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Biosynthesized MgONPs using *Syzygium cumini* seed extract: Characterization, *In vitro* anti-oxidant and anti-microbial activity

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ABSTRACT

The present study investigates *S. cumini* seed extracts which are considered as a promising and valuable source of bioactive compounds were prepared using different solvents such as methanol, ethanol, petroleum ether, acetone, chloroform, and diethyl ether. Among these solvents, methanol exhibited the highest extraction with a yield of 42 %. HPLC analysis revealed the highest concentration of quercetin flavonoids (49.62 mg/gm) in the methanolic *S. cumini* seed extract. Thus, the current work deals with the MgONPs synthesis through a biological approach using different *S. cumini* seed extracts. *In vitro* anti-oxidant properties were evaluated, which showed an IC_{50} value of 22.46 µg/mL for MgONPs synthesized from methanolic extract, surpassing the anti-oxidant potency of ascorbic acid by threefold. By leveraging the rich repository of bioactive compounds found within *S. cumini* seed extract, this study presents a novel approach to MgONPs synthesis. Exploring the symbiotic relationship between *S. cumini* seed extract and MgONPs, this research elucidates the pivotal role of bioactive compounds in guiding the formation and properties of nanostructures. Further anti-microbial studies on MgONPs from methanolic *S. cumini* seed extract were conducted against four different bacterial strains (*Escherichia coli, Bacillus subtilis, Staphylococcus aureus,* and *S. typhimurium*), revealing potent anti-microbial activity with 5.3 mm of inhibition for 100 µl against *S. typhimurium*. These findings suggest that *S. cumini* is a source of bioactive compounds responsible for the successful synthesis of MgONPs. Characterization studies of MgONPs were also carried out using UV–vis spectroscopy, FTIR, SEM, XRD, DSC and HPLC.

1. Introduction

Nanoparticles have been widely used in the field of anti-microbial treatment for their properties [1,2,]. The spatial properties have allowed them to exert physiological effects on living organisms [3]. Magnesium Oxide (MgO) stands out as a fundamental metal oxide with appealing traits, catching significant interest due to its stability across different processing conditions and its reputation as a safe substance for both humans and animals [4]. Among the different metal oxides, MgO is a functional semiconductor with numerous uses in optoelectronics, cell signaling, drug administration, and imaging, particularly as an effective, potent anti-bacterial and anti-oxidant agent combating the most dangerous antibiotic-resistant diseases [5]. Magnesium oxide nanoparticles (MgONPs) synthesized from *Syzygium cumini (S. cumini)* showed potential microbial inhibition against *Escherichia coli, Streptococcus pneumonia, Staphylococcus aureus,* and *Salmonella typhimurium* [6]. In recent years, there has been a growing interest in exploring the synthesis of nanoparticles using natural sources as reducing and stabilizing agents due to their eco-friendly nature and biocompatibility [7,8]. MgONPs have emerged as a versatile nanomaterial with diverse applications in biomedicine, catalysis, and environmental remediation [9]. The synthesis of MgONPs from plant extracts offers several advantages, including cost-effectiveness, scalability, and the potential to harness the inherent bioactivity of plant-derived compounds [10].

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Narrative Review

Role of probiotics in the management of cervical cancer: An update

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SUMMARY

Studies have extensively investigated a variety of health benefits associated with probiotic supplements, which often contain live microorganisms. The effect of probiotic supplements on cancer prevention and on chemotherapy effectiveness and toxicity are major areas that researchers have focused on. Recently, several researchers have concentrated on assessing the efficacy of probiotics in the treatment of cervical cancer, a leading malignancy in gynecology worldwide, especially in developing countries. To date, numerous clinical studies have demonstrated the efficacy of probiotics in preventing cervical cancer, but their dosages, bacterial strains, and duration of therapy are somewhat inconsistent. In this review, we have systematically updated the role of probiotics in cervical cancer management.

1. Introduction

Cervical cancer is one of the most common cancers affecting women's health worldwide, with a comparatively rare occurrence in developed countries, but about 80% of cases occur in developing or less developed countries [1]. It is usually asymptomatic during the early stages, but subsequent signs include discomfort during sexual intercourse, pelvic pain, irregular vaginal bleeding, tiredness, leg swelling, etc. [2]. Moreover, cervical cancer is considered the fourth most prevalent malignancy among women worldwide; most incidences occur between the ages of 35 and 44 during midlife, with the average diagnostic age being 50 [3]. Persistent infections of human papillomavirus (HPVs), which are the driving force behind global cervical cancers, are attributed in almost all instances [4] and other risk factors include chewing tobacco and multiple sexual partners [5].

HPVs are incredibly complex oncogenic viruses that comprise more than 200 genotypes which are known to infect humans and animals. They are small, non-enveloped DNA viruses that are normal in nature and form a wide family of viruses that are both benign and highly carcinogenic [6]. Based on their variations in pathogenicity, HPV types can be broadly divided into high- and low-risk categories [7]. Benign lesions such as lower-grade squamous intraepithelial lesions (LSIL) and genital warts are caused by low-risk types such as HPV6, HPV11, and HPV30, while high-risk types such as HPV16, HPV18, and HPV58 predominantly cause higher-grade squamous intraepithelial lesions (HSIL) that lead to cervical cancer [7,8]. In the cervix, by minor abrasions in the tissue, initial infection is thought to occur in the epithelial basal cells [9]. Once HPV has reached the target cells, it can remain latent in the genome-integrated nucleus or follow replication, terminating the synthesis and release from the superficial cells of infective viral particles [10].

HPV infections elicit immune responses, which clear most HPV viruses. Persistent infections greatly increase the risk for carcinogenesis. Understanding the mechanisms of HPV-caused cancer could be helpful for the prevention and treatment of the disease [11]. As key care strategies for cervical cancer, chemotherapy, radiotherapy, and surgery have been considered. These therapies, however, have been shown to increase toxicity and side effects, which can have a detrimental impact on the lives of women with this cancer [12,13]. While most HPV infections can be eradicated by the immune system, only a small percentage of women's immune systems fail to clear the infected HPV, causing malignancy of the

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SHORT COMMUNICATION

The Influence of Probiotics in Reducing Cisplatin-Induced Toxicity in Zebrafish (*Danio rerio*)

Kusuma Kandati[1,2] · Ankireddy Seshadri Reddy[1] · John Sushma Nannepaga[2] · Buddolla Viswanath[1]

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Abstract

In this work, the effects of probiotic supplementation on cisplatin toxicity in zebrafish (*Danio rerio*) were examined. For this study, adult female zebrafish were given cisplatin (G2), the probiotic, *Bacillus megaterium* (G3), and cisplatin+*B. megaterium* (G4) for 30 days, in addition to the control (G1). In order to investigate changes in antioxidative enzymes, ROS production, and histological changes after treatment, the intestines and ovaries were excised. The levels of lipid peroxidation, glutathione peroxidase, glutathione reductase, catalase, and superoxide dismutase were found to be significantly higher in the cisplatin group than in the control group in both the intestine and the ovaries. Administration of the probiotic and cisplatin effectively reversed this damage. Histopathological analyses showed that the cisplatin group had much more damage than the control group and that probiotic+cisplatin treatment significantly cured these damages. It opens the door to probiotics being combined with cancer-related drugs, which may be a more efficient approach for minimizing side effects. The underlying molecular mechanisms of probiotics must be further investigated.

Introduction

The burden of cancer is substantial and is increasing globally. Cisplatin, an antineoplastic drug, is the only one that the FDA has approved for the treatment of advanced cancers. This drug is well-known for its usage in the treatment of many solid tumours as well as various forms of cancer. It exerts anticancer activity through a variety of mechanisms, but its preferred mechanism includes the generation of DNA lesions through interacting with purine bases on DNA, blocking the production of DNA, mRNA, and proteins, arresting DNA replication, followed by the activation of numerous signal transduction pathways that ultimately result in the death of cancer cells [1]. Cisplatin is utilized in the treatment of cancer despite its inherent issues with side effects and drug resistance, which include major kidney difficulties, allergic responses, poor immunity to infections, gastrointestinal problems, haemorrhaging, and hearing loss, particularly in younger patients [2]. Three key pathways can lead to the development of drug resistance: greater DNA repair by the cell of platinum-induced damage, lower drug absorption into cancer cells, and enhanced drug degradation and deactivation before it reaches nuclear DNA. The primary lethal mechanism of cisplatin in proliferating (cancer) cells is DNA binding; nephrotoxicity and ototoxicity appear to be caused by hazardous levels of ROS and protein dysregulation in multiple cellular compartments [3]. The therapeutic limitations of cisplatin have led to the development of numerous cisplatin analogs. Only two, oxaliplatin and carboplatin, have received unanimity of opinion. But compared to cisplatin, the majority of platinum compounds don't seem to offer much of a benefit. Although soft nucleophiles like glutathione and other proteins and peptides containing cysteine or methionine sulphur residues are easily bound by platinum-based drugs, nuclear DNA is their primary target [4, 5]. Although the precise mechanism of cisplatin's cytotoxicity is unknown, it mainly causes toxicity by increasing the generation of ROS, decreasing endogenous antioxidant defences, and promoting inflammation [6].

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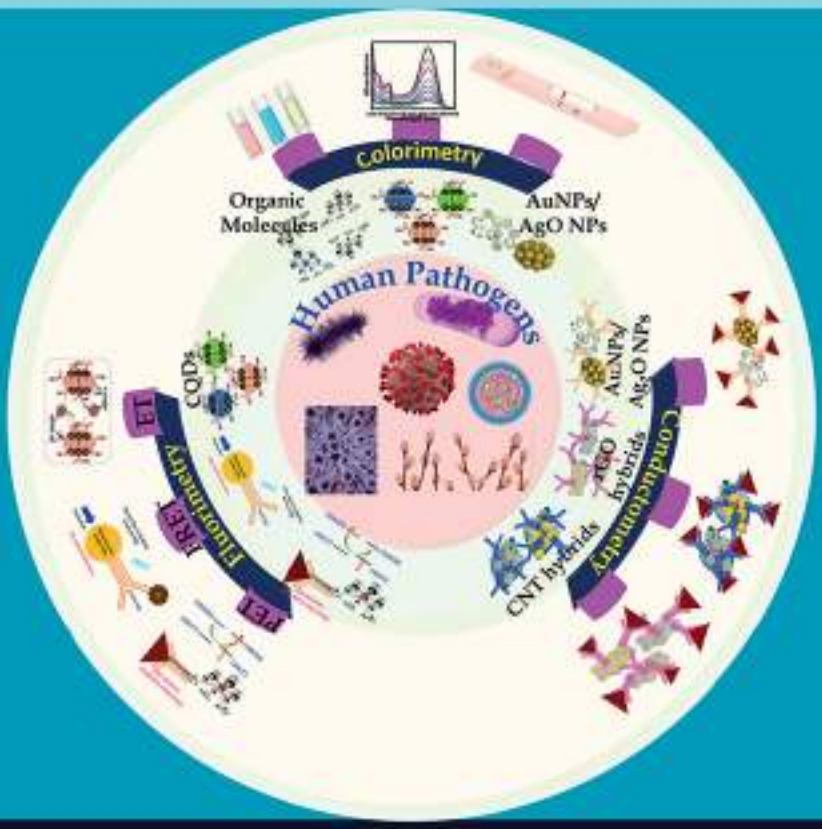
Developments in Applied Microbiology and Biotechnology



Recent Developments in Nanomaterial-based Sensing of Human Pathogens

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Role of molecular biomarkers in the diagnosis of fungal diseases using nanomaterial-based sensing platforms

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Abbreviations

BAL	bronchoalveolar lavage fluid
BDG	(13)-d-glucan
CSF	cerebrospinal fluid
CV	cyclic voltammetry
EIS	electrochemical impedance spectroscopy
ELISA	enzyme-linked immunosorbent assay
GM	galactomannan
IFA	immunofluorescence assay
IoT	the Internet of Things
MgO	magnesium oxide
NiO_2	nickel oxide
PCR	polymerase chain reaction
QA	quality assurance
QC	quality control
RT-PCR	real-time polymerase chain reaction
SPCE	screen-printed carbon electrode
ZrO2	zirconium oxide

Introduction

The majority of fungi produce skin infections or esthetic diseases, whereas bacteria and viruses cause serious and potentially fatal diseases. As a result, no one was particularly

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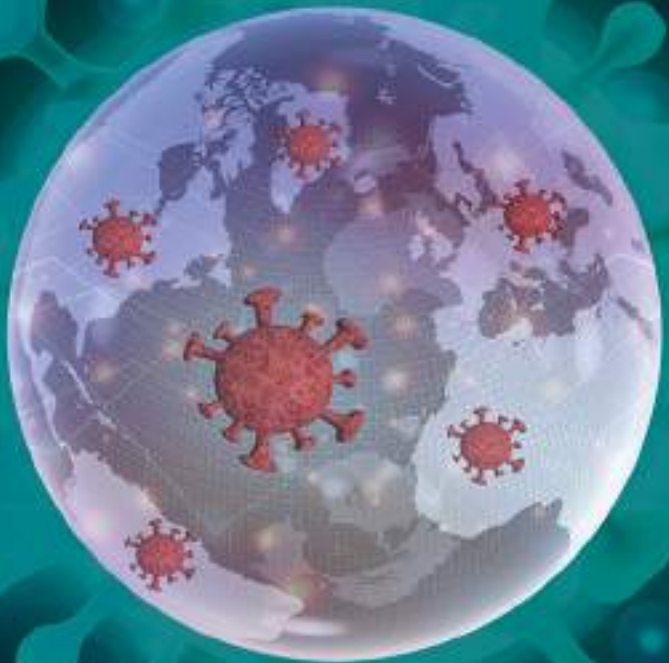
PANDEMIC OUTBREAKS IN THE 21st CENTURY

Epidemiology, Pathogenesis, Prevention, and Treatment



Chapter 1

Lessons learned from the first pandemic of the 21st century, global experience, recommendations, and future directions

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1.1 Introduction

Many infectious diseases have swept the world, taking the lives of millions of people. Viral outbreaks of varying frequencies and severities have caused panic and havoc across the globe throughout history [1]. The 21st century witnessed a few pathogenic and contagious virus outbreaks of zoonotic origin including severe acute respiratory syndrome coronavirus (SARS-CoV-1&2), Ebola virus, Middle East respiratory syndrome coronavirus (MERS-CoV), and Nipah virus [1]. SARS is an airborne virus and can spread through small droplets of saliva in a similar way to the cold and influenza. It was the first severe and readily transmissible new disease to emerge in the 21st century and showed a sustained human−human transmission along the routes of international air travel [2]. The 2003 outbreak of SARS shocked the world as it spread swiftly from continent to continent, resulting in >8000 infections, a total of 916 deaths globally with ~10% mortality and affecting local and regional economies [3]. In November 2002 the first case of SARS occurred in Foshan, China, and in June 2012, the first case of MERS died at a hospital in Jeddah, Saudi Arabia [4]. In November 2002 unusual cases of atypical pneumonia of unknown cause occurred in Foshan City, Guangdong province, in China, where many health care workers were infected [5]. Three laboratories—one each in Hong Kong, Germany, and the Centres for Disease Control and Prevention (CDCs) in Atlanta, Georgia, United States—nearly simultaneously isolated an apparently new coronavirus as the causative pathogen of SARS [3]. The infection was brought to Hong Kong on February 21, 2003, by a physician who had looked after similar cases of atypical pneumonia in the mainland China, leading to outbreaks in Hong Kong. On March 15, 2003, WHO officially declared an epidemic and labeled it as a SARS (later referred as SARS-CoV) [6−8]. The SARS-CoV epidemic quickly spread to 29 countries, but the global public health, medical, and scientific communities were not adequately prepared for the emergency. Chains of human-to-human transmission occurred in Toronto, Canada, Hong Kong Special Administrative Region of China, Chinese Taipei, Singapore, and Hanoi, Vietnam. The duration of the SARS epidemic was short and WHO declared the end of the SARS epidemic in July 2003 with a total of 8096 SARS cases and 774 deaths reported across 29 countries and regions [4]. The scientific effort demonstrated unusual international cooperation and was in turn facilitated by electronic communication. Media coverage provided accurate worldwide pictures to augment scientific data. As of March 1, 2004, there were 1695 citations related to SARS seen in the Medline [9]. One reason why SARS-CoV-2 spread is evidently much wider compared to SARS is the rapid urbanization and world trade network resulting in increased international travel during the last two decades. Hence, the control measures applied at the time of SARS-CoV-2 are no longer adequate in the current days, and more vigorous actions are required to control SARS-CoV-2 [10]. Besides, the duration in the infectious period between patients infected with SARS and those infected with SARS-CoV-2 is not the same. While in the former case, viral shedding peaks only when the patient's illness is advanced and respiratory symptoms appear [10], for SARS-CoV-2, the transmission can occur in the early phase of the illness, when the patients are completely asymptomatic [11]. Hence, isolation after the onset of symptoms might be ineffective in preventing virus transmission

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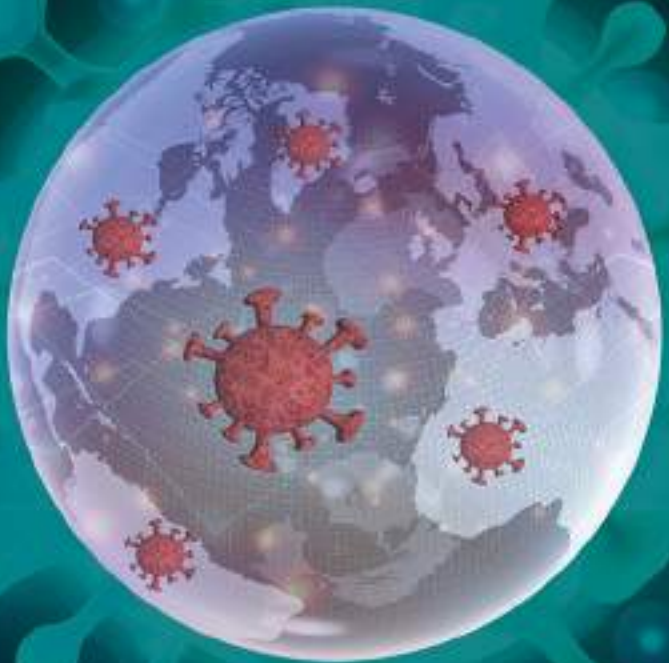
PANDEMIC OUTBREAKS IN THE 21st CENTURY

Epidemiology, Pathogenesis, Prevention, and Treatment



Chapter 7

Middle East respiratory syndrome: outbreak response priorities, treatment strategies, and clinical management approaches

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7.1 Introduction

Middle East respiratory syndrome (MERS) is a viral respiratory disease caused by a novel coronavirus (Middle East respiratory syndrome coronavirus, or MERS-CoV), which was initially discovered in Saudi Arabia in 2012 and it is one of six known human coronaviruses that cause respiratory disease in humans and, with a mortality rate >35% [1]. It is the first highly pathogenic human coronavirus to emerge since the global scare caused by the severe acute respiratory syndrome coronavirus in 2003 [2]. The first human MERS-CoV infection was found in Saudi Arabia, in June 2012 in a 60-year old man who developed renal failure [3]. Analysis revealed the disease is due to a novel virus which was named Middle East Respiratory Coronavirus [4]. The World Health Organization [5] has confirmed 2279 cases of human infections with MERS-CoV in 27 countries since 2012; 806 (35%) infected patients have died as of February 13, 2019 [6]. However, Saudi Arabia still has the highest reported MERS-CoV mortality rate where approximately 80% of the cases have been reported to occur there [7,8]. MERS-CoV remains a high-threat pathogen identified by WHO as a priority pathogen because it causes severe disease that has a high mortality rate, epidemic potential, and no medical countermeasures [9]. MERS-CoV belongs to the family *Coronaviridae*, order *Nidovirales*. It is one of the recently reported zoonotic viruses [10]. The family *Coronaviridae* is classified into four genera (α, β, γ, and δ). Each genus is divided into lineage subgroups. MERS-CoV belongs to lineage-C of the β coronaviruses [11]. Viral spread has been observed among healthcare workers and among individuals visiting MERS-CoV-positive patients. The control of some of these outbreaks has been achieved by the local center for disease control and prevention (CDC). Respiratory tract infections are the leading cause of mortality in resource-limited settings, accounting for more than 4 million deaths each year globally [12]. A hypothetical sequence of how humans and DCs (direct contact) lead to the spread of MERS cases is summarized in Fig. 7.1.

MERS-CoV infection may be implicated in transmission. As an emerging Betacoronavirus, Middle East respiratory syndrome coronavirus (MERS-CoV) causes illness characterized predominantly by mild-to-severe respiratory complaints, with most patients requiring admission to hospital because of pneumonitis or acute respiratory distress syndrome. Old age and the presence of comorbidities or immunosuppression seem to increase the risk of infection and are associated with severe forms of the disease [14].

Humans are thought to acquire MERS-CoV through contact with camels or camel products [15]. Despite the increase in the number of cases, the actual incidence of MERS-CoV among hospitalized patients with community-acquired pneumonia is low [16]. There are reports of the role of asymptomatic individuals in the transmission of MERS-CoV; however, the exact role is not known [16]. These observations indicate the need for understanding the human immune response to the virus to guide immunotherapy of severely ill patients and vaccine development and to

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