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Resveratrol, cancer and cancer stem cells: A review on past to future

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ABSTRACT

Cancer remains to be an unresolved medical challenge despite of tremendous advancement in basic science research and clinical medicine. One of the major limitations is due to the side effects of chemotherapy which remains to be palliative without offering any permanent cure for cancer. Cancer stem cells (CSCs) are the sub-population of cells in tumors that remain viable even after surgery, chemo- and radio-therapy that eventually responsible for tumor relapse. Hence, by eliminating non-stem cancer cells and cancer stem cells from the patient, permanent cure is expected. Phytochemicals have been under the intensive study to target these CSCs effectively and permanently as they do not cause any side effects. Resveratrol (RSV) is one such compound attaining lot of interest in recent days to target CSCs either alone or in combination. RSV has been used by several researchers to target cancer cells in a variety of disease models, however its CSC targeting abilities are under intensive study at present. This review is to summarize the effects of RSV under *in vitro* and *in vivo* conditions along with advantages and disadvantages of its uses against cancer cells and cancer stem cells. From the first reports on phytochemical applications against cancer and cancer stem cells in 1997 and 2002 respectively followed by later reports, up to date observations and developments are enlisted from PubMed in this comprehensive review. RSV is shown to be a potential compound having impact on altering the signal transduction pathways in cancer cells. However, the effects are variable under *in vitro* and *in vivo* conditions, and also with its use alone or in combination with other small molecules. Past research on RSV is emphasizing the importance of *in vivo* experimental models and clinical trials with different prospective combinations, is a hope for future promising treatment regimen.

1. Introduction

Resveratrol (RSV), is 3,4',5 – trihydroxy stilbene, a phytoalexin is widely distributed in variety of plants including red grapes, berries, peanuts, etc. Highest levels of RSV are found in Japanese knotweed (*Polygonum cuspidatum*) and muscadine grapes (*Vitis rotundifolia*) (Shrikanta et al., 2015). Though its occurrence is widely distributed about more than 70 plant species, its bioavailability is challenging upon its consumption (Gambini et al., 2015). Tome-Carneiro et al. (2013) have further shown, different levels of RSV concentrations are attributed for differential health impacts. Szekeres et al. (2010) in their review demonstrated that, due to the presence of three hydroxyl groups, it was known to act as a potent anti-oxidant by interfering with intracellular redox signaling. In many studies with different model organisms, RSV is shown to increase healthy life span mediated by SIRT1 (NAD-dependent deacetylase sirtuin-1) (Bhullar and Hubbard, 2015). RSV can reduce inflammatory stress through its effects on mitochondria. It activates a group of mitochondrial proteins of sirtuin family, particularly SIRT1. Lagouge et al. (2006) had shown that activation of sirtuin family protein can in turn related to the blood sugar stabilization in the body.

RSV effects on nitric oxide cycle were well known, through which it maintains the health of immune, nervous and vascular system. Nitric oxide in the body is synthesized by the enzyme Nitric Oxide Synthase (NOS) which has a critical role in inflammation. NOS can occur in

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Original Article

Aberrant signal transduction in Indian triple-negative breast cancer patients

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ABSTRACT

Aim of Study: The aim of this study is to correlate the prominin-1 or CD133 association with functional pathway markers of cancer stemness in Indian triple-negative breast cancer (TNBC) patient samples.

Materials and Methods: TNBC samples were confirmed for the absence of hormone receptors (estrogen receptor–ER/progesterone receptor) and human epidermal growth factor receptor-2 or proto-oncogene neu or erbB2 or CD340 by immunohistochemical analysis. Formalin-fixed paraffin-embedded samples of patients were used to collect the total RNA. Then, one-step reverse transcription-polymerase chain reaction (RT-PCR) was used to detect the cancer stemness-related transcript levels in the different samples. The RT-PCR products were analyzed semi-quantitatively on agarose gels. The band intensities of respective samples for different transcripts were analyzed by densitometry.

Results: TNBC-confirmed samples had shown increased levels of CD133 transcript than control tissues. Further, elevated CD133 transcripts are correlated with higher transcript levels of NOTCH1/FZD7/transforming growth factor-beta receptor Type III R/patched-1 pathway mediators.

Conclusions: This work has clearly indicated that there is a correlation between CD133 and functional pathways that control cancer stem cells in TNBC. These observations may indicate the possible association between cancer stemness and TNBC malignancy.

KEY WORDS: Cancer stem cells, FZD7, NOTCH1, patched-1, signal transduction, transforming growth factor-beta receptor Type III R, triple-negative breast cancer

INTRODUCTION

Breast cancers have been reported to be the second most common form of cancers among women with significant mortality in India and throughout the world.[1] Breast cancers exhibit significant heterogeneity with almost 21 distinct histological subtypes.[2] One of the classifications which is routinely used by clinicians that helps for planning effective treatment regimens is based on the presence or absence of hormone receptors (HR) (estrogen receptor-ER and progesterone receptor – PR) and human epidermal growth factor receptor-2 (HER2/neu).[3] The important molecular subtypes of breast cancer include luminal A ($HR^+/HER2^-$), luminal B ($HR^+/HER2+$), HER2-enriched ($HR^-/HER2+$), and triple-negative ($HR^-/HER2^-$) breast cancers (TNBCs).

Among all different subtypes, TNBC occurs at an incidence rate of about 31.9% in India.[4] TNBC incidence is reported to be more common in premenopausal women and those with BRCA1 gene mutation.[5] Other risk factors of TNBC incidence include obesity (35%), and women who had never given birth have 40% lower risk for the disease than those who had full-term pregnancy. Women with more than three children were reported to be at a high risk of getting TNBC.[6]

Existence and association of cancer stem cells (CSCs) has been evidenced in many cancers including leukemia and many other solid tumors.[7] The presence of CSCs is an ultimate reason for therapeutic resistance and tumor relapse. Thus, the CSCs will possess tremendous repopulation tendencies and can survive quiescently for extended periods.[8] CSCs will act as the tumor-initiating cells that can Self-renew by pluripotency and with immortality. This subpopulation of cells has shown to be responsible for cancer initiation, progression, metastasis,

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Synthesis, characterization, pharmacological evaluation and molecular docking studies of benzothiazole azo derivatives

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ABSTRACT

A series of novel benzothiazole based azo dyes were synthesized and fully characterized by using different analytical techniques. The antioxidant activity of synthesized azo dyes was studied with the DPPH, hydrogen peroxide, metal chelating and nitric oxide radical methods and compared with the known antioxidant ascorbic acid. Further, the anticancer properties of synthesized azo dyes were carried out against breast cancer (MCF-7) cell lines by MTT assay and results revealed that the synthesized compounds exhibited good anticancer property in micro-molar range. Additionally, the anti-inflammatory activities of target compounds were also investigated by protein denaturation method and were found to have effective anti-inflammatory property. In order to predict the binding modes and binding affinity of synthesized compounds, they were docked into the active sites of protein B-cell lymphoma-extra-large (Bcl-xL) to predict their anticancer property. The synthesized compounds were found to have good affinity for B-cell lymphoma-extra-large (Bcl-xL). A good correlation was found between in-silico docking analysis and in biological screening of all synthesized azo dyes with less binding energies and higher inhibition constants value against the target protein.

1. Introduction

When looking up early dyestuff industry, we saw the discovery of the principal dye chromogens employs various amines with benzene analogous [1]. In the last five decades of the dyestuff research trends have been focused on improved cost effectiveness and increased technical excellence in terms of brightness, high tinctorial strength and high fastness properties [2,3]. Therefore, in the earlier decades dyes were generally made by anthraquinone unit have excellent fastness properties. Although, the intrinsic disadvantages of antharaquinone dyes is having less tinctorial strength and production cost is higher [4]. Azo dyes are synthetic organic colorants bearing a chromophoric azo group (−N=N−). Commercially, these colorants are the largest and most versatile class of organic dyestuffs. The fine tuned taylor made properties of the azo dyes and their widest usage is due to the number of the variations in the chemical structures of starting materials and the methods of synthesis and their applications which are generally not complex [5,6]. Azo compounds, containing two phenyl rings separated by an azo (−N=N−) bond, are also versatile molecules and have received much attention in both fundamental and applied research areas. It is well known that these are used in many practical applications such as colouring fibers [7], photoelectronics [8], printing systems [9], optical storage technology [10], textile dyes [11] as well as in many biological reactions [12] and in analytical chemistry. Recently, heterocyclic azo dyes have attracted considerable interest and have played an important role in the development of the chemistry of dyes and dyeing process. Many of the heterocyclic azo dyes shows bathochromic shifts combined with brilliance of shade and high tinctorial strength compared with conventional anthraquionone dyes and aminobenzene azo dyes [13]. Among aryl hetero azo colorants, benzothiazole derivatives are relatively recent heterocyclic intermediates for the preparation of azo dyes because benzothiazole based azo dyes produce bright hues and are suitable for dyeing polyester, cotton, nylon fabrics etc.

Further, these classes of dyes have higher tinctorial strength and give relatively brighter hues than those derived from aniline-based diazo components and also provide a pronounced bathochromic

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Gestational and lactational exposition to di-*n*-butyl phthalate increases neurobehavioral perturbations in rats: A three generational comparative study

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ABSTRACT

Di-n-butyl phthalate (DBP) cause significant deficits in cognition and memory, however the neuroanatomical basis for impairments remain poorly understood. This study evaluates neurobehavioral changes in rats for three successive generations between non-siblings by administering DBP at 500mg/kg bw dose through oral gavage from gestation day-6 to 21 and lactation (3-weeks). Weaning period evaluations and developmental deficits assessed showed variations specific to generation and the toxic potential of DBP was confounded by behavioral deficits that include changes in sensorimotor development reflex response, poor performance, low memory retention and greater latency period. The cytoarchitectural alterations witnessed in hippocampus include condensed nuclei, vacuole formation and remarkable degeneration, shrinkage of pyramidal neurons in CA1 and CA3 regions; disorganized hilar cells and hyperplasia in dentate gyrus. Comparatively, the enlisted changes were high in subsequent generations than preceding and correlates assessed between cognitive impairment(s) and endocrine function confirm a link indicating vulnerability of immature animals as target to disrupt neural and endocrine functions.

1. Introduction

Di-*n*-butyl phthalate (DBP) is a ubiquitous environmental contaminant and widely used plasticizer, it is an additive to adhesives or printing inks [1]. Recent findings of De Toni et al. [2] reported the presence of phthalates as well as quantified phthalates namely, DEHP, DEP, DBP in pre-packed coffee capsules. Katsikantami et al. [3] in their review article have reported the maternal exposure to phthalates are able to cross the placental barrier and cause many health issues in humans. Its exposure to food and other materials at higher levels potentially induce abnormal fetal development [4]. Case studies reported by Colón et al. [5] have indicated anomalies such as premature breast development in female subjects while reduced anogenital distance [6], hypospadias [6] and decreased serum testosterone observed in male rats [7]. Arbuckle et al. [8] studies linked adverse reproductive effects and attention deficit disorders upon bisphenol-A exposure. Di (2-ethylhexyl) phthalate exposure shown to cause neurodevelopmental and behavioral deficits in rats [9]. Age-related effects reported upon exposure to phthalates are twice as high in children as adults with 40 % of children (age two to six years) showing higher urinary concentrations of phthalate metabolites [10]. Findings of Chopra et al. [11] indicated attention deficit disorder and learning disabilities in children of six to fifteen years upon exposure to phthalates. We have previously reported *in utero* and lactational exposure of DBP for three generations brought neuroanatomical perturbations in discrete brain regions and the severity of the effect was higher in subsequent generations [12].

Limited data available on cognitive aspects suggest that higher levels of phthalates adversely affect learning abilities in mice [13] and few studies reported an association between prenatal phthalate exposure and neurological impairments [14], however, the available information on phthalates is biased and inconclusive, especially on aspects of cognitive behavior. The brain weight in rodents was affected by di-2-ethylhexyl phthalate (DEHP) exposure [15,16]; in contrast, Rhodes et al. [17] observed no difference in brain weight upon phthalate-exposure in marmoset monkeys, suggesting changes in brain weight restricted only to rodents, while limited information available on cognitive aspects suggest DBP's toxic potential to cause distinct neurodegenerative changes in the hippocampus of neonatal and immature rats [14]. McIntyre et al. [18] indicated acetylcholine (ACh)

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Effect of radiation and antioxidant diet on the efficacy of silk synthesis of the silkworm, *Bombyx Mori*

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Abstract

Bombyx mori is a beneficial and environment friendly insect reared commercially for silk. In today's scenario, the silk farming shows a great downfall due to the promotion of synthetic materials. Thereby it is necessary to upsurge the production of silk fibres. The efficacy of silk is achieved through the growth and development of silkworms at a higher rate through supplementing their feed with antioxidant from the plant sources. Later the same worms were exposed to low dose radiation from the gamma source. These are considered as experimental groups while the worms without the supplement of antioxidant and radiation exposure, control group. The adaptability of the insects in terms of growth and economic parameters viz., silk filament, cocoon weight, shell weight and pupal weight was recorded. The total proteins in hemolymph and silk gland were assessed.

The present study results indicated the increase in the efficacy of silk as well as economic traits in all the experimental groups compared to the control group. The assessed total proteins showed an increment in the silk gland and hemolymph was statistically significant. The larvae exposed to gamma radiation at low doses reflects hormesis that has exerted stimulatory and beneficial effects on the efficacy of silk production.

Keywords: Sericulture, Radiation, Antioxidants, Total proteins, Economic traits, Silk.

Introduction

Silkworms are oligophagous insects which feed on mulberry leaves, spin cocoons; later cocoons are used to extract silk fibers. The silk thread extracted from cocoons depends on the silkworm feed that is on the quality of mulberry leaves, the sole source of the nutrients[1] which is not adequate for optimal silk performance. The growth and development of silkworms should be improvised significantly to result in the good cocoon varieties thereby leading to increase the silk yield. As a result, healthy and good quality mulberry leaves along with supplemented nutrients is a dire need for high and quality cocoon production. The pertinent studies[2] have shown that the efficiency of silk can be augmented by increasing the nutrients in the silkworm's diet. Besides, Bhattacharyya et al[3] concluded that the novel method of rearing silkworms by feeding worms with good quality of mulberry leaves and the diet supplemented with the high amount of nutrients is a pre-requisite to increase the silk production. The supplemented diet through feeding may increase the growth and development of silkworms which has a critical role in increasing the efficiency of silk. Besides the environmental factors such as temperature, humidity, light, air, feed quality[4] are also of prime importance to produce quality silk.

Fernandes et al[5] studied the effect of different concentrations (5, 10, and 20%) of Bordeaux mixture included in the diet of the silkworm caterpillars improved the cocoon production and structural and mechanical properties of the silk[5]. Besides, studies of Muniandy et al[6] showed fortification of mulberry leaves with supplementation of nutrients and feeding silkworms, a useful modern protocol to increase the economic value of cocoon. Each cocoon can produce 1000 to 2000 feet of silk filament made up of fibroin (75% - 90%) and sericin (10-25%). Furthermore, investigations of Saad et al[7] indicated the red beet supplement upsurges the silk performance along with improved traits such as weight of mature larvae, silk gland, fresh cocoon, pupae and cocoon shell significantly.

Radiation exposure at high dose levels was considered highly hazardous while radiation at low levels indicated favourable effects reflected as radiation hormesis shows an adaptive response[8]. The growth of silkworms was promoted and even bodyweight showed an increase upon continuous exposure to low-dose radiation[9]. Keeping in view the importance of silk performance and understanding the role of small cottage industries to uplift the rural economy, we hypothesized, the efficacy of silk production can be increased by supplementing the feed of worms with antioxidants and the exposure of worms to low dose radiation that enhances the growth, development and metabolism of *B. mori.*

Material and Methods

Chemicals/Labware: All chemicals (AR-grade) with chemical abstracts service registry number (CASRN) were purchased from Sigma-Aldrich Ltd. Spectrophotometer, Cooling REMI centrifuge, Geiger Muller counter (GM counter), Caesium 137- radioactive source, Microscope, Weighing scale, Screw gauge and Vernier calipers, rearing stands and trays, nylon nets, rotary or bamboo mountages or chandrike were used while rearing silk worms.

Antioxidants from the plant source: Silk filament, the animal fiber is white to begin with, later dyed with the

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Hepatotoxic evaluation of Di-*n*-butyl phthalate in Wistar rats upon sub-chronic exposure: A multigenerational assessment

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ABSTRACT

The extensive use of di–*n*-butyl phthalate (DBP) as a plasticizer in medical devices, personal care products, and industries, which is a major threat to humankind as it leaches out easily from the plastic matrix into the environment. Health risks posed to adults and children from the broad usage of DBP in cosmetics and infant toys observed predominantly due to repeated and prolonged exposure. Hence, this study was undertaken to evaluate the potential effect of DBP in the hepatic tissue of rats up to three generations. Wistar rats were induced at a dose of 500 mg DBP /kg body weight dissolved in olive oil by oral gavage throughout gestation (GD 6–21), lactation and post-weaning and reared by crossing intoxicated rats up to three generations. Results of the present study showed a significant increase in the relative weight of liver, while decreased levels of antioxidant enzymes *viz.*, superoxide dismutase (SOD), catalase (CAT), glutathione peroxidase (GPx), and reduced glutathione (GSH) was evident in DBP treated rats at $P < 0.05$. Besides hepatic marker enzymes *viz.*, alanine transaminase (ALT) and aspartate transaminase (AST) were elevated significantly in experimental rats compared to those of the control group. Furthermore, histological studies revealed congested central veins and dilated sinusoids in F_1 progeny while mild to severe focal inflammatory infiltrations were evident in F_2 & F_3 rats. Negative correlation observed between the levels of antioxidant enzymes and transaminase activity. In brief, DBP exposure elicits oxidative stress and alters the transaminase activity levels causing damage in hepatic tissue. F_3 progeny found to high vulnerability to the exposure of DBP than F_2 & F_1 rats.

1. Introduction

Phthalate esters (PE) are synthetic organic molecules extensively used as plasticizers in consumer products and has become indispensable in the human routine lifestyle. They are utilised as additives in production of PVC products, cosmetics and perfume industries owing to their nature of flexibility, stabilizer [1], adhesiveness [2], fixative and denaturing property [3]. Phthalate esters are classified into high molecular weight (MW) phthalate esters with 7–13 carbon atoms [Diisodecyl phthalate (DIDP), diisononyl phthalate (DINP), di-2-propylheptyl phthalate (DPHP), diisoundecyl phthalate (DIUP) and diisotridecyl phthalate (DTDP)] and low molecular weight phthalate esters with 3–6 carbon atoms [di-*n*-butyl phthalate (DBP), diisobutyl phthalate (DIBP), butyl benzyl phthalate (BBP) and di-2-ethylhexyl phthalate (DEHP)] in their backbone. As the usage of plasticizers is on the rise and their non-degradability has led to their ubiquitous presence in the environment. This has caused humans' exposure of phthalates through air, water, food, and dermal contact leading to many health hazards [4–8]. Recent investigations by Bi et al. [9] detected the presence of phthalates *viz.*, DEHP, BBP, DBP, and DIBP in the dust of various indoor environment. Once phthalates gain entry into the body through air [4], water [5], and food [6], dermal contact [8], later transform into their corresponding metabolites rapidly and eliminate through urine and feces. However their presence is detected in body fluids namely plasma, amniotic fluid, breast's milk and urine of humans [10,11]. The latest investigations indicated that the frequent usage of cosmetics during and before pregnancy was linked with the detection of phthalate metabolites in the hair [12]. Furthermore, many studies have shown that phthalates interfere with the endocrine system by acting as anti-androgens or mimic hormone (estrogen and androgen) which bring alteration(s) in the normal functioning of the reproductive system [13–16]. Phthalates along with their metabolites have the potential to cause toxicity in the reproductive system. For instance, a decline in sperm count, incidence of cryptorchidism, and hypospadias have been reported [16,17].

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Review

Fusarium oxysporum f. sp. *lycopersici* causal agent of vascular wilt disease of tomato: Biology to diversity– A review

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ABSTRACT

Tomato (*Lycopersicon esculentum*) is one of the widely grown vegetables worldwide. *Fusarium oxysporum* f. sp. *lycopersici* (*FOL*) is the significant contributory pathogen of tomato vascular wilt. The initial symptoms of the disease appear in the lower leaves gradually, trail by wilting of the plants. It has been reported that *FOL* penetrates the tomato plant, colonizing and leaving the vascular tissue dark brown, and this discoloration extends to the apex, leading to the plants wilting, collapsing and dying. Therefore, it has been widely accepted that wilting caused by this fungus is the result of a combination of various physiological activities, including the accumulation of fungal mycelia in and around xylem, mycotoxin production, inactivation of host defense, and the production of tyloses; however, wilting symptoms are variable. Therefore, the selection of molecular markers may be a more effective means of screening tomato races. Several studies on the detection of *FOL* have been carried out and have suggested the potency of the technique for diagnosing *FOL*. This review focuses on biology and variability of *FOL*, understanding and presenting a holistic picture of the vascular wilt disease of tomato in relation to disease model, biology, virulence. We conclude that genomic and proteomic approachesare greater tools for identification of informative candidates involved in pathogenicity, which can be considered as one of the approaches in managing the disease.

Contents

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Chapter 3
Beneficial Effects of *Trichoderma* on Plant–Pathogen Interactions: Understanding Mechanisms Underlying Genes

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Abstract *Trichoderma* is a genus of asexually reproducing filamentous fungi found in various ecosystems. It is among the utmost prevalent fungal genera commercially obtainable as a plant growth-promoting fungi (PGPF) and biocontrol agent. The biocontrol actions of *Trichoderma* are centered on the stimulation of various mechanisms such as competition for nutrients and space, mycoparasitism, alteration of the ecological conditions, antibiosis, and plant defensive mechanisms. Therefore, these fungi are commercially used in biocontrol of plant pathogens substituting the synthetic pesticides. The beneficial organism's genes and/or its products contain metabolites that reduce the harmful effects of plant pathogens and promote progressive responses in the plant. Certain genes have significant roles in the biocontrol process and are known as the biocontrol genes. These genes signal the secretion of enzymes and proteins that damage the plant pathogens. Some *Trichoderma* genes are also helpful in the control of different plant pathogens. In addition, *Trichoderma* produces plant growth-promoting molecules that stimulate growth and development of the plant. Within the rhizosphere, the conversation and recognition of signaling molecules by *Trichoderma* and plants may alter the physiological and biochemical characteristics of the plants as well as the biocontrol agent. A detailed realization of the molecular mechanisms underlying biocontrol would benefit from developing

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Chapter 11
Opportunistic Avirulent Plant Symbionts *Trichoderma*: Exploring Its Potential Against Soilborne Phytopathogens

Narasimhamurthy Konappa, Soumya Krishnamurthy, Nirmaladevi Dhamodaran, Udayashankar C. Arakere, Srinivas Chowdappa, and Niranjana Siddapura Ramachandrappa

Abstract A major threat to agriculture is soilborne diseases which extensively decline the crop yield. Control of soilborne phytopathogens is challenging because these pathogens persist for numerous years as sclerotia in soil or in organic matter under numerous environmental conditions. Pathogen management with the application of chemical pesticides imposes environmental threats and is potentially dangerous to humans and other living forms. The employment of biological control agents for disease reduction and improved yield provides an alternative for the chemical pesticides and this is a key aspect of disease management of plant pathogens. Various control agents such as fungi and bacteria are involved in biocontrol activity among control agents, the fungal genus *Trichoderma* shows a major role in the control of phytopathogens. *Trichoderma* spp. are extensively applied as biocontrol agents for the management of soilborne phytopathogens in agriculture. The control effects of *Trichoderma* on soilborne pathogens are higher in comparison to synthetic fertilizers and they exhibit prolonged persistence in soil post application. The mechanisms of biocontrol exerted by *Trichoderma* are generally antibiosis, mycoparasitism, and competition for nutrients, induced defense responses, or systemic resistance responses in the plants. *Trichoderma* spp. are well known for the secretion of cell wall degrading enzymes (CWDEs) and these enzymes play key roles in the degradation of the cell wall of the pathogens and the biocontrol

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CHAPTER

11

Biotechnological approaches for the enhancement of anticancer secondary metabolite production from endophytic fungi

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11.1 Introduction

Cancer is an abnormal growth of cells that can occur in various organs of the body, leading to the loss of the normal regulatory mechanisms that control cell growth and multiplication. The spread of cancer in the body cannot be controlled, leading to an increase in the mortality rate. Cancer may affect people of all age groups, and its severity increases with age. According to an estimate by GLOBOCAN on cancer incidence and mortality, 18.1 million new cases and 9.6 million deaths due to cancer were reported in 2018 (Freddie et al., 2018). Therefore, a multidisciplinary approach is required to overcome a variety of settings in clinical oncology. Chemotherapy using natural products as drugs to selectively kill cancer cells or its use for antiproliferation is a boon to cancer treatment. Since the early success of these initial treatments, the additional development of anticancer drugs has been increasing (Demain and Vaishnav, 2011).

The development of anticancer drugs by pharmaceutical companies from plant extractions as well as synthesis will raise the cost of the drug on the market, and development becomes a highly complex problem. Nowadays, the lifestyle of the population and the increases in cancer incidence have led to cancer treatments with cytotoxic drugs (Sloan and Gelband, 2007). Even if more selective therapies are developed, treatment schemes will continue to be associated with classical cytotoxic agents. Consequently, an increase in the cost of development and the requirement of cancer drugs should be addressed by reducing the production cost using advanced techniques (Kummar et al., 2006).

Natural anticancer drugs such as Taxol, vincristine, vinblastine, camptothecin, and its derivatives were originally derived from plant sources. Several classes of microbial-originated chemicals and distinct metabolites have been reported with anticancer activities (Wu et al., 2016). Among them, the endophytic fungi alone are valuable sources of diverse metabolites with potential as anticancer drugs (Ashish et al., 2017). Endophytic fungi precisely mimic the plant host metabolites such as camptothecin, Taxol, vincristine, and vinblastine from the respective hosts. However, the yield of these potential anticancer compounds from the plants or their endophytes is not enough to meet the daily dosage requirements of cancer chemotherapy (Isah, 2016).

A detailed understanding of the various enzymes and the pathways of biosynthesis of anticancer compounds would aid in identifying the key steps and methods targeting improvements in metabolite production (Tamano, 2014). The use of potential endophytic fungi for large-scale fermentation and plant cell culture are two methods that overcome the pitfall of the direct extraction of anticancer lead molecules from their sources (Kumar et al., 2019). However, enhancing the production of existing anticancer compounds in bioreactor cultures may be accomplished by implementing various techniques individually or in combination that include strain improvement, optimizing the

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Understanding the photoluminescence behaviour in nano $CaZrO_3:Eu^{3+}$ pigments by Judd-Ofelt intensity parameters

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ABSTRACT

$CaZrO_3$ ceramic pigment exhibits high chemical, thermal and structural stability. However, its application as a host for various luminophores/activators has not been clearly explored. In the present investigation, $CaZrO_3$ doped with Eu^{3+}, as a potential orange-red phosphor has been demonstrated. $Ca_{1-x}ZrO_3:Eu_x$ (x = 0.01–0.09) nanophosphor is prepared here through a low temperature, one pot solution combustion synthesis approach using glycine as the fuel. X-ray diffraction results show that all the samples are stabilized in orthorhombic crystal structure without any impurity phases. Scanning electron microscopy (SEM), transmission electron microscopy (TEM) and high resolution TEM are carried out to determine the microstructure of the phosphor. The particles are found to be significantly agglomerated and in the nano-regime (~40 nm). The observed excitation spectrum suggests that $Ca_{1-x}EuZrO_3$ can be efficiently excited using ultra-violet (UV), near-UV and UV blue (UVB), making it immediately relevant for current solid state lighting technologies. In fact with every ~1 at% doping increase, the primary excitation line intensity increases by a factor of ~1.5; this provides a simple parameter to enhance the UV excitability of the phosphor. The color coordinates are deduced using the Commission International De Eclairage (CIE) co-ordinates (x, y = 0.58, 0.40). The critical distance of energy transfer in this system is determined to be ~10.7 Å, making multipole-multipole interactions as the plausible reason for concentration quenching beyond 7 mol.% Eu doping. The luminescence behaviour of the material is evaluated using Judd-Offelt (JO) intensity parameters. Judd-Ofelt (JO) intensity parameters (Ω_2 and Ω_4) are calculated for the sample $Ca_{1-x}ZrO_3:Eu_x$ (x = 0.01–0.09), in order to understand the local structure around the activator. Irrespective of the concentration of Eu^{3+}, Ω_2 is found to be greater than Ω_4, indicating asymmetric environment around the activator. Furthermore, with increase in Eu^{3+}, Ω_2 increases suggesting an increase in covalency of Eu-O bonds with significant effect of host crystal field on Eu^{3+}.

1. Introduction

In the past decade, owing to emergence of sustainability oriented moves, and increasing awareness of need for energy efficient lighting, research and development of white light-emitting diodes (WLEDs) have gained significant interest. This is due to the relatively high luminous efficiency, concomitant low power consumption and reliability of WLEDs [1–3]. The most common method for building WLEDs is using phosphors that act as light transducers to convert near ultraviolet (NUV) or blue light into usable white light [4]. Among the many LEDs, one of the typical and most widely used WLEDs is fabricated using a combination of blue light emitting GaN chip and a yellow phosphor $Y_3Al_5O_{12}:Ce^{3+}$ (YAG). However, this phosphor suffers from high correlated color temperature (CCT > 6000 K) and low color rendering index (Ra < 80) [5]. This is due to the fact that YAG lacks high efficiency red-emitting component. This limits the choice of YAG for wide

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ORIGINAL ARTICLE

Green Synthesized Luminescent Carbon Nanodots for the Sensing Application of Fe^{3+} Ions

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Abstract
A single step hydrothermal mode of carbon nanodots (C-dots) synthesis from house-hold kitchen garbage such as snake gourd peel extract was successfully carried out. Characterisation of green synthesized C-dots were accomplished using UV-Visible and FTIR spectroscopy, Spectrofluorimetry and HRTEM. C-dots exhibited an appreciable quantum yield of 28.6%. Excitation-dependent photoluminescence emission properties and pH-sensitivity of C-dots were also studied in detail. C-dots exhibited strikingly selective detection of Fe^{3+} ions via fluorescence quenching mechanism. Linearity was obtained in a concentration range of 10–100 μM with detection limit of 0.398 μM in accordance with the Stern-Volmer relation. The existence of oxygen containing functional moieties in luminescent C-dots could be attributed to the effectual complexation between the metal ion and C-dots. The selective sensing property of C-dots towards Fe^{3+} ions provide avenue for biochemical analysis related to iron metabolism and diagnosis of anaemia.

Keywords C-dots · Green synthesis · Fluorescence · Fe^{3+} sensing · Sensors

Introduction

Fluorescent carbon nanoparticles otherwise termed as carbon dots (C-dots) are the latter most addition to the nanocarbon family with unique optical and chemical properties. Excellent biocompatibility, fluorescence properties, water solubility, chemical inertness and thermal stability justifies the outstanding appreciation grabbed by these interesting nanoparticles [1–4]. Carbon dots found tremendous applications in the field of bioimaging, bio- and chemo-sensing, photocatalysis, biolabelling etc. within a short time span since it is primarily reported [5–8].

Considering the current environmental scenario, development of green synthetic strategies is highly recommended. Abundant availability of natural sources allow the synthesis-design of carbon dots by ensuring environmental safety [9, 10]. Also the synthesis of carbon dots carried out in non-toxic solvents adhere strictly to green chemistry principles [11]. It is advantageous that the properties can be effectively controlled by altering carbon sources. Though different modes of synthesis are available, hydrothermal method is considered highly efficient owing to the possibility of introducing surface functional groups such as carboxylic, hydroxyl or amino groups. This method aids in conjugating C-dots with some target moieties of biological/environmental relevance. Synthesis of carbon dots from orange juice [12], sugarcane juice [13], watermelon peel [14], papaya [15], banana juice [16], apple juice [17], peanut [18], honey [19] etc. have been reported previously.

Ferric ion (Fe^{3+}) is one among the most indispensable metal ion which is abundantly available in the environment. These ions play significant role in maintaining many biological processes. Any change in the optimal level of ferric ions may disturb cellular process balance and can lead to several diseases like Alzheimer's disease, Parkinson's disease, heart failure, inflammation, hemochromatosis etc. [19, 20]. Hence sensitive and selective detection of Fe^{3+} ions are of considerable significance in biological applications.

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Original research article

Facile self-propagating combustion synthesis of MgO: Eu_{3+} orange-red nanophosphor and luminescence investigation by Judd-Ofelt intensity parameters

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ABSTRACT

In the present work we demonstrate the potential of one pot combustion derived Eu_{3+} doped nano MgO as efficient orange-red luminescent host. Surface morphology and size of the particles are characterized by scanning and transmission electron microscopic techniques. Optimization of the luminescence output is carried out by varying the dopant (Eu^{3+}) concentration of $Mg_{1-x}O:xSm^{3+}$ ($0.01 < x < 0.09$). Upon excitation at 395 nm the emission spectra of the phosphor show sharp peaks at 542, 577, 594, 653 and 690 nm corresponding to f-f transitions of rare earth dopant. The optimal Eu_{3+} content was found to be x = 0.05 at which MgO:xEu_{3+} show enhanced sharp or-ange red emission. Beyond x = 0.05 concentration, quenching was observed and critical distance calculations revealed the mechanism of quenching to be electric multipole-multipole interactions. Judd-Ofelt intensity parameters were calculated in order to evaluate the influence of the host lat-tice on the emission behaviour of the Eu^{3+} dopant in MgO. The branching ratios Ω_2 and Ω_4 were calculated and with increasing Eu^{3+} concentration, Ω_2 was found to increase. Further, $\Omega_2 > \Omega_4$ indicates that the covalency of Eu — O bonds increases and this suggests that host lattice crys-tal field has significant effect on Eu_{3+} emission. Thermoluminescence (TL) studies performed for γ-irradiated samples and TL glow curve suggest multiple types of traps in the host. TL intensity parameters were calculated and analysed in detail to understand the applicability of the phosphor for dosimetric use.

1. Introduction

The unique physical and chemical properties of nano magnesium oxide (MgO) makes it a unique functional material and the quantum confinement effect in nano regime gives novel properties superior to its bulk counterpart in many engineering application.

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Influence of Nitridation on Structural and Photoluminescence Behaviour of $CaZrO_3:Eu^{3+}$ Nanophosphors

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$Ca_{1-x}ZrO_3:xEu^{3+}$ (x = 0.05) phosphors have been prepared by using the low temperature solution combustion synthesis. The prepared nano phospors are well characterized by powder X-ray diffraction, scanning electron microscopy, Fourier infrared spectroscopy and transmission electron spectroscopy. PXRD results showed orthorhombic phase and SEM images showed porous agglomerated morphology. Influence of nitridation on structural and photoluminescence properties of the phosphor were investigated for wide range of nitridation time. The photoluminescence (PL) intensity was found to vary with nitridation with small shift in the photoluminescence emission peaks. The probable reasons for the variation of photoluminescence with nitridation are discussed.

Keywords: $CaZrO_3$, Solution combustion, Nitridation, Photoluminescence.

INTRODUCTION

White LEDs, owing to their excellent properties like brightness, durability, energy efficiency, eco-friendly, *etc*. have emerged as the new generation clean and energy saving technology in solid-state lighting devices. However, white light obtained by the combination of three distinct LEDs has major disadvantage of high production costs. Research on novel white LEDs combining suitable light emitting phosphors has therefore gained momentum [1]. Commercial WLEDs currently use blue-emitting GaN chip combined with yellow emitting YAG-doped Ce^{3+} phosphor [2]. However, because of lack of red component, these LEDs suffer low colour rendering index (RA < 80) and high correlated colour temperature (CCT > 6000 K). Development of novel efficient red phosphors with broad excitation band, which can produce high quality warm white-light emission LEDs, is therefore an area of current research interest.

In this context, rare earth (RE) doped with inorganic phosphor hosts having excellent red emissions have been vastly explored. Xiao *et al*. [3] have demonstrated enhanced red emission of Eu^{3+} doped ZnO phosphor compared to undoped phosphor. Role of Sm^{3+} activator in enhancing the photoluminescence of red light emitting phosphors, Sr_2CeO_4 and $Sr_3Sc(PO_4)_3$ has been reported by Monika *et al*. [4] and Ma & Liu [5]. Efficient red phosphors with Pr^{3+} as luminophore has also has been reported [6,7]. Despite several reported studies, Eu^{3+} still continues to be an extensively researched activator for red phosphors [8].

Eu^{3+} doped red phosphors exhibit intense emission band at ~600 nm *via* the $^5D_0 \rightarrow {}^7F_2$ transition [9]. However, commercial application of these phosphors are limited owing to poor excitation of $^5D_0 \rightarrow {}^7F_2$ transition by the near ultraviolet LEDs and low colour purity due to broad emission band resulting from 4*f*-5*d* transitions [10]. Red phosphors also have problems associated with low brightness and chemical instability. Lumi-

Electrochemical behavior of Heat treated Al 356 Alloy using N2-phenyl-1, 3, 5-triazine- 2, 4-diamine compound in 3.5% NaCl solution

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Abstract
In the present research work, corrosion behavior of heat treated Al 356 alloy in 3.5% NaCl with and without heat treatment in different concentration of inhibitors is studied. Rectangular specimen 2cm X 1cm X 1mm was subjected heat treatment for 2h, 4h and 6 hours in Muffle furnace at 550^{0}C. The specimen were tested for corrosion characterization of Electrochemical studies test. The result obtained is compared with heat treated and non-heat treated specimen. It was found that the heat treated specimen exhibits excellent corrosion Resistance when compared to non-heated specimen.

Keywords: Al 356 alloy, Muffle furnace, potentiodynamic polarization, impedance.

Introduction

Aluminum remains as one of the most desired metallic materials because of its numerous application areas which include automobiles, aerospace, constructions etc. It is also the third most abundant element constituting about 8.13 % in the earth's crust and it mainly exists in very stable combinations with other materials (particularly as silicates and oxides) in nature. Metals and alloys are the most important sources of engineering materials, and the demand for these materials with improved properties (i.e. strength, ductility, light weight) is always on the increase with the ever advancement of science and technology.

The advantages are such as light weight with acceptable strength, high conductivity and good corrosion resistance due to the presence of barrier oxide film layer. For instance, aluminum's light weight performances are highly benefitted in transport applications that are related to aerospace industry. The metal has been widely used as construction materials, heat exchangers, catalyst, combustion processes, and power lines. This research aims to investigate the corrosion resistance of 356 Al alloy of the heat treated specimens of peak age and over age tempers in 3.5% NaCl solution and compare the corrosion resistivity of different concentration of inhibitors.

The surface morphology was also investigated to observe any change in the microstructure of the heat treated specimens produced after corrosion immersion test in an aggressive 3.5% NaCl medium. These alloys show specific behavior in Retrogression and Re-aging (RRA) heat treatments. The most important feature of the aluminium alloy is to form oxide on surface which acts as a barrier. This barrier oxide breaks due to aggressive environments and thus study of the corrosion parameters of any alloy is required to understand to estimate the current and its reaction with a metal surface.

Material and Methods

The alloy selected for the work is Al 356alloy which is commercially available. Its composition is given in table 1.

Al 356 ingots which are available commercially were melted in a furnace to a temperature slightly above melting point. Then the melt is poured into preheated cast iron moulds. Cylindrical castings are subjected to machining to get specimens of size 2cm x 1 cm x 1 mm. The specimens were abraded with silicon carbide papers of different numbers 400, 800, 1200 and 2500 grade and then polished with the help of polishing wheel. Before immersing in the corrosion media, the specimens were cleaned using double distilled water, acetone and dried at room temperature.

Procedure: 4-chloro1,3,5-triasin-2-amine(500mg, 0.00384 mol, 1equiv) was dissolved in dry THF(5ml), the mixture was cooled to -10^0 C. DIPEA (497mg, 0.00384 mol, 1equiv) was added to aniline (357mg, 0.00384 mol, 1equiv) and dissolved in dry THF(2ml), the mixture was cooled to -10^{0}C, before this solution was added slowly to the 4-chloro1,3,5-triasin-2-amine solution while stirring. To ensure complete transfer, another 2ml of dry THF, cooled to -10^{0}C was used to flush all aniline into the reaction mixture.

Table 1
Composition of Aluminium 356 Alloy

ELEMENT	Al	Cu	Fe	Mg	Mn	Si	Ti	Zn	others
PERCENTAGE	93.2	0.10	0.12	0.03	0.05	7.5	0.20	0.05	0.15