome KRAS, as evidenced by the recent approval of sotorasib for the treatment of NSCLC and

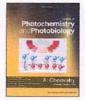
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Poly-L-lysine functionalized graphene quantum dots embedded zirconium metal—organic framework-based fluorescence switch on-off-on nanoprobe for highly sensitive and selective detection of taurine

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ARTICLEINFO

Keywords: Taurine Graphene quantum dots Metal-organic frameworks UiO-66@NH₂ MOF Cardiovascular disease

ABSTRACT

Taurine is now widely used as a novel diagnostic biomarker for cardiovascular disease. Unfortunately, engaged techniques for the analysis of taurine are suffering from low sensitivity, poor selectivity, and a tedious process. In this work, the poly-L-lysine functionalized graphene quantum dots embedded UiO-66@NH2 metal-organic framework (PLL-fGQDs@UiO-66@NH2 MOF) based turn 'On-Off-On' fluorescent nanoprobe was designed for taurine sensing. Initially, synthesized PLL-fGQDs, UiO-66@NH2 MOF, and PLL-fGQDs@UiO-66@NH2 MOF nanoprobe were confirmed using UV-Vis spectroscopy, FT-IR analysis, particle size analysis, fluorescence study, PXRD, SEM-EDAX, HR-TEM, etc. Here, anticipated PLL-fGQDs incorporation into UiO-66@NH2 MOF nanoprobe portrayed a highly fluorescent nanoprobe for taurine sensing. The copper (Cu2+) ions addition in the fluorescent nanoprobe resulted in fluorescence dampness followed by taurine addition showed the recovery of quenched fluorescence. Principally, it might be because of the greater binding affinity of Cu2+ ions towards taurinecontaining oxygen atoms of a sulfonic group and the nitrogen atom of an amine group. The linear concentration range, limit of detection (LOD), and limit of quantification (LOQ) of taurine were found to be 5 ng/mL to 360 ng/mL, 2.91 ng/mL, and 8.84 ng/mL, respectively. It also provides a high selectivity towards taurine in the occurrence of interfering agents whereas practical applicability was assured by spiked artificial serum samples analysis. In conclusion, the designed PLL-fGQDs@UiO-66@NH2 MOF nanoprobe offers high sensitivity, selectivity, good stability, repeatability, and practicability. In the future, it can be used as a new nanoprobe for taurine recognition with improved performance than the traditional methods.

1. Introduction

Presently, cardiovascular diseases (CVDs) are a leading consequence of mortality. Traditional approaches are unable to predict this increased risk [1]. In this shade, biomarker identification is pivotal in healthcare for diagnosis. Therefore, research scholars are now investigating for novel biomarkers for the diagnosis of plenty of serious disorders such as CVD [2]. Importantly, CVD can be managed satisfactorily at a preliminary phase by monitoring divergent biochemical values. In a sense, it is imperative to emphasize that CVD can be spotted at an initial stage by adopting an innovative biosensing strategy [3]. Taurine (2-aminoethanesulfonic acid) [4] is a free and necessary amino acid. It is present in a variety of body fluids, including plasma and urine. As well, it is

committed to a variety of crucial biological processes [5]. As a result, taurine is a significant biomarker for the earliest identification of CVD [6]. In the literature, multiple methods have been developed for the determination of taurine [7,8]. Nonetheless, there are several shortcomings of these methods such as the difficult extraction, need for modern equipment, high pricing, prolonged detection process, etc., [9] that need to be overcome using advanced methods.

Carbon-based zero-dimensional (0D) nanomaterials namely graphene quantum dots (GQDs) are ordinarily prioritized for biomedical applications encompassing such diagnostics and others [10]. Mainly, GQDs are tiny graphene particles with diameters less than 100 nm [11]. It offers superior and dynamic physicochemical features which are important for the development of the sensing approach [12]. The surface

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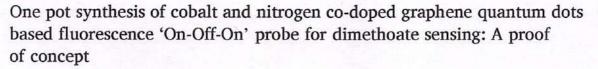


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ARTICLEINFO

Keywords: Cobalt/ nitrogen doping Graphene quantum dots Dimethoate Fluorescent sensor

ABSTRACT

Dimethoate, which is widely used in agriculture, has harmful effects on organs. To address this issue, advanced sensors are crucial for detecting it in real samples. Notably, graphene quantum dots (GQDs)-centered fluorescent sensors offer numerous advantages such as high sensitivity, selectivity, and good stability. Therefore, in this work, we designed a new cobalt/nitrogen co-doped GQD (Co/N-GQD) fluorescence switch "On-Off-On" sensor to achieve selective dimethoate detection. In brief, the synthesis of Co/N-GQDs, achieved through the hydrothermal method, involves Pithecellobium dulce fruit peel as a green precursor, along with cobalt (Co) and urea as dopant sources. Extensive spectral characterizations, including FTIR, UV-Vis spectroscopy, zeta potential analysis, particle size analysis, HR-TEM, Raman, PXRD, and fluorescence studies, were conducted to validate the fabrication of Co/N-GQDs. The resulting nanosized Co/N-GQDs exhibited an enhanced quantum yield of 49.78 %. In terms of sensing, the fluorescence intensity of Co/N-GQDs is selectively quenched ("Turned Off") by Cu2+ through a dynamic quenching mechanism. When dimethoate is included in the quenching system, a proportional correlation is observed between dimethoate concentration and fluorescence reactivation. This phenomenon is attributed to the potential of dimethoate, which contains amide and phosphorodithioate functionalities, to displace Cu2+ from the electrostatic complex through chelation. Remarkably, the sensor achieves a limit detection limit (LOD) of 64.08 ng/mL, offering a broad linear range spanning from 10 to 300 ng/mL. In addition, it exhibited real-time applicability, good stability, and reproducibility. In conclusion, the design of Cu2+-Co/N-GQDs can be used as a proof of concept for dimethoate sensing within various sample contexts.

1. Introduction

In today's modern era, organophosphorus pesticides (OPPs) play an important role in crop protection globally. These pesticides are highly regarded for their potent insecticidal action, water solubility, and rapid degradation [1]. Despite their benefits, long-term OPP presence in agriculture, soil, and water threatens health and survival [2]. Dimethoate, a thio-organophosphate, finds global use but is banned in Europe due to harm [3]. Still, it is used in parts of Asia, Africa, Brazil, and the USA, raising significant concerns about its potential risks and effects [4]. Dimethoate exerts its toxicity by irreversibly inhibiting the enzyme acetylcholinesterase (AChE), leading to organ dysfunction and death [5]. In alignment with this, the World Health Organization (WHO) has established a supremely acceptable dose of dimethoate at 0.002 mg/kg of total body weight [6]. This chemical can harm multiple organs [7].

Hence, it is crucial to closely monitor and control the presence of OPPs in food, water, and the environment, demanding special attention to each of these aspects. Numerous conventional techniques have been explored for monitoring dimethoate, such as spectrophotometry [8], thin layer chromatography (TLC) [9], liquid chromatography-mass spectrometry (LC-MS) [10], high-performance liquid chromatography (HPLC) [11], and gas chromatography (GC) [12]. These methods offer highly sensitive, selective, and quantitative monitoring of dimethoate. However, they come with inherent drawbacks such as expensive equipment, complex operations, time-consuming pre-treatment, and the need for experienced operators [13]. Consequently, the academic and scientific community is closely focusing on alternative sensor technologies to track various pesticides. In brief, inorganic quantum dots, such as cadmium telluride/cadmium sulfide-based sensors, have been utilized for monitoring OPPs. However, they have some drawbacks in terms of

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RESEARCH



Functionalized Graphene Quantum Dots (GQDs) based Label-Free Optical Fluorescence Sensor for CD59 Antigen Detection and Cellular Bioimaging

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Abstract

Cluster of differentiation (CD59), a cell surface glycoprotein, regulates the complement system to prevent immune damage. In cancer, altered CD59 expression allows tumors to evade immune surveillance, promote growth, and resist certain immunotherapies. Targeting CD59 could enhance cancer treatment strategies by boosting the immune response against tumors. Herein, we present a one-step synthesis of Polyethyleneimine (PEI) functionalized graphene quantum dots (*Lf-GQDs*) from weathered lemon leaf extract. The fabricated *Lf-GQDs* were successfully used for the quantitative detection of the cluster of CD59 antigen that is reported for its expression in different types of cancer. In this work, we utilized orientation-based attachment of CD59 antibody (Anti-CD59). Our findings reveal that, instead of using random serial addition of antigen or antibody, oriented conjugation saves accumulated concentration offering greater sensitivity and selectivity. The Anti-CD59@*Lf-GQDs* immunosensor was fabricated using the oriented conjugation of antibodies onto the *Lf-GQDs* surface. Besides, the fabricated immunosensor demonstrated detection of CD59 in the range of 0.01 to 40.0 ng mL⁻¹ with a low detection limit of 5.3 pg mL⁻¹. Besides, the cellular uptake potential of the synthesized *Lf-GQDs* was also performed in A549 cells using a bioimaging study. The present approach represents the optimal utilization of Anti-CD59 and CD59 antigen. This approach could afford a pathway for constructing oriented conjugation of antibodies on the nanomaterials-based immunosensor for different biomarkers detection.

 $\textbf{Keywords} \ \ \text{Functionalized graphene quantum dots} \cdot \text{CD59 antigen} \cdot \text{Oriented conjugation} \cdot \text{Turn `on-off' sensor} \cdot \text{Bioimaging}$

Introduction

Cancer represents a daunting rise in mortality rate and leads to an imperative barrier in the healthcare system. Fresh estimates from the World Health Organization (WHO), have declared cancer a foremost cause of death globally [1]. Apart from this, the tumor microenvironment and the new hallmarks of cancer propagation have been explored day by day [2]. In response to this, the incorporation of novel diagnostics and treatment strategies needs to be demonstrated to minimize the burden and patient suffering worldwide. In this framework, novel strategies for the early detection and diagnosis of cancer are being developed using different cancer biomarkers. A cluster of differentiation (CD59) a membrane protein anchored with glycosylphosphatidylinositol highly expressed in several cancer cell lines as well as tumor tissues. It also plays a vital role in different functions and regulation of immune cells in the tumor microenvironment [3]. Several studies reported the occurrence of CD59 in lung cancer, especially NSCLC and their role in the development of resistance to chemotherapy via complement activation [4, 5]. Early detection of CD59 expression in cancer is crucial for effective management. The role of CD59 as a complement system regulator provides a unique opportunity to identify early-stage malignancies. Monitoring CD59 levels in blood or tissues can serve as a reliable biomarker, enabling prompt treatment and

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Design of lactoferrin functionalized carboxymethyl dextran coated egg albumin nanoconjugate for targeted delivery of capsaicin: Spectroscopic and cytotoxicity studies

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Keywords: Lactoferrin Colorectal cancer Carboxymethyl dextran Egg albumin Capsaicin

ABSTRACT

The increased mortality rates associated with colorectal cancer highlight the pressing need for improving treatment approaches. While capsaicin (CAP) has shown promising anticancer activity, its efficacy is hampered due to low solubility, rapid metabolism, suboptimal bioavailability, and a short half-life. Therefore, this study aimed to prepare a lactoferrin-functionalized carboxymethyl dextran-coated egg albumin nanoconjugate (LF-CMD@CAP-EGA-NCs) for the targeted CAP delivery to enhance its potential for colorectal cancer therapy. Briefly, LF-CMD was synthesized through an esterification reaction involving LF as a receptor and CMD as a shell. Concurrently, CAP was incorporated into an EGA carrier using gelation and hydrophobic interactions. The subsequent production of LF-CMD@CAP-EGA-NCs was achieved through the Maillard reaction. Spectral characterizations confirmed the successful synthesis of smooth and spherical-shaped LF-CMD@CAP-EGA-NCs using LF-CMD and EGA-CAP nanoparticles, with high entrapment efficiency and satisfactory drug content. Furthermore, LF-CMD@CAP-EGA-NCs demonstrated a sustained release of CAP (76.52 \pm 1.01 % in 24 h, R^2 = 0.9966) in pH 5.8 buffer with anomalous transport (n = 0.68) owing to the shell of the CMD and EGA matrix. The nanoconjugate exhibited enhanced cytotoxicity in HCT116 and LoVo cell lines, which is attributed to the overexpression of LF receptors in colorectal HCT116 cells. Additionally, LF-CMD@CAP-EGA-NCs demonstrated excellent biocompatibility, as observed in the FHC-CRL-1831 cell line. In conclusion, LF-CMD@CAP-EGA-NCs can be considered as a promising approach for targeted delivery of CAP and other anticancer agents in colorectal cancer treatment.

1. Introduction

Colorectal cancer ranks third in prevalence and second in severity among various cancer types [1]. Surgery remains the most favorable option for treating early colorectal cancer [2]. Unfortunately, over half of cancer patients experience recurrence and metastasis following surgical resection [3,4]. In such patients, chemotherapy and radiation have emerged as reliable treatment options [5]. For instance, clinical trials have shown the potential of irinotecan, oxaliplatin, and capecitabine in treating colorectal cancer [2]. However, prolonged chemotherapy results in drug resistance and significant damage to normal tissues [6,7]. While useful, both radiation and chemotherapy suffer from multiple

limitations such as lack of selectivity, dose-dependent toxicity, and development of resistance [5,8]. Systemic delivery of chemotherapeutic agents has shown to be useful in managing colorectal cancer [9]. Studies have reported the efficacy of systemically administered FOLFIRI (5-fluorouracil/leucovorin and irinotecan) and FOLFOX (5-fluorouracil/leucovorin and oxaliplatin) in the treatment of metastatic colorectal cancer [10]. The implementation of systemic treatment in colorectal cancer improves the survival of cancer patients [11]. In addition, the use of modified nanocarriers along with anticancer drugs has yielded synergistic benefits, including targeted delivery and the potential for concurrent administration in systemic treatment [9].

Capsaicin (CAP) has gained considerable attention in cancer therapy

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Scientific paper

Zinc Metal-Organic Frameworks- Graphene Quantum Dots Nanocomposite Mediated Highly Sensitive and Selective Fluorescence "On-Off-On" Probe for Sensing of Quercetin

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Abstract

The current study presents a fluorescence-based 'On-Off-On' nanoprobe composed of rose petal-derived graphene quantum dots embedded in zinc metal-organic frameworks (RP-GQDs@Zn-MOFs) as a proof of concept for quercetin sensing. The particle size and HR-TEM analysis confirmed the synthesis of a uniformly distributed nanosized probe, while the zeta potential (+33.03 mV) verified its good stability. The fluorescence analysis confirmed that the introduction of copper ions (Cu^{2+}) resulted in fluorescence quenches, while the inclusion of quercetin forms quercetin- Cu^{2+} complex, leading to recovery of quenched fluorescence in RP-GQDs@Zn-MOFs due to static quenching. The nanoprobe demonstrated a wide concentration range and a low detection limit of 100 ng/mL to 1400 ng/mL ($R^2 = 0.99$) and 37.8 ng/mL, respectively. Selectivity analysis highlighted pronounced specificity for quercetin, attributed to Cu^{2+} coordination between carbonyl oxygen atom and the 3-OH group of quercetin. Furthermore, designed probe exhibited excellent stability, repeatability (RSD < 5), and potential for real-time analysis.

Keywords: Zinc metal-organic frameworks; graphene quantum dots; copper ions; quercetin; high sensitivity; high selectivity

1. Introduction

Metal-organic frameworks (MOFs) are preferred for various applications, including biomedical and environmental uses. This preference stems from their distinctive characteristics, such as their ability to modify surfaces, their large surface area, and their adjustable structure. It provides a highly porous structure through the association of metal ions with carefully selected organic linkers via strong bonding. To date, various types of MOFs have been developed for numerous applications, including drug delivery, biosensing, chemical sensing, gas separation, and more. At present, they are widely employed for biosensing purposes, offering low detection limits, high sensitivity,

excellent responsiveness, and good stability, among other benefits. Despite these groundbreaking merits, MOFs suffer from major drawbacks, primarily the collapse of their structure and pore shrinkage. As a result, there is a need for complementary nanoparticles that can help overcome these significant drawbacks while preserving the original features of MOFs.

Currently, significant efforts are underway to develop innovative MOFs-centered composites to address the genuine needs of the scientific community. Encapsulating nanosized components within MOFs represents a novel advancement in the biomedical field.^{5,6} In this context, it is worth noting that fluorescence-mediated sensing tech-



Nangare et al.: Zinc Metal-Organic Frameworks- Graphene Quantum ...

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RESEARCH ARTICLE



Discovery of New Quinazoline Derivatives as VEGFR-2 Inhibitors: Design, Synthesis, and Anti-proliferative Studies



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> Abstract: Background: In cancer, Receptor tyrosine kinases (RTKs) are powerful oncoproteins that can lead to uncontrolled cell proliferation, angiogenesis, and metastasis when mutated or overexpressed, making them crucial targets for cancer treatment. In endothelial cells, one of them is vascular endothelial growth factor receptor 2 (VEGFR2), a tyrosine kinase receptor that is produced and is the most essential regulator of angiogenic factors involved in tumor angiogenesis. So, a series of new N-(4-(4-amino-6,7-dimethoxyquinazolin-2-yloxy)phenyl)-N-phenyl cyclopropane-1,1dicarboxamide derivatives as VEGFR-2 inhibitors have been designed and synthesized.

> Methods: The designed derivatives were synthesized and evaluated using H-NMR, C13-NMR, and Mass spectroscopy. The cytotoxicity was done with HT-29 and COLO-205 cell lines. The potent compound was further studied for Vegfr-2 kinase inhibition assay. Furthermore, the highest activity compound was tested for cell cycle arrest and apoptosis. The molecular docking investigation was also done with the help of the Glide-7.6 program interfaced with Maestro-11.3 of Schrodinger 2017. The molecular dynamics simulation was performed on the Desmond module of Schrodinger.

Results: Compound SQ2 was observed to have promising cytotoxic activity ($IC_{50} = 3.38$ and $IC_{50} = 3.38$) in comparison to the reference drug Cabozantinib (IC₅₀ = 9.10 and 10.66 μM) against HT-29 and COLO-205, respectively. The synthesized compound SQ2 showed VEGFR-2 kinase inhibition activity (IC₅₀ = 0.014 µM) compared to the reference drug, Cabozantinib (IC₅₀ = 0.0045 μM). Moreover, compound SQ2 strongly induced apoptosis by arresting the cell cycle in the G1 and G2/M phases. The docking study was performed to understand the binding pattern of the new compounds to the VEGFR-2 active site. Docking results attributed the potent VEGFR-2 inhibitory effect of the new compounds as they bound to the key amino acids in the active site, Asp1044, and Glu883, as well as their hydrophobic interaction with the receptor's hydrophobic pocket. The advanced computational study was also done with the help of molecular dynamics simulation.

Conclusion: The findings show that the developed derivatives SQ2 and SQ4 are equally powerful as cabozantinib at cellular and enzymatic levels. The apoptosis and cell cycle results show that the proposed compounds are potent. This research has provided us with identical or more potent VEGFR-2 inhibitors supported by the results of docking studies, molecular dynamics simulation, cytotoxic actions, in vitro VEGFR-2 inhibition, apoptosis, and cell cycle arrest.

Keywords: Quinazoline, molecular modeling, anti-proliferation, VEGFR-2, cell cycle, apoptosis.

1. INTRODUCTION

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Cancer is a serious global health issue and a potential cause of death in the future [1, 2]. Furthermore, it was anticipated that by 2030, there might be 22 million new instances of cancer worldwide [3, 4]. Despite cancer prevention and treatment advancements, it continues to be the second most common cause of death worldwide [5-7]. The process of cancer angiogenesis is essential to the development of tumors [8]. The formation of new capillaries from existing blood capillaries enables the delivery of oxygen and nutrients to divide cells, which may aid in cancer growth, survival, and metastasis [9, 10].

Recently, the development of more precise chemotherapeutics and the identification of novel biological targets have emerged as major research priorities [11]. Receptor tyrosine kinases (RTKs) are crucial for controlling intracellular signal transduction pathways and numerous cellular activities [12]. RTKs are powerful oncoproteins that can lead to uncontrolled cell proliferation, angiogenesis, and metastasis when mutated or overexpressed, making them crucial targets for cancer treatment. RTK inhibitors have potent antitumor effects that have been proven, and some of them are now being investigated in clinical studies or have previously received approval [13, 14]. Numerous factors stimulate cancer angiogenesis [15]. In endothelial cells, one of them is vascular endothelial growth factor receptor 2 (VEGFR2), a tyrosine kinase receptor that is produced and is the most essential regulator of angiogenic factors involved in tumor angiogenesis [5, 16, 17]. By binding to VEGF and stimulating subsequent signaling cascades and specific endothelial responses, such as enhanced endothelial cell proliferation and improved vascular permeability, VEGFR-2 can promote angiogenesis. The VEGFR receptor underwent a conformational change after binding VEGF, which was followed by phosphorylation and dimerization. Thus, inhibiting VEGF and VEGFR-2 is an effective

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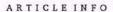


Review article

Design of carbon and graphene quantum dots based nanotheranostics applications for glioblastoma management: Recent advanced and future prospects

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Keywords: Glioblastoma Carbon quantum dots Graphene quantum dots Bioimaging Nanotheranostics applications



The primary challenges in combating Glioblastoma multiforme (GBM) include the lack of early detection methods and precision therapies. In response to this pressing need, this review discusses the applications of carbon-based fluorescent nanomaterials, such as carbon quantum dots (CQDs/CDs) and graphene quantum dots (GQDs), which have ushered in a new era of innovative approaches for early detection and treatment of GBM at the cellular level. The exceptional properties exhibited by GQDs and CQDs have expanded the horizons of GBM management. Surface modifications of these nanomaterials in the context of GBM treatment have yielded promising results, providing excellent biocompatibility and stability for normal cells while exerting toxicity against cancer cells, thereby demonstrating exceptional selectivity. The remarkable photo-physical attributes of CQDs and GQDs have underscored their suitability for advanced anticancer therapies, including photodynamic and photothermal therapies. Furthermore, integrating anticancer agents into CQDs and GQDs, along with receptor-based targeting systems, has significantly enhanced their potential in combating GBM due to their remarkable specificity. Research involving GBM-associated cell lines and animal models has validated the bioimaging capabilities of these nanomaterials, primarily owing to their distinctive fluorescence properties. Finally, the development of GBM biosensors utilizing CQDs and GQDs-based fluorescent and electrochemical platforms has demonstrated a high degree of selectivity, sensitivity, and real-time applicability. In conclusion, the adoption of fluorescent CQDs and GQDs for both diagnostic and therapeutic purposes has emerged as a promising alternative to conventional GBM management strategies.

1. Introduction

1.1. Glioblastoma multiforme

Glioblastoma multiforme (GBM) is the most common and lethal type of primary brain tumor, accounting for over 60% of all adult brain tumors. It is classified as a grade four (IV) malignancy by the World Health Organization (WHO) [1]. According to the literature, it is the most aggressive type of cerebral tumor in adults [2]. Principally, GBM is responsible for 2.5% of all cancer-related mortality, with a worldwide incidence of 3.2 cases per 100,000 people. Data suggests that the median age for GBM diagnosis is 64 years [3]. There are two forms of GBM: primary and secondary GBM. Primary GBM constitutes the majority

(90%) of GBM cases and primarily affects elderly individuals as an aggressive and highly invasive neoplasm. There is no clinical or histological evidence of a lower-grade antecedent lesion in primary GBM. Secondary GBM is associated with children and adolescents and progress over months or years from widespread low-grade or anaplastic astrocytoma [4]. In GBM, changes in the cellular biology of newly mature GBM cancer cells can be confirmed using a light microscope. These changes manifest as hallmarks related to tissue and cell alterations. The genetic information in GBM undergoes alterations, resulting in changes, suppression, and expression of genes compared to normal cells (astrocytes). These alterations also affect the extracellular matrix in the brain region. In summary, these pathological conditions can be used for the diagnosis of GBM [5]. In GBM tissues, GBM cancer stem cells represent

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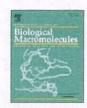


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Platinum-alginate-chitosan nanobioconjugate decorated carbon backbone layered biosensor for highly sensitive and selective detection of BACE-1

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Keywords: β-Secretase Chitosan Platinum nanoparticles Surface plasmon resonance Alzheimer's disease Sodium alginate Layer-by-layer assembly

ABSTRACT

Chitosan (CS) and sodium alginates (SA) have been revealed for the design of layer-by-layer (LbL) assembly to develop pharmaceutical dosage forms owing to their versatile characteristics. Recently, the preference for unique LbL assemblies in biosensor development has offered the modified performance for detection interest analyte. Beta (β)-site amyloid precursor protein-cleaving enzyme 1 (BACE-1) is a pivotal biomarker of Alzheimer's disease (AD) and demands high sensitivity and selective identification for the early-stage diagnosis. In this work, CS-SA-platinum nanoparticles (Pt-NPs) LbL-based nanobioconjugate decorated carbon backbone-layered affinity surface plasmon resonance (Anti-BACE-1-LbL@Pt-NPs-GO-SPR) biosensor was designed for extremely sensitive and selective sensing of BACE-1. Primarily, LbL nanobioconjugate was synthesized by integrating cationic 'CS' and anionic 'SA' on the face of green-made Pt-NPs. Here, the amines of 'CS' offers a softer surface for anti-BACE-1 immobilization that leads to maintaining the bio-functionality of bioreceptors, provides the specific orientation for bioreceptors, etc. As well, the synthesized graphene oxide (GO, 2D carbon backbone) was preferred as nonplasmonic nanomaterials due to their plenty of merits in biosensors. Here, the designed biosensor provides a low detection limit (LOD) of 5.63 fg/mL and a wide linear range from 5 fg/mL to 150 ng/mL. Moreover, selectivity and real-time analyses in spiked samples exhibited their practical usefulness in complex specimens for BACE-1 detection. Hence, the decorating of antibody-immobilized CS-SA coated Pt-NPs nanobioconjugate on the face of GO has various benefits mainly extremely sensitive and superb specificity. Overall, CS and SA coated Pt-NPs bioconjugate decorated GO layered SPR biosensors can provide highly sensitive, selectivity, rapid, label-free, etc. detection of BACE-1 in clinical samples.

1. Introduction

Alzheimer's disease (AD) is a long-term, severe, irreversible, and progressing neurodegenerative health concern [1]. Since its inception, there is a tremendous demand for sensitive and specific assessment of biomarkers of particular ailments to reach an earlier diagnosis [2]. Therefore, numerous strategies for the prognosis and diagnosis of AD have been presented to date [3]. Herein, several AD biomarkers have been documented for diagnosis of AD in clinical samples mainly beta-amyloid (A β), tau protein, lactoferrin, β -Site amyloid precursor protein-cleaving enzyme 1 (BACE1), etc. [1]. Herein, BACE-1 (also referred to as Beta-secretase 1) is a critical biomarker for the timely identification of AD [4]. In recent times, it has been detected using fluorescence-based biosensors [5], electrochemical biosensors [6], quantitative proteomics [7], enzyme-linked immunosorbent assay (ELISA) [6], etc. Notwithstanding these reports on BACE-1 and other AD

biomarkers, the rapid and direct assessment of AD biomarkers in supplied clinical samples at clinically meaningful amounts remains the key rate-restricting hurdle for AD and other neurodegenerative illnesses. Since its inception, the plasmonic biosensor has offered remarkable characteristics as diagnostics for biomarker detection [8]. In the case of plasmonic biosensors, surface plasmon resonance (SPR) is a cutting-edge optical biosensor technique that detects analytes with high speed, higher sensitivity, selectivity, label free, etc. [9]. Importantly, the SPR-based technique permits the label-free identification of extremely minute amounts of a target with great accuracy and efficiency [10]. Unfortunately, to the best of our knowledge reports on the detection of BACE-1 using SPR-based biosensors are less explored.

Graphene-based carbon backbone nanostructures such as 2D nonplasmonic graphene oxide (GO) have been disclosed for the construction of upgraded SPR biosensors. Herein, SPR shifts are made possible by their optical properties [11]. Moreover, it has a large surface area,

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pubs.acs.org/journal/abseba Review

Stimuli-Responsive Design of Metal-Organic Frameworks for Cancer Theranostics: Current Challenges and Future Perspective

Jidnyasa Pantwalawalkar, Prachi Mhettar, Sopan Nangare, Rushikesh Mali, Anil Ghule, Pravin Patil, Suhas Mohite, Harinath More, and Namdeo Jadhav*



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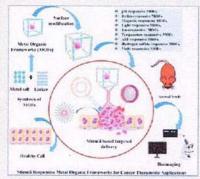


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ABSTRACT: Scientific fraternity revealed the potential of stimuli-responsive nanotherapeutics for cancer treatment that aids in tackling the major restrictions of traditionally reported drug delivery systems. Among stimuli-responsive inorganic nanomaterials, metal—organic frameworks (MOFs) have transpired as unique porous materials displaying resilient structures and diverse applications in cancer theranostics. Mainly, it demonstrates tailorable porosity, versatile chemical configuration, tunable size and shape, and feasible surface functionalization, etc. The present review provides insights into the design of stimuli-responsive multifunctional MOFs for targeted drug delivery and bioimaging for effective cancer therapy. Initially, the concept of cancer, traditional cancer treatment, background of MOFs, and approaches for MOFs synthesis have been discussed. After this, applications of stimuli-responsive multifunctional MOFs-assisted nanostructures that include pH, light, ions, temperature, magnetic, redox, ATP, and others for targeted drug delivery and bioimaging in cancer have been thoroughly discussed. As an outcome, the



designed multifunctional MOFs showed an alteration in properties due to the exogenous and endogenous stimuli that are beneficial for drug release and bioimaging. The several reported types of stimuli-responsive surface-modified MOFs revealed good biocompatibility to normal cells, promising drug loading capability, target-specific delivery of anticancer drugs into cancerous cells, etc. Despite substantial progress in this field, certain crucial issues need to be addressed to reap the clinical benefits of multifunctional MOFs. Specifically, the toxicological compatibility and biodegradability of the building blocks of MOFs demand a thorough evaluation. Moreover, the investigation of sustainable and greener synthesis methods is of the utmost importance. Also, the low flexibility, off-target accumulation, and compromised pharmacokinetic profile of stimuli-responsive MOFs have attracted keen attention. In conclusion, the surface-modified nanosized design of inorganic diverse stimuli-sensitive MOFs demonstrated great potential for targeted drug delivery and bioimaging in different kinds of cancers. In the future, the preference for stimuli-triggered MOFs will open a new frontier for cancer theranostic applications.

KEYWORDS: Metal-organic frameworks, stimuli-responsive, anticancer, nanotheranostics, bioimaging

1. INTRODUCTION

Cancer is the most distressing health issue globally. Principally, it is distinguished by an alteration in regulatory mechanisms that monitor the cell cycle, corresponding to the uncontrolled proliferation of malignant cells. Although the exact mechanism of cancer leading to mortality is yet to be illuminated, several controllable variables, viz. smoking, excessive body weight, and uncontrollable variables like genetic factors can contribute to the pathogenesis of cancer, either consecutively or concurrently. Reportedly, 19.3 million cancer patients were diagnosed worldwide in 2020. Correspondingly, 10.2 million deaths in the same year emphasize its ferocity. Moreover, Global Cancer Observatory (GCO) forecasted 30 million cancer-endorsed deaths annually from 2030. 1,4

1.1. Approaches for Cancer Treatment. A multitude of treatments have been devised for the management of cancer. But current therapies pose numerous challenges. Therefore, continuous progression in approaches to treat cancer successfully is of the utmost importance. Current cancer therapies mostly comprise surgical resection, biological therapy, chemotherapy (CT), radiotherapy, etc. in the solitary or combination form. Surgical excision is widely employed to control solid tumors. Although it is advantageous for the amputation of massive tumors that cannot be treated with radiation or chemotherapy, it may induce cancer cells to shed into the blood circulation, upsurge migration, and invade the target site. Additionally, it suppresses immunity, which favors

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Principal

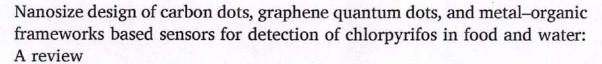


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Review Article





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ARTICLEINFO

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ABSTRACT

Chlorpyrifos (CPS) is a pesticide that is extensively used in agriculture. Despite their significant advantages in agriculture, small amounts of CPS in food and water have serious negative effects on human health and the environment. As a result, the detection of CPS with high sensitivity and selectivity is an urgent need. Unfortunately, conventional methods have numerous shortcomings such as low sensitivity, poor selectivity, low stability, complex procedures, etc. Nowadays, smart nanomaterials such as carbon dots (CDs), graphene quantum dots (GQDs), and metal-organic frameworks (MOFs) are widely reported for sensing CPS because of their unique characteristics such as good stability, tunability, high surface area, optical and electrical properties, etc. Therefore, the present review article provides insights into advanced nanoarchitecture-based smart nanomaterials namely CDs, GQDs, and MOFs mediated sensors for highly sensitive and selective sensing of CPS in water and food. Initially, the concept of CPS toxicity and the need to detect CPS are reviewed. Following this, smart advanced nanomaterial-based fluorescent, electrochemical, and colorimetric sensors for CPS monitoring in food and water are described. Finally, the current challenges and future promises of CDs, GQD, and MOF-based smart nanomaterials for CPS sensing are addressed. As an output, CDs, GQD, and MOF-based sensors provide the lowest detection limits down to femtograms (fg) for CPS detection. In addition, the reported sensors show high selectivity, good stability, and real-time applicability. In conclusion, CDs, GQDs, and MOFs-based sensing systems for CPS revealed superior performance over conventional methods. Therefore, in the future, this study will provide insights to budding researchers to design ultramodern smart nanomaterial-mediated sensors for realtime applications.

1. Introduction

Since their inception, organophosphorus pesticides (OPPs) have been utilized most effectively to kill insects [1]. According to a literature review, pesticide utilization increased from 3.1 to 4.1 million tons between 1999 and 2018 [2]. Mainly, OPPs are categorized into four prigroups such as phosphates, phosphorothioates, phosphorodithioates, and phosphorothiolates [3]. In this case, a few of the most popularly utilized OPPs include diazinon, dichlorvos, dimethoate, fenitrothion, quinalphos, monocrotophos, CPS, malathion, parathion, etc. [4]. Despite the plenty of merits of OPPs, the residues of OPPs are frequently found in air, soil, groundwater, and even agricultural commodities. Moreover, these pesticides are extremely poisonous and their residues are detrimental to living organisms and the atmosphere

[5]. Out of these pesticides, CPS is a potent insecticide employed in crop fields to eradicate termites, mosquitoes, roundworms, maize rootworms, flea beetles, flies, fire ants, and other pests [6]. It gives the broadspectrum ability to kill weeds and insects [7]. Primarily, China is the world's largest producer of CPS and India is a major consumer of CPS. Also, it is widely used in the United States, Brazil, and Cyprus [8]. To the best of our knowledge, the CPS was invented by a German scientist in the 1930 s. Later, in 1965, Dow Chemical Corporation introduced CPS to the United States for household and agricultural applications [9]. As per WHO categorization, CPS is a second-class OPPs with moderate toxicity. As well, CPS (C₉H₁₁C₁₃NO₂PS; O, O-diethyl-O-(3,5,6-trichloro-2-pyridinyl) phosphorothioate) is a non-systemic chlorinated OPPs insecticide. Also, it is used as an acaricide and nematicide. The CPS is a crystalline solid that is white or colorless and has a faint mercaptan

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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.

 $\textbf{Keywords} \ \ Carbon \ quantum \ dots \cdot Polyaspartic \ acid \cdot Functionalized \ carbon \ quantum \ dots \cdot Calcium \ (II) \ ions \ sensing \cdot Glutathione \ sensing \cdot Fluorescent \ probe$

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 of pirfenidone loaded chitosan-polyvinyl alcohol-graphene oxide-based scaffold: Spectroscopical characterizations and antibacterial activity

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Keywords: Chitosan Polyvinyl alcohol Graphene oxide Pirfenidone Antibacterial activity

ABSTRACT

The antibacterial activity against Staphylococcus aureus (S. aureus) in diabetic foot wound treatment is an appealing area for budding researchers. In this case, drug-loaded chitosan (CS)/polyvinyl alcohol (PVA)/graphene oxide (GO)-based composites can be used as an excellent option for antibacterial activity in diabetic foot wound treatment. Therefore, the present study aims to design a pirfenidone-loaded CS/PVA/GO nanocomposite (PFD-CS/PVA/GO) based scaffold via solvent casting method for improved antibacterial activity. In brief, CS with PVA forms the polyelectrolyte complex due to hydrogen bonding between amine functionality (CS) and a hydroxyl group (PVA). The GO nanosheet addition into CS/PVA resulted in covalent bonding between the amine functionality (CS) and the carboxylic functionality (GO) whereas PFD was fixed in CS/PVA/GO via π-π stacking. In this study, optimized PFD-CS/PVA/GO (6% w/w) scaffold percent entrapment efficiency, tensile strength, moisture content, % drug release, % swelling degree, % elongation at break, and water retention capacity were found to be 77.60%, 70.35 g/cm2, 16.39%, 50.60% (7 days), 236%, 45%, and 543.47%, respectively. Release kinetics assured that the Higuchi matrix was the best-fit model (R2 = 0.99). Interestingly, the GO avoids burst drug release at the beginning followed by extending the release whereas CS into PFD-CS/PVA/GO provides a good adhesive ability. Finally, antibacterial activity against S. aureus of PFD-CS/PVA/GO (6% w/w) shows a high (12.06 mm) zone of inhibition over a separate component of the scaffold. Concisely, optimized PFD-CS/PVA/GO (6% w/w) scaffolds provide improved antibacterial potential owing to their combined benefits of CS, and GO. In the future, anticipated PFD-CS/PVA/GO scaffolds will open a new door for antibacterial potential in diabetic foot wound healing.

1. Introduction

Diabetes mellitus (DM) is a critical condition in the healthcare sector. Epidemiological studies indicate approximately 285 million cases of DM in 2010 whereas it would be more than 360 million cases of DM in 2030. As per the literature, DM patients are susceptible to several problems wherein diabetes chronic foot wounds are one of them [1]. Unfortunately, diabetes chronic foot wounds take longer to heal because of disruptions in the process of collagen synthesis [2]. In addition, diabetic food infection is associated with poly-microbial infections. In that,

Staphylococcus aureus (S. aureus) is the most common pathogen. Presently, with the continuous preferences for antibiotics, there are chances of antimicrobial resistance for this pathogen [3]. To treat this critical healing condition of patients, several types of advanced approaches have been revealed. Current treatment approaches incorporating active for particular tasks, such as nanoparticles, nanogels, beads, biofilms, bandages, nanofibrous membranes, and so on, are unable to provide the necessary effects [2]. In addition, available therapies including tissue transplants, bioengineered skin, growth factors, hyperbaric oxygen treatment, and negative pressure wound therapy have shown healing

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Artificial Intelligence in the Paradigm Shift of Pharmaceutical Sciences: A Review

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Abstract

Al has emerged as a revolutionary technology in the pharmaceutical and biomedical fields. This review explores its transformative role, particularly in drug development, the discovery of future interventions in the pharmaceutical sector. By leveraging AI, these processes have become more efficient, cost-effective, and capable of delivering personalized medicine to individual patients. Moreover, AI's potential in disease prevention and outbreak prediction is promising, as it can analyze vast datasets to identify crucial patterns and trends, leading to targeted interventions for combating diseases. In biomedical research, AI has proven highly beneficial, especially in genomics, proteomics, and metabolomics, where it enables researchers to comprehensively analyze complex biological data, uncovering new insights and accelerating scientific discoveries. The impact of AI is also evident in the patient-physician interface, as it enhances diagnostic accuracy and treatment efficiency, ultimately improving patient care.

Keywords: artificial intelligence (AI); pharmaceutical research; drug discovery; academic research; precision medicine; job market

Introduction

Artificial intelligence (AI) has brought about a significant revolution in various sectors, with pharmaceutical research being no exception. This cutting-edge technology holds tremendous potential to accelerate medication development, improve patient outcomes, and reduce costs. Pharmaceutical research is a complex and time-consuming process encompassing drug discovery, development, clinical trials, and regulatory approval. AI's integration into these stages, as well as academic and industrial research and the biomedical industry, can prove

highly impactful [1]. The initial phase of pharmaceutical research involves drug discovery and development, which includes identifying and validating therapeutic targets, designing molecules, and testing their efficacy and safety. This step typically takes years and requires substantial resources and expertise. However, AI can streamline the process by analyzing vast datasets, predicting molecular interactions, and optimizing drug design [2].

For instance, AI algorithms can efficiently analyze genomic and proteomic data to identify potential drug targets and predict the effectiveness of specific drug



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