Collaborative publications during calendar year 2023

INDEX

Sr. No.	Calendar Year	Number of Research Papers Published
1	2023	16
Total		**16**

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Collaborative publications 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
Calendar Year 2023 (Number of Publications: 16)								
Development of amino acid salt-based curcumin@ lysine acetate co-amorphous system using liquid-assisted grinding for improved solubility and dissolution	U Patil, S Rawal, J Pantwalawalkar, SN Nangare, D Dagade, PO Patil, NR Jadhav	01/01/2023	The Thai Journal of Pharmaceutical Sciences	2023	1905-4637	https://digital.car.chula.ac.th/tjps/vol46/iss6/11/	https://digital.car.chula.ac.th/tjps/vol46/iss6/11/	https://www.scopus.com/sourceid/19700175006
Design of polyacrylamide grafted sesbania gum-mediated pH-responsive IPN-based microbeads for delivery of diclofenac sodium: In-vitro-in-vivo characterizations	P Devkar, SN Nangare, LR Zawar, NR Shirsath, PS Bafna, PG Jain	27/01/23	International Journal of Biological Macromolecules	2023	0141-8130	https://www.sciencedirect.com/science/article/abs/pii/S0141813023002465?via%3Dihub	https://doi.org/10.1016/j.ijbiomac.2023.123360	https://www.scopus.com/sourceid/17544
Medicinal Benefits of Black Rice (Oryza Sativa L. Indica): A Review	S Bhardwaj, D Javere, P Bagad, L Akotkar, VK Chatap, U Aswar	15/07/23	Advances in Pharmacology and Pharmacy	2023	2332-0044	https://www.hrpub.org/journals/article_info.php?aid=13191	https://doi.org/10.13189/app.2023.110303	https://mjl.clarivate.com://search-results?issn=2332-0036&hide_exact_match_fl=true&utm_source=mjl&utm_medium=share-by-link&utm_campaign=search-results-share-this-journal

Graphene Quantum Dots Incorporated UiO-66-NH2 Based Fluorescent Nanocomposite for Highly Sensitive Detection of Quercetin	SN Nangare, S Patil, K Chaudhari, ZG Khan, A Patil, PO Patil	01/03/23	Nano Biomedicine and Engineering	2023	2097-3837	https://www.sciopen.com/article/10.26599/NBE.2023.9290005	https://doi.org/10.26599/NBE.2023.9290005	https://www.scopus.com/sourceid/19900195033
Development and Evaluation of Vasoactive Intestinal Peptide Freeze Dried Injection	AR Bukkawar, AK Jain, VK Chatap	25/06/23	International Journal of Drug Delivery Technology	2023	2588-8943	https://ijddt.com/volume13issue2/	https://doi.org/10.25258/ijddt.13.2.21	https://www.scopus.com/sourceid/20500195212
Design, Development and Characterization of Ropinirole Mouth Dissolving Film by using Spin Coating Technique	B Akhade, VK Chatap, P Jain, MR Bhat	25/06/23	International Journal of Drug Delivery Technology	2023	2588-8943	https://ijddt.com/volume13issue2/	https://doi.org/10.25258/ijddt.13.2.10	https://www.scopus.com/sourceid/20500195212
Synthesis and Characterization of Hydroxypropyl Sesbania Galactamannan Seed Gum for Pharmaceutical Application	VK Chatap, G Choudhari, P Jain, MR Bhat	25/06/23	International Journal of Pharmaceutical Quality Assurance	2023	0975-9506	https://ijpqa.com/volume14issue2/	https://doi.org/10.25258/ijpqa.14.2.11	https://www.scopus.com/sourceid/21100204506
Preparation, characterization, and in vitro cytotoxicity activity of isothiocyanate embedded polymeric nanoparticles for potential breast cancer targeting	PB Patil, JK Patel	11/09/23	Breast Cancer	2023	2374-4677	https://link.springer.com/article/10.1007/s12282-023-01501-1	https://doi.org/10.1007/s12282-023-01501-1	https://www.scopus.com/sourceid/83418
A Review Article: Formulation of Topical Gel by QbD Approach	PG Karamkar, A Agrawal, VK Chatap	15/05/23	Advances in Pharmacology and Pharmacy	2023	2332-0045	https://www.hrpub.org/journals/article_info.php?aid=12828	https://doi.org/10.13189/app.2023.110202	https://mjl.clarivate.com://search-results?issn=2332-0036&hide_exact_match_fl=true&ut

								m_source=mjl&utm_medium=share-by-link&utm_campaign=search-results-share-this-journal
Formulation Development and Evaluation of Freeze-dried Aviptadil Injection using Mannitol as Cryoprotectant	AR Bukkawar, AK Jain, VK Chatap	07/09/23	International Journal of Pharmaceutical Quality Assurance	2023	0975 9506	https://ijpqa.com/volume14issue3/	https://doi.org/10.25258/ijpqa.14.3.13	https://www.scopus.com/sourceid/21100204506
Recent progress in targeting KRAS mutant cancers with covalent G12C-specific inhibitors	LS Rathod, PS Dabhade, SN Mokale	18/03/23	Drug Discovery Today	2023	1878-5832	https://www.sciencedirect.com/science/article/abs/pii/S1359644623000739?via%3Dihub	https://doi.org/10.1016/j.drudis.2023.103557	https://www.scopus.com/sourceid/21196
Functionalized Graphene Quantum Dots (GQDs) based Label-Free Optical Fluorescence Sensor for CD59 Antigen Detection and Cellular Bioimaging	RS Tade, A Kalkal, PO Patil	17/11/23	Journal of Fluorescence	2023	1053-0509	https://link.springer.com/article/10.1007/s10895-023-03501-y	https://doi.org/10.1007/s10895-023-03501-y	https://www.scopus.com/sourceid/25282
Zinc metal-organic frameworks- graphene quantum dots nanocomposite mediated highly sensitive and selective fluorescence "On-Off-On" probe for sensing of quercetin	SN Nangare, P Sangale, A Patil, PO Patil	29/11/23	Acta Chimica Slovenica	2023	3812-4653	https://acsi-journal.eu/index.php/ACSi/article/view/7870	https://doi.org/10.17344/acsi.2022.7870	https://www.scopus.com/sourceid/22658
Discovery of New Quinazoline Derivatives as VEGFR-2 Inhibitors: Design, Synthesis, and Anti-proliferative Studies	SA Dhawale, PS Dabhade, SN Mokale	31/08/23	Anti-Cancer Agents in Medicinal Chemistry	2023	1875-5992	https://www.eurekaselect.com/article/132916	https://doi.org/10.2174/1871520623666230714152455	https://www.scopus.com/sourceid/29318

Design of carbon and graphene quantum dots based nanotheranostics applications for glioblastoma management: Recent advanced and future prospects	SN Nangare, S Chandankar, PO Pati	14/10/23	Journal of Drug Delivery Science and Technology	2023	1773-2247	https://www.sciencedirect.com/science/article/abs/pii/S1773224723009127?via%3Dihub	https://doi.org/10.1016/j.jddst.2023.105060	https://www.scopus.com/sourceid/22204
Stimuli-Responsive Design of Metal–Organic Frameworks for Cancer Theranostics: Current Challenges and Future Perspective	J Pantwalawalkar, P Mhettar, SN Nangare, R Mali, A Ghule, PO Patil, S Mohite, H More, N Jadhav	01/08/23	ACS Biomaterials Science & Engineering	2023	2373-9878	https://pubs.acs.org/doi/10.1021/acsbiomaterials.3c00507	https://doi.org/10.1021/acsbiomaterials.3c00507	https://www.scopus.com/sourceid/21100461927

OFFICE SEAL

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Original Article

Thai Journal of Pharmaceutical Sciences

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

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ABSTRACT

Curcumin, multivalued 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 curcumin-lysine acetate COAM was confirmed using Fourier-transform infrared spectroscopy, differential scanning calorimetry, and powder X-ray diffraction. COAM tablet formulation showed optimum evaluation characteristics with improved drug dissolution. Therefore, the amino acid salt-based co-amorphous system can be used for solubility and dissolution improvement of curcumin and other multivalued 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

Co-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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ARTICLE INFO

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 3^2 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, ^{1}H 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 % (12*h*) which was non-significant ($p > 0.05$; f2 = 79 ~ 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.*

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

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

1. Introduction

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

Research Article

Nano Biomed Eng

Graphene Quantum Dots Incorporated UiO-66-NH_2 Based Fluorescent Nanocomposite for Highly Sensitive Detection of Quercetin

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Citation: S. Nangare, S. Patil, K. Chaudhari, et al. Graphene quantum dots incorporated UiO-66-NH_2 based fluorescent nanocomposite for highly sensitive detection of quercetin. *Nano Biomedicine and Engineering*, 2023.

http://doi.org/10.26599/NBE.2023.9290005

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-NH_2 metal–organic framework-based nanoprobe (GQDs@UiO-66-NH_2) 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-NH_2. The addition of quercetin to GQDs@UiO-66-NH_2 leads to fluorescence dampening due to the adsorption potential of UiO-66-NH_2. 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 NH_2; 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].

RESEARCH ARTICLE

Development and Evaluation of Vasoactive Intestinal Peptide Freeze-Dried Injection

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ABSTRACT

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

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

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

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

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

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

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Source of support: Nil.

Conflict of interest: None

INTRODUCTION

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

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

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

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RESEARCH ARTICLE

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

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ABSTRACT

The aim of the research was to develop a ropinirole mouth-dissolving film employing solvent casting and spin coating methods with sesbenia gum acting as a film-forming agent. Parkinson's disease is treated with ropinirole. Sesbenia gum was designed as a film-forming ingredient in the 25 to 600 mg concentration range for solvent casting and 50 to 250 mg for spin coating. For both procedures, the concentration of the plasticizer propylene glycol was optimized between (0.3 and 1.0 mL). Film-forming agent and plasticizer effects at various concentrations were examined. For the solvent casting and spin coating processes, the plasticizer concentration was 0.3 mL for each, while the optimal film-forming agent concentrations were 50 and 150 mg, respectively. Ropinirole MDFs were made employing an enhanced concentration and more excipients. In comparison to the solvent casting approach, the spin coating process produced films with better surface morphology, a 24 seconds shorter disintegration time, good tensile strength of 3.2 (N/mm^2), a thinner thickness of 0.2 mm, and a maximum drug content of 93.14%. Sesbenia gum has been discovered to have greater potential for the spin-coating method of developing a ropinirole mouth-dissolving film.

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

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Conflict of interest: None

INTRODUCTION

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

A novel oral fast-dissolving dose form combines the convenience of dosing without water or beverage with the simplicity of administration. Despite their quick disintegration/ dissolution times, some patient groups still worry about swallowing solid pills and run the danger of choking. Fast-dissolving film eliminated The possibility of choking.[2] Oral films can be divided into the following three categories.[3]

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

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

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

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RESEARCH ARTICLE

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

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ABSTRACT

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

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

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INTRODUCTION

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

According to Duke *et al.*, the endosperm, or outermost layer, of a seed of the species *Sesbania grandiflora* (Leguminosae) is used to make *Sesbania* gum. According to 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 cold-water dispersion of gum, as reported as.[3,4]

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

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

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ORIGINAL ARTICLE

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

Prashant Bhagwan Patil[1,2] · **Jayvadan Kantilal Patel**[1,3]

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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

RESEARCH ARTICLE

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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INTRODUCTION

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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ELSEVIER

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

POST-SCREEN

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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. $KRAS^{G12C}$ 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[4]. Among all KRAS mutations, the $KRAS^{G12C}$ 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.[7] For example, Shokat and colleagues reported the novel identification of the first selected cysteine 12 (Cys12) $KRAS^{G12C}$ covalent inhibitors in 2013, suggesting that $KRAS^{G12C}$ covalent inhibitors of Cys12 interfere with the KRAS signaling process via covalent bonding.[8]

Further research resulted in enhanced covalent $KRAS^{G12C}$ inhibitors, which reached clinical trials, including adagrasib and ARS-1620. Direct targeting of $KRAS^{G12C}$ 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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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.

Keywords Functionalized graphene quantum dots · CD59 antigen · Oriented conjugation · Turn 'on–off' sensor · 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 glycosyl-phosphatidylinositol 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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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.[1] It provides a highly porous structure through the association of metal ions with carefully selected organic linkers via strong bonding.[2] To date, various types of MOFs have been developed for numerous applications, including drug delivery, biosensing, chemical sensing, gas separation, and more.[3,4] At present, they are widely employed for biosensing purposes, offering low detection limits, high sensitivity, excellent responsiveness, and good stability, among other benefits.[4] Despite these groundbreaking merits, MOFs suffer from major drawbacks, primarily the collapse of their structure and pore shrinkage.[2] 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-

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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-1,1-dicarboxamide 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 10.55 μM) in comparison to the reference drug Cabozantinib (IC_{50} = 9.10 and 10.66 μM) against HT-29 and COLO-205, respectively. The synthesized compound SQ2 showed VEGFR-2 kinase inhibition activity (IC_{50} = 0.014 μM) compared to the reference drug, Cabozantinib (IC_{50} = 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.

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

1. INTRODUCTION

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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ABSTRACT

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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Review

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

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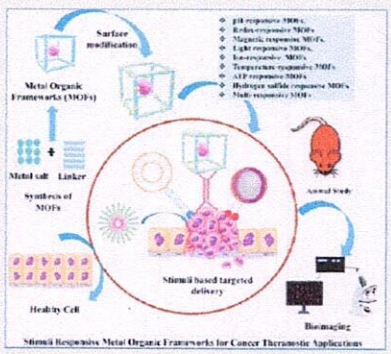
ABSTRACT: Scientific fraternity revealed the potential of stimuli-responsive nanotherapeutics for cancer treatment that aids in tackling the major restrictions of traditionally reported drug delivery systems. Among stimuli-responsive inorganic nanomaterials, metal–organic frameworks (MOFs) have transpired 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.[1] 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.[2] Reportedly, 19.3 million cancer patients were diagnosed worldwide in 2020. Correspondingly, 10.2 million deaths in the same year emphasize its ferocity.[3] 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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