CRITICAL REVIEWS IN ANALYTICAL CHEMISTRY
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Nanoarchitectured Bioconjugates and Bioreceptors Mediated Surface Plasmon Resonance Biosensor for *In Vitro* Diagnosis of Alzheimer's Disease: Development and Future Prospects

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ABSTRACT

Alzheimer's disease (AD) is an obvious neurological disorder characterized by progressive brain cell death that resulted in memory loss, cognitive decline, and finally dementia. Besides, AD is also affected by a multifunctional pathway, which leads to alteration in the biomolecular level as AD steps forward. Notwithstanding numerous diagnosis techniques, the conventionally engaged technology permits the detection of AD biomarkers with low sensitivity and poor selectivity. Concerning this, in recent years bioconjugates and bioreceptors based AD biomarkers recognition is gaining huge prospective to improved selectivity and sensitivity of AD at the molecular level. The present review deals with the recent progress in bioreceptors and bioconjugates mediated surface plasmon resonance (SPR) biosensor for *in vitro* diagnosis of AD. Fascinatingly, this review inculcates the information of assorted important AD biomarkers viz. beta-amyloid (Aβ), Tau protein, apolipoprotein (apoE4), 17-β-hydroxysteroid dehydrogenase type 10 (17β-HSD-10), acetylcholine, etc. In addition, this review sheds light on the utmost and unique methods of bioconjugates synthesis, which is holding the huge attention of researchers for AD biomarker detection and contributed to the development of simplistic, rapid, and socioeconomic sensitivity enhancement methods. Concisely, this review gives insight into the analytical performance of nanoarchitectured bioconjugate and bioreceptor-mediated SPR biosensor and their revolutionary benefits in terms of selectivity and sensitivity for *in vitro* diagnosis of AD biomarkers. Overall, this review gives a detailed overview of research done to date in the meadow of SPR biosensors in the *in vitro* diagnosis of AD, which paves the new pathway for futuristic biomedical applications.

KEYWORDS

Alzheimer's disease; surface plasmon resonance; bioconjugates; bioreceptors; *in vitro* diagnosis

HIGHLIGHTS

- AD recent updates and its biomarkers reviewed.
- There is no leading technology to rapidly sense and monitor AD.
- Bioconjugates as potential biosensing elements.
- Conjugation methods to link bioreceptors to nanomaterials have been highlighted.
- Role of bioconjugates and bioreceptors in AD biosensing through SPR biosensor have been discussed.

GRAPHICAL ABSTRACT

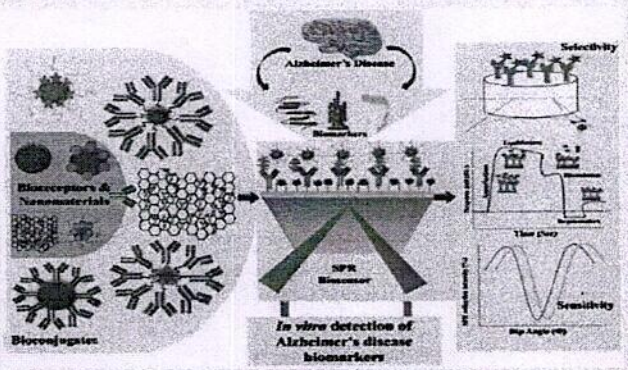

Figure 1. Nano-architectured bioconjugates and bioreceptors mediated SPR biosensor for highly sensitive and selective in vitro diagnosis of AD biomarkers.

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Functional Composites and Structures

PAPER

One-pot *in situ* synthesis of eco-friendly cellulose magnetic nanocomposite (Cf-MNCs) for dye adsorption application

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Keywords: cellulose fibers, *in-situ* synthesis, magnetic nanocomposites, dye adsorption

Abstract

Cellulose-based magnetic nanocomposites (Cf-MNCs) have been introduced using a modified one-pot *in situ* co-precipitation method using iron salts with various concentrations in the alkali solution. Fabricated nanocomposites investigated for structural and functional properties with different spectroscopic characterization techniques prior to use in dye degradation study. The scanning electron microscopy revealed the morphological structure of the synthesized nanofibers and nanocomposites. The elemental analysis and vibrating sample magnetometry emphasized the presence of Fe elements attributed to the iron salts. The HRTEM analysis showed a destructed cellulose fiber network indicating its arrangement into nanocomposites. Moreover, the crystal properties of the Cf-MNCs were accomplished using x-ray powder diffraction (79.3% crystallinity). The Fourier transform infrared analysis and differential scanning calorimetry gives the idea about the structural and functional changes in the cellulose fibers loaded with iron oxide nanoparticles. The functional adsorption properties of the prepared nanocomposites have been evaluated using methylene blue and Alizarin red S carcinogenic dyes. The dye adsorption of the fabricated Cf-MNCs nanocomposites was found to be 93%. We affirmed that this novel eco-friendly degradable polymer-based nanocomposite has great potential in the field of catalyst fabrication for the degradation of organic pollutants in wastewater.

1. Introduction

In recent years, nanocellulose has exploited for abundant applications in materials chemistry, nano-biomedicine, drug delivery, and green composite materials. Cellulose-based nanocomposites (CbNCs) combine the distinct features of cellulose with specific nanomaterials incorporated in it with high specific surface area and add-on characteristics. Commonly, cellulose nanofibers (CNFs) and cellulose nanocrystals (CNC) have been used for the fabrication of CbNCs [1]. Nanocellulose can be obtained from native fibers by acid hydrolysis, high pressure homogenization (HPH) or different methods [2, 3]. Amongst all methods, acid hydrolysis results in highly crystalline and rigid nanofibers, ranging in size from 100 nm to 1 μm than that of the HPH route. Recently, the use of cellulose-based magnetic nanocomposites (Cf-MNCs), acclaimed fame in a short duration of time in the catalytic and different allied applications. The length-to-diameter (L/d) is a major factor that controls the mechanical properties of nanocomposites and determines the percolation threshold value called 'geometrical aspect ratio', which further benefits the reinforcing effect [4]. As mentioned earlier, the large surface area, high porosity and biodegradability allowed investigators too many customary modifications in their structures can be availed using cellulose nanofibers (CNF). The use of iron oxide nanoparticles (IONPs) was realized for magnetodielectric properties and ease of separation [5]. To develop the ideal Cf-MNCs, the IONPs should be well dispersed in the fibrils either as an over-attached form or in the lumen. The dispersion of IONPs in the cellulose matrix can be monitored by setting the process parameters, like temperature, pH, solvent properties and other process attributes. The Cf-MNCs can be prepared by *in situ* as well as *ex-situ* methods such as microwave reflux, co-precipitation, hydrothermal treatment, etc. These reinforced Cf-MNCs can be explored for *in vivo* MRI as superparamagnetic or negative

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REVIEW Open Access

Flavonoids as natural phenolic compounds and their role in therapeutics: an overview

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Abstract

Background: Natural plants and plant-derived formulations have been used by mankind from the ancient period of time. For the past few years, many investigations elaborated the therapeutic potential of various secondary chemicals present in the plants. Literature revealed that the various secondary metabolites, viz. phenolics and flavonoids, are responsible for a variety of therapeutic action in humans.

Main body: In the present review, an attempt has been made to compile the exploration of natural phenolic compounds with major emphasis on flavonoids and their therapeutic potential too. Interestingly, long-term intake of many dietary foods (rich in phenolics) proved to be protective against the development and management of diabetes, cancer, osteoporosis, cardiovascular diseases and neurodegenerative diseases, etc.

Conclusion: This review presents an overview of flavonoid compounds to use them as a potential therapeutic alternative in various diseases and disorders. In addition, the present understanding of phenolics and flavonoids will serve as the basis for the next scientific studies.

Keywords: Phenolics, Flavonoids, Secondary metabolites, Therapeutic action

Background

Polyphenols is one of the major classes of naturally occurring compounds having at least one phenol group in their structure, present in the plants, including vegetables, fruits, cereals and dry legumes [1–3]. As these compounds show multiple physiological effects, when consumed as a component or dietary supplement, polyphenolics become a subject of interest in a scientific fraternity [4]. Polyphenols are secondary metabolites consisting of polyhydroxy phytochemicals of the plant kingdom and effective defense against pathogenic aggression and ultraviolet radiation [5]. These secondary compounds are biosynthesized through shikimic acid and phenylpropanoid pathways and believed to be participative in adapting the plants in a stressed situation due to environmental changes [6]. From this extensive class of polyphenolic compounds, more than 8000 have been already isolated, identified and described in detail [7].

In food, initially, polyphenols are used to manipulate astringency, bitterness, flavor, color, odor and oxidative stability. Throughout evolution in various plant lines, the ability to synthesize phenolic compounds was selected when these compounds met unique needs, allowing plants to cope with continuously evolving environmental conditions over evolutionary time [8]. Afterward, various epidemiological research activities and accompanying meta-analyses intensely recommended protection offered against the development of diabetes, cancer, osteoporosis, cardiovascular diseases and neurodegenerative diseases by long-term intake of plant polyphenols in our daily diet [9, 10]. These compounds, based on their chemical structures, are divided into various subclasses like phenolic acids, flavonoids, tannins, coumarins, lignans, quinones, stilbenes and curcuminoids [1].

Flavonoids are ubiquitously occurring polyphenolic compounds and comprise the broad class of natural products. To date, it has documented over 8000 different flavonoids and most of them are present in the cells or surfaces of various plant tissue organs [11]. A large variety

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Functional Composites and Structures

TOPICAL REVIEW

Fundamental aspects of graphene and its biosensing applications

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Keywords: graphene, sensor scale-up aspects, biosensing applications, immunosensing, pathogen sensing

Abstract

The worldwide frontiers of research have experienced a flood of developments in advanced nanomaterials. Among these, graphene, a member of the carbon family, has now replaced many traditional materials and broadened the horizons of material chemistry, analytical chemistry, pharmaceutics, and other multidisciplinary fields. Owing to the exceptional properties of graphene, it has been widely utilized in various nanocomposites as a reinforcing material and for biosensing components. The present review serves as a familiarization for budding researchers in the materials science and analytical fields, where the use of graphene in biosensing-related applications had long been foreseen. Furthermore, we also offer a brief review of graphene's tunable properties for biosensing. This article describes the actual mechanisms of interfaces that interact with graphene, such as immunogenic agents, bacteria, and other biomolecules. We also discuss the application of graphene-based materials to the biosensing of a range of analytes, and the challenges and future perspectives of graphene. Thus, this review gives a detailed insight into biosensing with graphene, graphene's fundamental properties, and application perspectives.

1. Introduction

Over the last couple of decades, graphene-based materials (GBMs) have gained tremendous research interest owing to their excellent physicochemical properties [1]. Interestingly, graphene exists in many forms, and can be customized in numerous ways as per the application requirements [2]. Common to all graphene forms, the lattice-configured nanostructure of graphene, i.e. graphene oxide (GO) has been thoroughly investigated for several biomedical and pharmaceutical applications [3], possibly due to its very tunable properties. Because of this, it offers several benefits for the fabrication of biosensing elements or parts thereof [4]. The fascinating characteristics of graphene or GO including a large specific area, abundant surface functional groups viz. carboxyl, epoxy, etc, offer a choice of materials for the immobilization of various important biomolecules (e.g. enzymes). Moreover, the high chemical stability and remarkable optical properties of GO are suitable for electrochemical (ECL) biosensing [5]. Moreover, its electrical properties, high conductivity, and superb electron mobility help in the fabrication of thin films and plasmonic biosensors for the detection of various biomolecules. From 2010 onwards, several research groups have been engaged in the design, fabrication, and analysis of various types of biosensors based on graphene platforms for heavy metal detection [6, 7], ferric ion detection, DNA detection [8], antibody detection [9, 10] as well as many biological metabolite detections [11], etc.

Graphene has an electrical conductivity of the order of 1000 mho m^{-1} and thermal conductivities of between 1500 and 2500 W $m^{-1} K^{-1}$. It is the strongest material ever tested, with a tensile strength of around 130 GPa [12, 13]. Graphene exhibits a broad ECL window of approximately 2.5 V in a 0.1 mol l^{-1} when tested in phosphate-buffered saline. It offers a low charge-transfer resistance of around 6.5 MΩ cm^2. These properties prove that graphene is an ideal material for use in multifunctional fast sensors.

Since graphene was discovered, it has started to emerge and be developed in many scientific studies. Despite these advances, the fundamental science behind graphene is, unfortunately, not completely explained. More work is needed on this problem in areas such as graphene surface absorption mechanisms, biomolecular orientations, and the way in which these interactions affect graphene's transport properties, etc

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REVIEW Open Access

Pharmaceutical applications of citric acid

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Abstract

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

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

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

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

Background

Citric acid (CA, 2-hydroxy2, 3-propanetricarboxylic acid, tricarboxylic acid) is the largest organic acid contained in the tonnage. Generally, it is a universal plant-and animal-metabolism intermediate. CA is a commodity chemical processed and widely used around the world for plentiful pharmaceutical applications (Fig. 1) [1]. To begin with 1784, Carl Scheele (a Swedish chemist) isolated the CA (Molecular Weight: 210.14 Da) from the lemon juice. Whereas in1893, at the first time Wehmer demonstrated the culture medium includes sugars and inorganic salts, *Penicillium glaucum* (*Citromyces*) accumulating CA. Amusingly, CA was first commercially manufactured in England from the imported Italian lemons. In 1917, Currie discovered that some of the *Aspergillus niger* strain generated CA into adequate nutrient mediums that contain high levels of sugar plus mineral salts and along with that preliminary medium pH (2.5–3.5). Despite these notable findings, lemon juice was still a commercial source for the manufacturing of CA until 1919. This provided the foundation for industrial CA production with *Aspergillus niger* [2]. As per literature, CA has been unrevealed by Krebs in the late 1930s as a key ingredient in the metabolism of all aerobe species [3, 4]. The developmental stages of the discovery and manufacture of CA from 1784 to 2020 [4] are represented in Fig. 2.

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

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ORIGINAL ARTICLE

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

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Abstract

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

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

How to cite this article

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INTRODUCTION

Even though the investigation on allotropic forms of carbon was begun before 1990, but the most intuitive form of carbon allotrope i.e. carbon nanotubes (CNTs) were reported in 1991[1]. Numerous classical approaches for the synthesis of CNTs are reported by academic researchers and industry experts for their promising physicochemical properties. In case of CNTs, the

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Nano Biomed Eng
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Research Article

Fabrication of N-Doped Graphene@TiO_2 Nanocomposites for Its Adsorption and Absorbing Performance with Facile Recycling

Pravin Onkar Patil[1], Sopan Namdev Nangare[1], Pratiksha Pramod Patil[1], Ashwini Ghanashyam Patil[2], Dilip Ramsing Patil[2], Rahul Shankar Tade[1], Arun Madhukar Patil[2], Prashant Krishnarao Deshmukh[3], Sanjay Baburao Bari[1]

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Abstract

The present work aims to synthesize nitrogen-doped reduced graphene oxide-titanium dioxide nanocomposite (N-rGO@TiO_2) using a simple, eco-friendly method and its applications in spectroscopic detection of heavy metal ions such as lead (Pb^{2+}), mercury (Hg^{2+}), and chromium-VI [Cr(VI)] in potable water. Initially, TiO_2 nanoparticles loaded N doped rGO sheets were fabricated by an ecological method using *Gossypium hirsutum* (cotton) seeds extract as a green reducing agent. Then, the N-rGO@TiO_2 nanocomposites were subjected for characterizations such as spectroscopic techniques, particle size analysis, zeta potential analysis, and spectroscopic sensing. Notably, the results of this study confirmed that N-rGO@TiO_2 exhibited countless stupendous features in terms of sensing of an analyte. Briefly, the UV-visible spectroscopy and Fourier transform infrared (FTIR) spectroscopy confirmed the successful synthesis of N-rGO@TiO_2. The SEM images showed the wrinkled, folded, and cross-linked network structures that confirmed the surface modification and nitrogen doping in the rGO sheet and synthesis of N-rGO@TiO_2. The EDAX study confirmed the elemental composition of the N-rGO@TiO_2 nanocomposite. Finally, due to the larger surface area, porous nature, high electron mobility, etc. the N-rGO@TiO_2 probe provides the lower detection limit for Pb^{2+}, Hg^{2+}, and Cr (VI) as low as 50 nM, 15 µM, and 25 nM, respectively. Concisely, our study affirms the admirable sensitivity of N-rGO@TiO_2 nanocomposite to the Pb^{2+}, Hg^{2+}, and Cr (VI) in potable water can provide better environmental remediation.

Keywords: Graphene oxide, N-rGO@TiO_2, Nanocomposite, Cotton-seed, Heavy metals, Biodegradable, Sensing

Introduction

Over the past two decades, graphene-based materials are gaining tremendous attention from a scientific fraternity in various fields [1-3]. It may because of its astonishing properties and potential to revolutionize the scientific sector [3-5]. Graphene can be used to fabricate several dimension materials such as 1D nanostructure [6], 2D layer stacked films [7], 3D graphene hydrogel [7-9], and aerogel [10-13], etc. Out

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Black Phosphorus Nanostructure Based Highly Sensitive and Selective Surface Plasmon Resonance Sensor for Biological and Chemical Sensing: A Review

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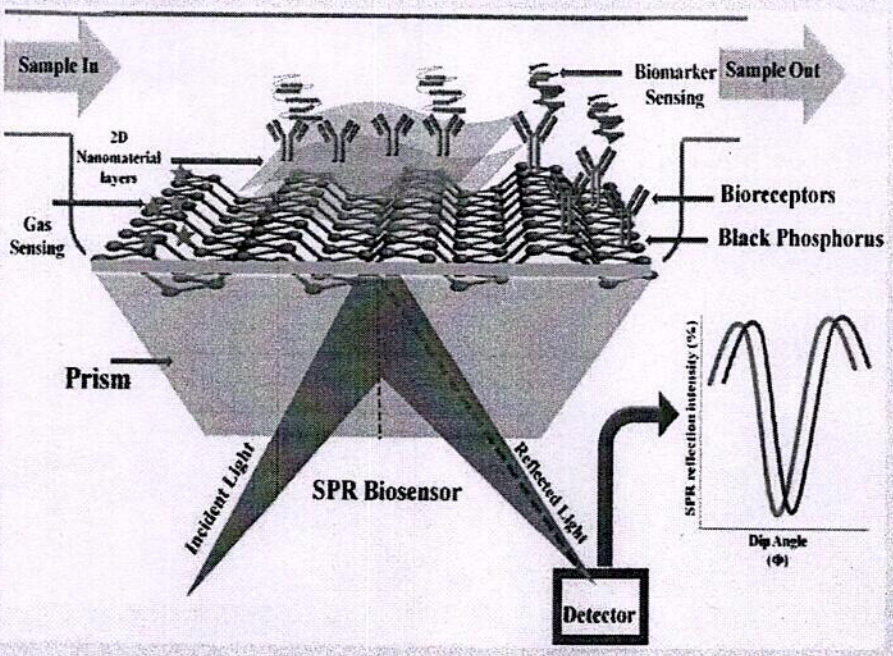
ABSTRACT

Surface plasmon resonance (SPR) is an attention-grabbing sensor type, which offers the sensitive and selective detection of biomolecules and environmentally toxic substances. Notably, the SPR sensor gives excellent rewards including real-time, *in-situ*, and label-free measuring capability as compared to existing sensing technologies. As a result, these noteworthy merits of the SPR sensor make it straightforward to investigate the molecular events and chemical/gas molecule interaction. Unfortunately, there are different binding events including smaller molecular mass substances, which cannot be detected at the SPR sensor. Accordingly, this downside of the SPR sensor eventually led to the design and implementation of new approaches for sensitivity and selectivity improvement for sensing applications in different fields. Recently, the black phosphorus (BP) derived 2D nanomaterial is stand out as a distinctive nanostructure in comparison to recently reported other 2D nanomaterials. Substantial and functional characteristics of BP including simplicity of operation, optical properties, high carrier mobility, stronger immobilization of receptors and biomolecules, electronic bridging playing important role in the highly selective and sensitive assessment of analyte. The designed BP nanostructures are mostly serving to accelerate the plasmon material signals followed by improved molecular sensing that may due to 40-times faster-sensing responses of BP nanostructure than reported 2D nanomaterials. Therefore, the present review article sheds light on the latest significant advances in biological and toxic gas detection through 2D BP nanostructures based SPR sensors. In the future, this review will facilitate detailed insights into the development of BP-based groundbreaking frameworks for highly sensitive and selective recognition of biomolecules and environmental pollutants.

KEYWORDS

Black phosphorus; biosensing; in-vitro diagnosis; sensitivity enhancement; surface plasmon resonance

GRAPHICAL ABSTRACT



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RESEARCH Open Access

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

Mohan G. Kalaskar[1*], Rakesh E. Mutha[2], Anilkumar U. Tatiya[1], Sandip D. Firke[1], Sanjay J. Surana[1], Komal A. Dhoka[1] and Komal Heda[1]

Abstract

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

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

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

Keywords: Neem gum, Sedimentation volume, Redispersibility, Flowability

Background

Pharmaceutical excipients are additives with unique physicochemical properties that help to transform the drug substances into an effective type of dosage suitable for patient administration. Demand for new and updated excipients for drug delivery systems has been growing in order to meet the needs of new, better formulations. To be used as pharmaceutical excipients, natural polymers are readily available, biodegradable, non-toxic and cost-effective, to be used as an excipient for a range of pharmaceutical formulations [1].

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

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

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RESEARCH ARTICLE

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

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ABSTRACT

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

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hydration; chrysin;
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Introduction

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

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

Out of the many approaches used for drug encapsulation, liposomes are widely used for both hydrophilic and hydrophobic drugs such as antioxidants, antimicrobials and other pharmacologically important compounds [8]. However, organic residual effect, leakages of active compounds and instability during storage of traditional liposomes may restrict their applications [9,10]. So as to conquer these limitations, polycationic polymer like chitosan could be used as a coating material which forms polyelectrolyte complex with oppositely charged polymeric r ial by intermolecular electrostatic deposition [11,12].

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

The main objective of the present study was to encaps CHR in liposomal form using the electrostatic deposition nique for protection and further enhancement in bioavailal For the same, biocompatible and biodegradable biological m molecules viz. chitosan (CHN) and soya lecithin (SOL) were which form a polymeric nanoshell with the aim to shield against degradation and to enhance its biocompatibility [1 Being a polycationic macromolecule, chitosan, through inte lecular electrostatic deposition, form polyelectrolyte compl with oppositely charged macromolecules [17]. Developed ch liposomes (CLPs) were further characterized using different p cochemical parameters like particle size (PS), polydispersity i (PDI), zeta potential (ZP), entrapment efficiency (% EE), drug l ing (% DL), differential scanning calorimetry (DSC), transmis

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Cissus quadrangularis L: A comprehensive multidisciplinary review

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ABSTRACT

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

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

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

Results: Phytochemical assessment as a whole indicated the presence of flavonoids, triterpenoids, alkaloids, saponins, iridoids, stilbenes, vitamins, steroids, and glycosides. A toxicity study revealed that its LD_{50} value is above 3000 mg/kg in animals indicating its safety. A variety of pharmacological studies of aerial parts of this herb by different extracts have demonstrated analgesic, anti-inflammatory, anticonvulsant, antimicrobial, anticancer, anti-osteoporotic activity and other bone-related disorders to justify its name as *Hadjod*. Still, the herb has been utilized in clinical practice and several patents were filed in India and US for its antiosteoporotic property.

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

1. Introduction

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

Natural products, notably those extracted from plants, tend to provide valuable leads in the drug development process (Balunas and Kinghorn, 2005). The initial process in drug research is to gather data on materials that have previously been used to cure a disease. Due to the custom of verbal transfer of the information regarding medicinal plants and their relevant techniques of use (Bhatia et al., 2014), there is concern that aboriginal herbal medicine knowledge is being endangered (Ssegawa and Kasenene, 2007). It is a need of time to conserve and document this traditional and advanced knowledge of plants proven through various experimentation and study protocols so that it will work as a lighthouse for the future researchers and give guideline with respect to safety, efficacy and specific uses (Bunalema et al., 2014).

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

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Review Article

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

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Gout, uric acid
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Colorimetric biosensor

ABSTRACT

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

1. Introduction

From its inception, arthritis is a severe health issue of a joint in almost all developed and developing nations. Arthritis is a term that derives from the Greek word "disease of the joint." Commonly, it can be stated as acute inflammation or chronic inflammation of the joint that is sometimes with the effect of pain and sometimes co-exists with structural damage [1]. As many as 100 classes of arthritis have been characterized according to the research. Generally, it can be classified into two type's namely non-inflammatory arthritis and inflammatory arthritis. In the first category, non-inflammatory arthritis is commonly known as osteoarthritis, while inflammatory arthritis is categorized

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Perspective

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

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

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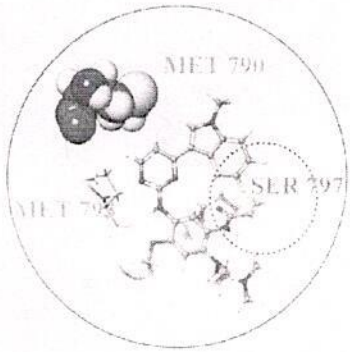
ABSTRACT: The pyrimidine core-containing compound Osimertinib is the only epidermal growth factor receptor tyrosine kinase inhibitor (EGFR-TKI) from the third generation that has been approved by the U.S. Food and Drug Administration to target threonine 790 methionine (T790M) resistance while sparing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



1. INTRODUCTION

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

The EGFR-independent pathway also contributes to the resistance to Osimertinib in addition to the acquired C797S mutation.[15,16] The EGFR-independent pathway (bypass pathway) is ascribed to the modification of other signaling molecules, such as MET amplification, MEK activation, ALK activation, FGFR amplification, HER2 amplification, AKT activation, BRAF activation, and AXL activation.[17,18] The tertiary undruggable C797S mutation in the EGFR kinase domain, which causes more than 20% of the incidence rate in clinical results, is the most difficult to deal with of all these potential mechanisms.[19−21] The focus of this review is to provide an exhaustive overview of Osimertinib resistance mechanisms and use the available information to develop potential strategies to overcome the associated resistance problem.

2. EGFR-MEDIATED SIGNALING PATHWAYS IN NSCLC

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

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Fabrication of polyethyleneimine surface-functionalized fluorescent carbon dots and its applications towards highly sensitive and selective detection of glutathione in aqueous medium and in vitro cell imaging of HeLa cells

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ABSTRACT

The present study aimed to synthesize polyethyleneimine (PEI) surface-functionalized fluorescent carbon dots (CDs)-based biosensor (GP-PEI-CDs) for highly sensitive and selective detection of glutathione (GSH). In brief, green pea (GP) shells were utilized for green synthesis of blue luminescent GP-CDs through hydrothermal method. The obtained GP-CDs were surface functionalized with PEI to improve surface defects and quantum confinement effects. The surface functionalization of GP-PEI-CDs was confirmed by different spectroscopic techniques, including FTIR, XPS, etc. Switch "on" of GP-PEI-CDs was quenched by Cu(II) ions (turn "off"), and the limit of detection (LOD) of Cu(II) was found to be 23 nM along with a linearity range as 0 μM to 50 μM. Then, turn "On" process enabled the restoration in fluorescence of surface-functionalized GP-PEI-CDs when different concentrations of GSH in phosphate buffer saline (PBS, pH 7.4) was added. This could be due to split up of Cu(II) from Cu(II)@GP-PEI-CDs complex by presenting selective affinity with thiol (–SH) group of GSH among the various biomolecules. The LOD of GSH was found to be 38 nM and linearity in the range of 0 to 25 μM. The cytotoxicity study confirmed the biocompatibility of surface-functionalized GP-PEI-CDs. Furthermore, a confocal analysis indicated exceptional penetrations of GP-PEI-CDs into the cell cytoplasm and nucleus, demonstrating the created probe's suitability for GSH sensing at the cellular level. The method was successfully applied to determine GSH in in human serum sample.

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

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Abstract

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

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

1. Introduction

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

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

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ABSTRACT

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

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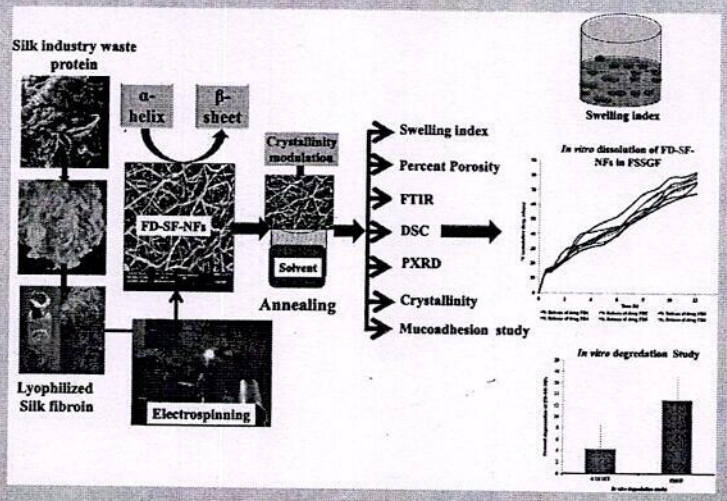
Silk fibroin; electrospun nanofibers; crystallinity modulation; felodipine; floating drug delivery; controlled release

GRAPHICAL ABSTRACT



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

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REVIEW

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

Sopan N. Nangare[1] · Sayali R. Patil[1] · Ashwini G. Patil[2] · Zamir G. Khan[1] · Prashant K. Deshmukh[3] · Rahul S. Tade[1] · Mahendra R. Mahajan[1] · Sanjaykumar B. Bari[1] · Pravin O. Patil[1]

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Abstract

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

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

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Design and synthesis of poly-L-lysine-functionalized graphene quantum dots sensor for specific detection of cysteine and homocysteine

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HIGHLIGHTS

- Waste material (pistachio shells) used for synthesis of graphene quantum dots (GQDs).
- Novel poly-L-lysine (PLL) surface functionalized GQDs (PLL-GQDs) based sensor was developed.
- The fabricated probe (PLL-GQDs) exhibited low cytotoxicity and excellent biocompatibility.
- The probe demonstrated highly sensitive and selective detection of cysteine (cys) and homocysteine (hcys) in real samples.

ARTICLE INFO

Keywords:
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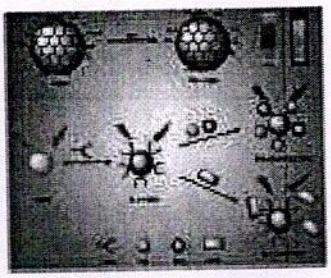
Poly-lysine
Functionalized graphene quantum dots
Cysteine and homocysteine
Sensing
Fluorescent probe

GRAPHICAL ABSTRACT



ABSTRACT

In this paper, a novel poly-L-lysine (PLL) surface functionalized graphene quantum dots (GQDs) based sensor was developed for detection of cysteine (cys) and homo cysteine (hcys). A fluorescent probe (PLL-GQDs) was then fabricated by surface functionalizing GQDs with PLL, a biodegradable polycationic electrolyte to improve the sensitivity and selectivity towards cys and hcys. The detection was based on the specific binding of cys and hcys to PLL at the PLL-GQDs surfaces, which enabled dynamic quenching via electrostatic and hydrophobic interactions. This fluorescent probe provided good linearity for the tested biothiols, ranging from 0 to 150 nM for cys, from 0 to 100 nM for hcys, with limit of detections (LODs) of 2.38 and 1.94 nM, respectively in BPS (pH 7.4). Interestingly, fabricated probe was also able to display a significant selectivity towards cys and hcys against known interfering molecules. The cytotoxicity study confirmed the biocompatibility of PLL-GQDs, enabling its future scope for cell adhesion and other biomedical applications. Besides, confocal study revealed the excellent penetrations of PLL-GQDs into cell cytoplasm and nucleus that validate the practical application of developed probe to detect cys and hcys at cellular level. The method was successfully applied for detection of cys and hcys in human serum sample. We expect the design concept presented here would be broadly used for selective and sensitive estimation of cys and hcys.

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REVIEW ARTICLE

Graphene quantum dots (GQDs) nanoarchitectonics for theranostic application in lung cancer

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ABSTRACT

Lung cancer (LC) is heading up as a substantial cause of mortality worldwide. Despite enormous progress in cancer management, LC remains a crucial problem for oncologists due to the lack of early diagnosis and precise treatment. In this context, numerous early diagnosis and treatment approaches for LC at the cellular level have been developed using advanced nanomaterials in the last decades. Amongst this, graphene quantum dots (GQDs) as a novel fluorescent material overwhelmed the horizons of materials science and biomedical fields due to their multifunctional attributes. Considering the complex nature of LC, emerging diagnostic and therapeutic (Theranostics) strategies using GQDs proved to be an effective way for the current practice in LC. In this line, we have abridged various approaches used in the LC theranostics using GQDs and its surface-engineered motif. The admirable photophysical attributes of GQDs realised in photolytic therapy (PLT), hyperthermia therapy (HTT), and drug delivery have been discussed. Furthermore, we have engrossed the impasse and its effects on the use of GQDs in cancer treatments from cellular level (*in vivo-in vitro*) to clinical. Inclusively, this review will be an embodiment for the scientific fraternity to design and magnify their view for the theranostic application of GQDs in LC treatment.

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KEYWORDS
Lung cancer; graphene quantum dots; theranostics; photolytic/hyperthermia therapy; drug delivery

Introduction

Global cancer risk is elevating gradually and results in a greater mortality rate per year. As per the fresh report of GLOBOCAN 2020, about 19.3 million cases and nearly 10.0 million deaths by cancer were recorded in 2020. Epidemiologists suggested that there would be probable 28.4 million new cases of cancer to befall nearly in 2040. Amongst all cancers, lung cancer (LC) has positioned on second diagnostic occurrence followed by breast cancer (11.7%) and crossed about 11.4% mortality rate, led by 1.8 million deaths (18%) in 2018 [1]. Besides, LC mortality is probable to reach 2.45 million globally by 2030. Principally, LC is a complex form of (adenocarcinoma) which increasing worldwide as an utmost cause of mortality. Generally, adenocarcinoma is known as the cancer of glandular mucus-producing cells (especially lungs). As per literature, LC is classified into four types: invasive adenocarcinoma (IA), adenocarcinoma in-situ (AIS), and minimally invasive adenocarcinoma (MIA) and other variants (e.g. lipidic) (Figure 1(A)). Besides this, the World Health Organisation (WHO) gives a sub-classification of lung adenocarcinomas as per their cellular origin. It includes acinar cells, papillary cells, bronchoalveolar, and mucus-secreting [2]. Literature survey advocated that there is a scarcity in our current knowledge of cancer statistics due to changing epidemiological trends of LC amongst developing countries [3]. In this context, it is observed that there is a vital role of the Human Development Index (HDI) in cancer mortality and morbidity in several countries. Both developed and developing countries experiencing an evident rise in the augmented effects of cancer risk factors. Moreover, there is an alarming rise in LC incidents in non-smokers as well. Notably, some major risk factors associated with the LC are smoking, exposure to second-hand smoke, previous radiation therapy, exposure to radon gas, exposure to asbestos and other carcinogens, and hereditary history of LC. Besides, the world is evidenced by the residual burden of different respiratory infections associated with LC. For example, Coronavirus disease 2019 (COVID-19), its emergence in 2020, and recurrence in 2021 have been overwhelmed the global healthcare systems. At this juncture, COVID-19 is becoming a major risk factor for LC patient's treatment. However, an extensive survey regarding the precise impact of COVID-19 associated with a patient suffering from LC is not available to date [4,5].

Current diagnostics and management strategies for LC

Despite the significant development in cancer therapeutics, several risk factors escalating in front of the developed and developing nations. Recently, Sung et al. reviewed the global cancer prevalence, which suggested the frequent diagnostic appearance as well as morbidity of LC up to 2020 which raised significantly after 2018 (Figure 1(B)) [1,6].

The traditional methods including X-ray, magnetic resonance imaging (MRI), Computed tomography (CT), or positron-electron microscopy (PET) scanning are commonly used for the diagnosis of cancer. Primary screening of LC by traditional methods is dependent on the severity and phases of LC. Unfortunately, the lack of site-specific localisation or inability to detect micrometer-sized tumours becomes inconclusive in the early detection of LC. Apart from this, sputum cytology, biopsy, and bronchoscopy methods are commonly used for the diagnosis of LC.

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nthesis, molecular modelling study of the methaqualone analogues anti-convulsant agent with improved cognition activity and inimized neurotoxicity

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ABSTRACT

In the current research, methaqualone derivatives were synthesized and assessed for their anti-convulsant activity. Among them, compounds **3, 4, 6, 7** and **11** exhibited significant anti-convulsant activities with ED_{50} values of 132.23 mg/kg, 120.34 mg/kg, 100.78 mg/kg, 145.89 mg/kg, and 148.46 mg/kg, respectively. The toxicity profiling (TD_{50}) of these compounds (**3, 4, 6, 7** and **11**) demonstrated that these drugs caused only a minor neurological impairment. The PI scores of these compounds (**3, 4, 6, 7** and **11**) were higher than the reference drug (methaqualone PI: 1.99). The acetylcholinesterase enzyme level is significantly reduced in these compounds, indicating the enhancement of cognition activity. Pharmacophoric modelling and molecular docking studies against the human GABA-A receptor are in close agreement with each other. Molecular dynamic simulation of compound **6** indicates that it remains stable with the human GABA-A receptor for a 100 ns time span.

ntroduction

Epilepsy is among the oldest medical disorders recorded in his- [1]. Despite the wide and expanding range of antiepileptic gs (AEDs) available for treatment, around 30% of epileptic pa- nts have suboptimal seizure control, and another 25% have seri- side effects [2]. Epilepsy is linked to a higher incidence of neu- sychological disorders, including emotional disturbance, cogni- deficits, and psychiatric disorders, all of which have a severe pact on quality of life [3–7]. Therefore, there is an immense e to develop new AEDs that are both effective and have a her safety profile. Methaqualone has a tumultuous past as both nedicinal and a recreational substance [8,9]. In the early 1960s, thaqualone was sold under the trade names Parest, Quaalude, onal, Somnafac, and Mandrax, as a non-barbiturate hypnotic h a broad safety margin and limited abuse potential [1]. In er years, methaqualone became one of the world's best-selling lative-hypnotic agents with other structural analogues (collectively known as "quaaludes") [1]. Although the clinical characteristics of methaqualone are quite typical for a sedative-hypnotic medication, some of its *in vivo* effects differ from those produced by conventional central nervous system (CNS) depressants. [10,11]. As compared to benzodiazepines and barbiturates, methaqualone, purportedly facilitates a rapid induction of a more natural deep sleep, resulting in less severe dizziness/dullness, and headaches in insomnia patients [10,11].

Several quinazoline derivatives have been identified and reported to stimulate GABA-A receptors [12]. The GABA-A receptor is an ionotropic ligand-gated ion channel receptor, and γ-aminobutyric acid (GABA) is an endogenous ligand that is the primary inhibitory neurotransmitter in the CNS. Upon activation, the GABA-A receptor primarily flows Cl^-*via* its pore, causing the neuron to hyperpolarize. This inhibits neurotransmission by inhibiting the action potential [13–15]. Many quinazolinones with structural similarities to methaqualone have been discovered and investigated for anti-convulsant action (Fig. 1) [12].A continuous issue faced with these compounds emanates from the fact that nearly every analogue evaluated in combined neurotoxicity and anti-convulsant testing revealed neurotoxicity values (TD_{50}) that were less than or only slightly higher than the effective doses

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Scientific paper

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

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Abstract

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

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

1. Introduction

Pharmaceutical experts have long struggled with the formulation and development of poorly water-soluble drugs, and these challenges are projected to worsen since more than 40% of new chemical entities discovered by drug discovery are poorly aqueous soluble.[1] Whereas, it is more problematic in the case of poorly soluble drugs with poor absorption profile, and bioavailability because it is dissolution rate-limited and can be affected by patient fed or fasted state condition[2]. Traditional approaches including solubilization by surfactant, surfactant dispersion, micronization, use of the oily solution, permeation enhancers, which evolved too earlier, that address the challenges of formulation and have limited use.[2,3] The major milestone has been achieved in the development of poorly water-soluble drugs using various newer technology, but to date, there is no universal thumb approach applicable to all active pharmaceutical ingredients.[3] Consequently, a new approach has been progressively required to deal with formulation issues that are associated with the delivery of poorly soluble drugs, to enhance their therapeutic efficacy and maximize their pharmacodynamics therapy.[2]

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

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Article

Fabrication of Poly-L-lysine-Functionalized Graphene Quantum Dots for the Label-Free Fluorescent-Based Detection of Carcinoembryonic Antigen

Rahul Shankar Tade and Pravin Onkar Patil*

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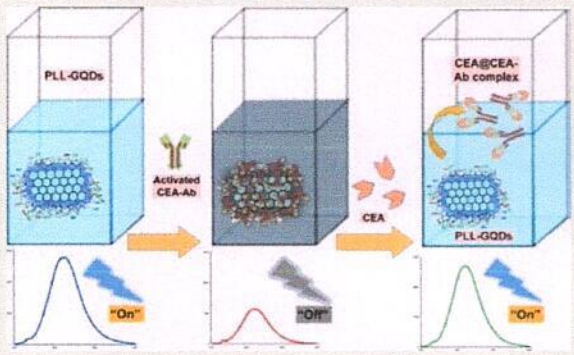
ABSTRACT: The diagnosis of tumor biomarkers is an attentive approach for the early detection and treatment of cancer. However, a cost-effective, simple, rapid, selective, and sensitive method is a basic prerequisite for diagnostic research. Herein, we present a novel fluorescence-based label-free sensing strategy for the sensitive and selective detection of carcinoembryonic antigen (CEA) using poly-L-lysine (PLL)-functionalized graphene quantum dots (GQDs). The GQDs were synthesized using a greener method by employing carbonized peanut shell (PNS) waste as a carbon source, and functionalization was accomplished using PLL (PLL-GQDs). The fluorescence stability of the PLL-GQDs was tested in a variety of solvent systems and pH solutions. When compared to nonfunctionalized GQDs (PNS-GQDs), prepared PLL-GQDs demonstrated increased fluorescence lifetime, high quantum yield, excellent photostability, biocompatibility, and greater cellular uptake. The PLL-GQDs with abundant surface amine and carboxylic groups showed selective interactions with an activated CEA antibody (CEA-Ab), resulting in the quenching of fluorescence signals. Because of the strong bioaffinity of CEA to the CEA-Ab, the antibody was unwrapped, resulting in the formation of an antibody−antigen complex and the recovery of fluorescence. As a result of this relationship, a turn "on−off−on" sensing mechanism with a strong response to CEA concentration (0.01 ng mL^{-1} to 100 μg mL^{-1}) and a detection limit of 1.19 pg mL^{-1} was demonstrated. Furthermore, the fabricated CEA immunosensor (CEA-Ab@PLL-GQDs) performed admirably in real sample analysis, with an average recovery of 98.32%. The cellular uptake performance of PLL-GQDs was also demonstrated in the A427 cell lines, exhibiting a greater cellular uptake potential than PNS-GQDs. The cellular bioimaging study demonstrates that PLL-GQDs can be used for additional therapeutic and biological applications.



KEYWORDS: *graphene quantum dots, poly-L-lysine functionalization, carcinoembryonic antigen, turn "on−off−on" sensing, bioimaging*

1. INTRODUCTION

Cancer is a major global health problem and is becoming a leading cause of death globally. In a recent report, GLOBOCAN with the International Agency for Research on Cancer has estimated the increasing burden of mortality and morbidity due to cancer.[1] Furthermore, low- and middle-income countries are disproportionately affected by the lack of early, accurate, and low-cost diagnosis services. As a result, the cure rate that can be achieved at an early stage lags behind, putting a strain on the society and, ultimately, to the country.[2,3] Concerning this, in recent years, the urge for an early detection and management strategy for cancer was implicated by the researchers.[4]

Researchers have developed many tumor biomarker-based bioanalytical strategies for the early detection of cancer in recent years. Tumor markers are biological molecules that have gained diagnostic utility in the early detection of various types of cancer. The assessment of cancer biomarkers plays a significant role not only in the early diagnosis of cancer but can also assist with tumor subtype, the extent of tumor spread, and response to ongoing therapy.[5,6] Carcinoembryonic antigen (CEA) is typically one of the tumor markers involved in the detection of many cancers, including colorectal cancer,[7] breast cancer,[8] malignant pleural effusion,[9] gastric carcinoma,[10] lung cancer,[11−14] and so forth. CEA is a glycoprotein that is found in cellular interactions. It is typically secreted between fetal growths but ceases production before birth. CEA is found in the blood of healthy people at about 0−2.5 ng mL^{-1} and at a

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COMPARATIVE PHYTOCHEMICAL INVESTIGATION ANTIOXIDANT AND ANTIMICROBIAL ACTIVITY OF LEAVES, BARK AND STEM EXTRACT OF *MUNTINGIA CALABURA*

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Abstract

Bioactive compound found in medicinal plants are used to treat a variety of human ailments and serve a vital part in healing. *Muntingia calabura* L. is a species of Muntingia. (*M. calabura*, Elaeocarpaceae) has long been utilized to treat a variety of pain-related issues. The goal of this study is to investigate at the phytochemicals, antioxidants, and antibacterial capabilities of *M. calabura* leaves, bark, and stem. By using the soxhletion method, the dried leaves, stem, and bark of *M. calabura* were successively extracted with n-hexane, ethyl acetate, and methanol solvents and the solvents from the extracts were evaporated under vacuum. The well-known test procedure was used to determine the qualitative analysis of various phytochemical elements as well as the quantitative analysis of total phenolic, flavonoids, and alkaloid content. The antioxidant activity of ethyl acetate and methanolic extracts of the leaves, bark, and stem was measured in vitro using the DPPH model. The presence of numerous phytoconstituents in each extract was discovered through preliminary phytochemical analysis. To determine antimicrobial activity, a well diffusion method was used to test an ethyl acetate extract of *M. calabura* (leaves, bark, and stem) against three different strains, and it showed considerable inhibitory action against all of them. The present study concluded that the all the three part (leaves, bark and stem) of *M. calabura* is a rich source of secondary phytoconstituents which impart significant antioxidant potential. The findings of the present study will be helpful to phytochemists, pharmacologists and pharmaceutical industries.

Keywords: Medicinal plants, *Muntingia calabura,* Phytochemical, Antioxidant activity, antimicrobial study.

INTRODUCTION

Currently, the focus of research has been placed on searching new natural antioxidants, in particular of plant origin, has steadily increased. Plants have been an inexhaustible source of medicines and recently, a lot emphasis has been made to find new therapeutic agents based on medicinal plants. Today, a folk favor to use medicinal plants rather than chemical drugs [1]. The antioxidants have high importance in terms of its reducing power of oxidative stress which is one of the causes that could damage biological molecules [2]. The species of *M. calabura* belong to the family Elaeocarpaceae, it is one of the Philippine medicinal plants and widely distributed throughout the world. *M. calabura* is commonly known as Jamaican Cherry tree and is also known as capulin or capuli in Latin America. In Southern Taiwan, *M. calabura* plant was cultivated in gardens and along the road side for edible and ornamental purposes. The various parts of the *M. calabura* plant have been documented for several medicinal uses. In traditional medicine, flowers can be used as an antiseptic and treat abdominal cramps. The leaf infusion can be drunk as tea like beverage. It can be used for the treatment of cold and headache.

The fruits are widely eaten by children as it is sweet and also cooked in tarts and made into jam.

The *M. calabura* have nutritional values, scientifically a number of flavonoids and phenolic compounds have been isolated from various part of the plant and structures were elucidated by spectroscopic analysis. 8- Hydroxy-7, 3, 4, 5- tetramethoxyflavone and 8, 4-dihydroxy-7, 3, 5-trimethoxyflavone were isolated from the stem bark and root and screened the cytotoxic activities against A549 and HT-29 cells respectively [4, 5]. The leaves of M. calabura have potential antibacterial activity [3], free radical

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Pharmacognostic Studies on *Anisomeles Heyneana* Benth. (Labiatae)

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ABSTRACT

Adulteration is considered to be the main cause for the production of inferior and sometimes unsafe and toxic drug. So correct identification and selection of crude drugs becomes utmost important to avoid further health complications. Out of the various techniques available, morphological and microscopic evaluation is found to be most suitable and promising for the plant drug authentication. The present work deals with the study of morphological and microscopical characteristics along with phytochemical, physicochemical and fluorescence analysis of leaf, petiole and stem of *Anisomeles heyneana* Benth. Along with morphological study, detail microscopical study gives more authenticity in the identification of medicinal plant. The microscopy of dorsiventral lamina of the leaf shows adaxial and abaxial epidermal cells, palisade and spongy parenchyma. The petiole consists of a central and two lateral vascular bundles. The stem of the herb is quadrangular with very narrow phloem and collenchymatous hypodermis. Microchemical tests of leaf revealed occurrence of phenolic compounds, lignin, starch, etc. Phytochemical analysis revealed occurrence of phytosterols, triterpenes, phenolic compounds, flavonoids, tannins, saponins, etc when studied using different extracts. Physicochemical evaluation of the herb was done using parameters such as extractive values, ash values, foreign matter, moisture content, water insoluble matter and volatile oil content. Variation in the fluorescence colour response was detected in fluorescence analysis using different solvents. This finding may be useful as identifiers of herb parts and serve as a guiding path for the development of official monograph and detailed standardization of *Anisomeles heyneana*.

Keywords: *Anisomeles heyneana*, Leaf, Petiole, Stem, Micrometry.

INTRODUCTION

Anisomeles Linn. R. Br. is thought to be important genera of family Lamiaceae, This genus comprises herbs or under-shrubs, scattered from Africa to India, South East Asia to North East Australia and east from China to Taiwan, Japan and Philippines. In India, Anisomeles genus is represented by three species viz. *A. indica*, *A. malabarica* and *A. heyneana*. *Anisomeles heyneana* commonly called as Western Hill Catmint in English or Gopali in Marathi. It's a tall, upright herb with slim stems and quadrangular branches that may reach 1 to 1.5 meters in height. Leaves are 5 to 12 cm long, ovate lance-like, and oppositely oriented. Flowers are tiny, white with pink tinges, and 2-lipped, and appear in lengthy cymes in October-November. The flowers resemble cow's earlobes [1]. Till date *A. indica* and *A. malabarica* have been investigated for various pharmacognostical and pharmacological studies. These species and essential oil obtained from them was already explored for their antibacterial activity [2,3]. With this, these two herbs are also investigated for the presence of various fatty acids from their fixed oil [4]. Whereas, *A. heyneana* has been investigated for the presence of various phyllocladane diterpenes and evaluated for inhibition of *Mycobacterium tuberculosis* [5]. The pharmacognostical study (morphological and microscopical) of *A. heyneana* is not done yet so far. The rationale made here to row up the most valuable medicinal plant *A. heyneana* like *A. indica* and *A. malabarica*. So that this species undertaken to study and make it familiar throughout the world in view of at least morphological, microscopic, phytochemical, physicochemical and fluorescence analysis. The objective of the present investigation is to figure out an overall pharmacognostic assessment of the *A. heyneana*.