

Online ISSN: 2682-2628  
Print ISSN: 2682-261X

# IJC CBR

## INTERNATIONAL JOURNAL OF CANCER AND BIOMEDICAL RESEARCH

<https://jcbr.journals.ekb.eg>

Editor-in-chief

Prof. Mohamed Labib Salem, PhD

**Special Issue: Thesis Abstracts**

May, 2021



PUBLISHED BY

**EACR** EGYPTIAN ASSOCIATION  
FOR CANCER RESEARCH

Since 2014

## **Welcome letter from Editor-in-Chief**



Welcome to the Int J Cancer and Biomedical Research (IJCBR)!

It is with great pleasure that I write this editorial to welcome you to the IJCBR. This journal provides a platform for publication of original and reviews research articles, short communications, letter to editor, thesis abstract, conference report, and case studies. These types of publication are directed at the interface of the fields of cancer and biomedical research.

The IJCBR relies on a distinguished expert of the Advisory and Editorial Board Members from the top international league covering in depth the related topics. They timely review all manuscripts and maintain highest standards of quality and scientific methodology and ethical concepts. Meanwhile, we take all possible means to keep the time of the publication process as short as possible.

I take this chance to welcome your contributions to the IJCBR and have every expectation that it will soon become one of the most respected journals in both the fields of cancer and biomedical research.

A handwritten signature in blue ink that reads "Mohamed L. Salem". The signature is fluid and cursive.

**Mohamed L. Salem,**

Editor in Chief

## Role of postgraduate researchers in advancing cancer and biomedical research

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### ABSTRACT

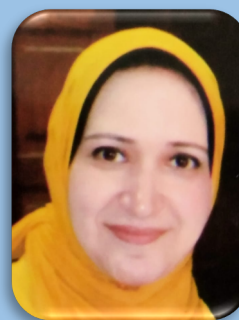
This special issue of IJCBR "Role of postgraduate researchers in advancing cancer and biomedical research" aims to raise awareness of the importance of postgraduate scientific research in the fields of cancer and biomedical research among scholars and junior researchers. There is always a need to discover safe natural materials or novel synthetic compounds to treat different types of cancer as well as other diseases. The master and PhD theses' abstracts presented in this special issue cover six topics, including Anticancer therapeutics, Cancer biology and immunology, Drug discovery, Biological activities of biochemicals, Nanotechnology, and Medicine and Nursing.

In Anticancer therapeutics section, several synthetic compounds as well as extracts from marine organisms and plants showed effective anti-cancer cell capabilities, opening new avenues for their use as a possible adjuvant to cancer therapy. In Cancer Biology and Immunology section, the studies have shown some intrinsic and extrinsic features of cancer cells as well as the potential as cancer immunotherapeutic. In Drug Discovery Section, certain materials extracted from micro and marine algae, and probiotic bacteria showed as anti-diabetic and anti-bacterial, and anti-schistosomiasis, as well as stimulators for immune response against hepatitis C Virus and as a flavoring agent in some foods. In Biological Activities of Biochemicals section, synthetic chemicals such as heterocyclic compounds, bicyclic, and polycyclic rings demonstrated potential effects as anti-microbials, anti-oxidants, and anti-tumor capabilities. In Nanotechnology section, green metal nanoparticles biosynthesized using *Moringa oleifera* plants and blue green algae expressed anti-microbial, anti-oxidant, anti-viral, and anti-cancer properties. In Medicine and Nursing, the studies recommended that nurses should be educated with programs such as burn, PICC line in order to develop their awareness and practice.

Overall, the studies presented several natural and chemical compounds with different biological activities, including anti-diabetic, anti-microbial, anti-cancer, as well as immune enhancer, opening new avenue for drug discovery. I do believe that the scientific findings from the presented theses are of great importance and add values for the biomedical research in general and cancer research in particular. These studies highlight the fundamental role of postgraduate students in advancing biomedical research and innovation.

Editor-in-Chief: Prof. M.L. Salem, PhD - Article DOI: 10.21608/IJCBR.2021.75093.1210

### ARTICLE INFO



#### Article history

Received: May 3, 2021

Revised: May 6, 2021

Accepted: May 6, 2021

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**SECTION 1**

**Medicine and Nursing**

## The effect of implementing peripherally inserted central catheter educational program on nurses' knowledge, practice, and neonatal outcomes

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**Background:** The peripherally inserted central catheters (PICCs) have become among the most common technologies employed in the intravenous therapy of neonates as they allow safe long-term intravascular access, comfort, and ease of transition to home therapy that contributed to the increased survival of those newborns. **Aim:** This study aimed to evaluate the effect of implementing peripherally inserted central catheter educational program on nurses' knowledge, practice, and neonatal outcomes. **Materials and Methods:** pretest-posttest quasi-experimental design was conducted on 45 neonatal nurses working at neonatal intensive care units affiliated to Mansoura University Children Hospital (MUCH) with a purposive sample of (20) neonates admitted to NICU throughout six months and need PICC line insertion was enrolled in the study. Tools of data collection: Data were collected by using three tools: Peripherally inserted central catheter insertion questionnaire sheet, PICC line insertion and care observational checklist and neonatal assessment sheet. **Results:** Majority of studied nurses had poor knowledge and more than half had competent skills about PICC before program implementation while after program implementation there was more than half had average knowledge and two third had competent practices as well as there is decrease in the prevalence of neonatal complication. **Conclusion:** There was apposite effect of the educational program on nurse's knowledge and skills as well as neonatal. Recommendation: Continuing of nursing education and practices about PICC lines.

**Keywords:** Educational program; knowledge; Neonates; Neonatal nurse; PICC line

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Editor-in-Chief: Prof. M.L. Salem, PhD - Article DOI: 10.21608/JCBR.2021.59939.1137

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## Current nursing practices for managing children with burn injuries

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■■■

**Background:** Burns are one of the most common forms of trauma in children. Providing adequate care for burnt children properly is the most important contribution to the successful management. **Aim:** This study aimed to describe the current nursing practice provided for managing children with burn injuries and to identify the most common causes of burn injuries among children. **Materials and Methods:** A descriptive exploratory research design was utilized in the study. The study was carried out in burn unit at Plastic, Reconstructive and Burn Surgery Center and Mansoura International Hospital at Mansoura city on a convenient sample of 56 nurses and 100 pediatric patients. Data were collected by using three tools. Current nursing practices for managing children with burn injury structure questionnaire sheet, Burn care observation checklist and clinical data sheet for children with burn injury. **Results:** The most common cause of burn was boiling water, more than three quarter of studied nurses had poor knowledge about burn and its management, two fifth of them had competent practice about wound dressing, more than two third of studied nurses had competent practice about pain and there was statistical significance difference between severities of burn and children death. **Conclusion:** The present study indicated that the nurses' knowledge regarding burn was poor and were incompetent in the care practice regarding burn injuries. The study recommends that there is a need for burn training program that should be provided to nurses in order to improve their knowledge and practices regarding burn management.

**Keywords:** Burn injuries; Children; Management; Nursing practice

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Editor-in-Chief: Prof. M.L. Salem, PhD - Article DOI: 10.21608/JCBR.2021.60540.1145

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## Effectiveness of Educational Program on Mothers' Knowledge and Practices for The Prevention of Sudden Infant Death Syndrome

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**Background:** Sudden infant death syndrome (SIDS) is a common cause of infant mortality below one year, and its causes remain unknown. However, simple protective practices in infant sleep and sleep environment can dramatically reduce its incidence. **Aim:** Evaluating the effectiveness of educational program on mothers' knowledge and practices for the prevention of SIDS. **Materials and Method:** A quasi-experimental research was conducted in postnatal department at the general hospital in Kafr Elsheikh city, Egypt, on 180 newly delivered mothers, free from eclampsia, chronic diseases and a delivered baby did not have health problem as neonatal jaundice or respiratory distress syndrome. Interview questionnaire sheet was used to collect data about characteristics of mothers and their infant; mothers' knowledge and reported practices about SIDS. **Results:** More than three-quarters of the mothers did not hear about SIDS and had poor knowledge level about SIDS before the program. In addition, about half of the mothers demonstrated unsatisfactory practice level about SIDS prevention before the program. While the majority of them had good knowledge and satisfactory practices level after program application. There was positive effect of the educational program in improving the mothers' knowledge, preventive practices about SIDS. **Conclusions:** A regular health education program is essential for improving the newly delivered mothers' knowledge and practices regarding SIDS prevention and safe sleep recommendations should be done by the medical staff in the neonatal care unit and on every health visit for the infant in his first year.

**Keywords:** Educational program; Knowledge; Mother; Safe sleep practice; Sudden infant death syndrome

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Editor-in-Chief: Prof. M.L. Salem, PhD - Article DOI: 10.21608/JCBR.2021.59429.1129

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## Assessment of the relationship between psychological locus of control and immune status in breast cancer patients

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**Background:** Several recent studies confirm the immune disturbances in cancer patients in comparison with the healthy individual. Other studies confirmed the effective role of psychological status on the immune system. In breast cancer patient, depression associated with decreased inflammatory and immune function. Several studies suggested relationship between locus of control and depression as an external locus of control individuals have more symptoms of depression. **Aim:** To investigate the direct relation between immune status and locus of control in breast cancer patients. **Materials and Methods:** Patients and participators responded to three questionnaires (God health locus of control, multidimensional health locus of control, and Rotter internal/external locus of control). The numbers and phenotype of CD4+ T cells, Treg cells and NK cells by flow-cytometry were measured. The gene expression of pro-inflammatory cytokines was assessed by real time PCR. **Results:** There is a significant direct co- relation between IHLC and CD4+ T cells, IHLC and NK cells. **Conclusion:** There is a relationship between psychological locus of control and immune status in breast cancer patients.

**Keywords:** Breast cancer; Immune status; Locus of control

Editor-in-Chief: Prof. M.L. Salem, PhD - Article DOI: 10.21608/JCBR.2021.61774.1164



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SECTION 2

**Nanotechnology**

## Bionanoparticles from moringa as antimicrobial activity and Its application in water purification

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**Background:** Nanotechnology is the greatest promising technique for generating new applications in water purification. Green synthesis of silver nanoparticles and copper oxide nanoparticles is an eco-friendly, cheap and non-toxic more than chemical and physical methods. **Aim:** This study focuses on green synthesis, characterization, antibacterial activities of silver nanoparticles and copper oxide nanoparticles synthesized using *Moringa oleifera* leaf and stem extract and its application in water purification. **Materials and Methods:** The green synthesis of silver nanoparticles was done by using *Moringa oleifera* leaf and stem extract and 1mM of silver nitrate solution while copper oxide nanoparticles were synthesized by using *Moringa oleifera* leaf and stem extract and 10mM of copper sulfate pentahydrate solution. pH, temperature and the mixture reaction time are parameters affecting the formation of silver nanoparticles and copper oxide nanoparticles. **Results:** In this study, various techniques and devices used to characterize and confirms the formation of silver nanoparticles and copper oxide nanoparticles included visual observation, UV-Vis spectroscopy, TEM, FTIR, and EDX. Silver nanoparticles and copper oxide nanoparticles showed antimicrobial activity against *E. coli* ATCC 8739 and *S. typhi* ATCC 14028 and isolated microorganisms from tested water sample which included *Pseudomonas aeruginosa* and *Klebsiella variicola*. Cellulose filter paper which coated with silver nanoparticles and copper oxide nanoparticles showed good effect in water purification as its good antimicrobial activity against microorganisms, increasing pH value and reducing conductivity, total alkalinity values and Pb concentration value. **Conclusion:** The results from this study indicate that bionanoparticles from moringa have an antimicrobial activity that can be applied in water Purification.

**Keywords:** Cellulose filter paper; Copper oxide; Nanoparticles; *Moringa oleifera*; Nanotechnology; Silver

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Editor-in-Chief: Prof. M.L. Salem, PhD - Article DOI: 10.21608/JCBR.2021.60450.1146

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## Biosynthesis of metal nanoparticles using blue-green algae (Cyanobacteria) and their possible applications

Rehab S. Ghobashy, Mostafa M. Elsheekh, Gehan A. Ismail and Saly F. Gheda

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**Background:** Silver nanoparticles has attracted much attention as its appropriate solvent systems and ecological reducing agents so, its synthesis was of wide prominence and were functional in many fields. **Aim:** The present work was designed for the biosynthesis of AgNPs by seven cyanobacterial species using their filtrate and biomass separately and also their crude phycobiliproteins extract of *Nostoc linckia* and *Spirulina platensis* which scored the highest quantities. **Results:** Appearance of surface plasmon band at 400 nm for filtrate and biomass while at 420 nm crude phycobiliproteins extract that indicated the biosynthesis of AgNPs. FTIR analysis suggested that proteins were responsible for their capping and stabilization. XRD analysis confirmed its spherical crystalline shape. Zeta potential recorded -15.9 mV and -16.8 mV for *S. platensis* and *N. linckia* AgNPs, respectively confirming its stability. TEM images revealed that AgNPs had a mean average size of 21.2 and 21.05 nm for *S. platensis* and *N. linckia*, respectively. AgNPs showed potent antimicrobial activity against Gram positive, Gram negative bacteria and *Candida albicans* using the disk diffusion method. The antioxidant activity of AgNPs was promising by using three assays of DPPH radical scavenging activity, total antioxidant capacity and ferric reducing antioxidant power. The cytotoxicity of AgNPs was tested on HepG2 cell line through neutral red assay and the NPs of both species proved to be safe in low concentrations. Significant antiviral activity against HCV (64.976%) was recorded for AgNPs of *N. linckia* which was comparable to Ribavirin (66.67%) as a standard drug while *S. platensis* AgNPs recorded 48.3%. **Conclusion:** Biosynthesis of metal nanoparticles using blue-green algae (Cyanobacteria) can express potential anti-cancer activities.

**Keywords:** Antiviral; AgNPs; Antimicrobial; Antioxidant; Cyanobacteria

Editor-in-Chief: Prof. M.L. Salem, PhD - Article DOI: 10.21608/JCBR.2021.59664.1133

## The use of iron oxide nanoparticles in hyperthermia of Ehrlich tumor

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■■■

**Background:** Nanotechnology offers important new tools expected to have a great impact on many areas in medical technology. It provides extraordinary opportunities to improve materials and medical devices and they contain several chemical, physical, engineering and biological sciences. Magnetic hyperthermia is a relatively new method used for cancer therapy. Magnetic nanoparticles are an attractive option because they can be remotely targeted by application of external magnetic field gradients or other active and passive targeting methods. **Aim:** Given that tumor cells are more sensitive to a temperature increase than healthy ones, this property can be used in vivo to increase the temperature of tumor tissue (40-43°C) to destroy the pathological cells by hyperthermia. **Materials and Methods:** It was found that, magnetic fluid based on superparamagnetic Fe<sub>3</sub>O<sub>4</sub> nanoparticles coated by biocompatible layer is suitable for hyperthermia because the particles have a high magnetic moment, strong magnetic specific loss power (SLP) and non-toxicity. **Results:** This study presents results of research on preparing the magnetic fluid based on Fe<sub>3</sub>O<sub>4</sub> nanoparticles by co-precipitation method and its potential hyperthermia application. The magnetic fluid was used as a mediator for heating by Neel relaxation when exposed to ultrasound and / or microwave energy. The magnetic fluid hyperthermia (MFH) results caused a significant anti-tumor effect on cancer cells. Ultrastructural changes were evaluated by (TEM). **Conclusion:** These results indicate that intra-tumoral injection of monodisperse MNPs can attenuate the tumor cells after exposure to ultrasound energy followed by microwave energy.

**Keywords:** Heating effect; Heating mechanism; Magnetic fluid hyperthermia; Magnetic nanoparticles; Ultrasound and Microwave energy

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Editor-in-Chief: Prof. M.L. Salem, PhD - Article DOI: 10.21608/JCBR.2021.60623.1154

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## Evaluation of silver nanoparticles caffeic folate complex compound as new potential therapeutic agent against cancer xenograft in mice

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**Background:** In the last few decades the properties of silver compounds have been of interest as potential cancer treatments. **Aim:** The present work was designed to study the effect of new conjugated caffeic and folic acid with silver nanoparticle with definite molecular size applied with and without gamma radiation exposure, as an antitumor agent against experimentally induced Ehrlich tumor and attempted to identify their potential molecular mechanisms of action throughout determination of anti-tumor activities using MTT cytotoxic assay against two human carcinoma cell lines in vitro. **Materials and Methods:** Apoptosis analysis by flow cytometry through caspase-8, caspase-3 and TNF determine in vivo. Adult female albino mice were used and divided into five groups, Animals were scarified and the following parameters were estimated, glutathione, glutathione peroxidase, superoxide dismutase in blood and caspase8, caspase 3 and TNF from scarified tumor tissue. The tumor specimens were processed for histopathological examination. **Results:** Nano-silver folate caffeic (NSFC) complex compound treatment resulted in a growth inhibition in Hep-G2 and MCF-7 cells (IC50 7.70  $\mu$ M and 14.50  $\mu$ M, respectively). Flow cytometric analysis revealed that (NSFC) with radiation exposed has apoptotic effect at caspases 8, 3 and TNF more than any compound of them alone. That disturbance was found to be associated with a kinetic induction of apoptosis and showed modulation of antioxidant system beside its high percentage of necrotic cells by histopathological studies. **Conclusion:** The novel synthetic nano-silver folate Caffeic complex compound may potentially present a new hope for the development of breast cancer therapeutics, which should attract further scientific and pharmaceutical interest.

**Keywords:** Apoptosis; Conjugated caffeic and folic acid; Radiation; Silver nanoparticles; Tumor

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Editor-in-Chief: Prof. M.L. Salem, PhD - Article DOI: 10.21608/JCBR.2021.62150.1174

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## Preparation and evaluation of graphene oxide based-materials for anticancer drug delivery in an experimental mice tumor

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**Background:** Graphene oxide (GO) is a multifunctional carbon nanomaterial with tremendous potential in medical science including cancer therapy. It has unique physical, and chemical properties to be used as a drug carrier such as Doxorubicin (DOX). Aim: This study aimed to load DOX on (GO) and supramagnetic iron oxide GO (GO/Fe<sub>3</sub>O<sub>4</sub>) as a passive and active forms with or without folic acid (FA) and to compare the anti-tumor effects of these conjugates to free DOX. **Materials and Methods:** GO was synthesized by Hummers method, then loaded with DOX, FA or Fe<sub>3</sub>O<sub>4</sub>. All conjugates were characterized by FT-IR, TEM and TGA techniques, then their anticancer properties were investigated in vitro using EAC cell lines. In vivo study was performed using EAC-bearing mice which were divided and treated with DOX, GO/DOX, rGO/DOX/FA, GO/Fe<sub>3</sub>O<sub>4</sub>/DOX, rGO/Fe<sub>3</sub>O<sub>4</sub>/FA/DOX, GO/Fe<sub>3</sub>O<sub>4</sub>/DOX+IR and rGO/Fe<sub>3</sub>O<sub>4</sub>/FA/DOX+IR. After 10 days, number of tumor cells, splenocytes and white blood cells (WBC), apoptosis, and cell cycle of tumor cells were analyzed. **Results:** In vivo results showed that GO conjugates induced significant decrease of the total numbers of EAC cells. Interestingly rGO/Fe<sub>3</sub>O<sub>4</sub>/FA/DOX+ IR treatment showed increases in late apoptosis whereas GO/DOX and rGO/Fe<sub>3</sub>O<sub>4</sub>/FA/DOX induced necrotic cells as compared to free DOX. Free DOX induced leukopenia in spleen, however treatment with GO/DOX or GO/FA/DOX induced lesser effects. Treatment with GO/DOX conjugates induced significant increases in the blood leukocytes as compared to treatment with DOX and GO/DOX/FA which induced leukopenia. **Conclusion:** These results demonstrate that GO composites may be a highly biocompatible nanomaterial with practical applications in cancer therapy.

**Keywords:** Cancer; Doxorubicin; Ehrlich ascites; Folic acid, Graphene oxide

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Editor-in-Chief: Prof. M.L. Salem, PhD - Article DOI: 10.21608/JCBR.2021.61754.1167

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## Biochemical studies on the effect of nano particles of some nutrients on apoptosis modulation of breast cancer cells in experimental animals

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**Background:** Nano micronutrients and their relationship to health or disease is one of the domains of modern needs of many of extensive researches and studies. **Aim:** This work was carried out to study the effect of some nano nutrients to induce apoptosis in breast cancer and the inhibitory effect of them on development of toxic material of mammary tumor for 180 days against injected intraperitoneally a single dose of (50 mg/kg) N-methyl-N-nitrosourea (MNU) in female rats. Experimental animals in this study divided into two categories, first category: include (78 rats) which induced breast cancer by injecting a single dose of MNU intraperitoneally. Two weeks after MNU treatment, a time by which the animals had recovered from MNU-induced toxicity, the rats were divided into 13 groups (6 for each). Finally, all the experimental results evaluated, tabulated and statistically analyzed. **Results:** Parameters in normal treatments showed agreement with the results of many previous biochemical studies, especially the results of folic acid, vitamin C and apoptosis. While the biochemical results of nano treatments showed many unexpected differences in cancer diseases, especially increasing the level of folic acid, vitamin B12 and vitamin C. There was a high release of those nano nutrients from the diseased cells. In addition to the inability of the diseased cells to keep them, which may be in a different the status for the natural form. The treatment of nano yeast showed nearly the best results among all other treatments. We will need more research to support these results. Results of nano treatment on diseased cancer cells and normal cells indicated to difference in biochemical pathways from normal cells. This will require further studies. **Conclusion:** Parameters in normal treatments showed agreement with the results of many previous biochemical studies, while the biochemical results of nano treatments showed many unexpected differences in cancer diseases. The treatment of nano yeast showed nearly the best results among all other treatments.

**Keywords:** Apoptosis; Breast Cancer; Mammary tumor; Nano Particles; Nutrients

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Editor-in-Chief: Prof. M.L. Salem, PhD - Article DOI: 10.21608/jcbr.2021.60576.1149

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CANCER AND BIOMEDICAL RESEARCH

SECTION 3

**Cancer Biology and  
Immunology**



## Detection of circulating cancer stem cell and matrix Metalloproteinase-2 in patients with hepatitis C Virus and their correlation with hepatocellular carcinoma

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**Background:** Hepatitis C virus (HCV) infection is a major health problem. In majority of infected patients, HCV can effectively evade innate immunity resulting in chronic hepatitis, cirrhosis and hepatocellular carcinoma (HCC). Similar to most tumors, HCC contain poorly differentiated cancer stem cells (CSCs) that initiate tumorigenesis. The interaction of stem cell with microenvironment is key regulatory mechanism in maintenance of its self-renewal capacities. Matrix metalloproteinase (MMPs) are proteolytic enzymes that plays a role in degradation of extracellular matrix which is necessary for metastasis. **Aim:** The present work attempted to study the mRNA expression of CSC markers (CD133 and CD44) as well as levels of MMP-2 in HCV patients and their correlation with progression towards cirrhosis and HCC. **Materials and Methods:** Peripheral blood mononuclear cell (PBMC) prepared from HCV patients (either with or without complications) were probed for mRNA expression of CD133 and CD44 by RT-PCR and compared to that of non-HCV cirrhotic patients as well as healthy controls. Also, MMP-2 levels were measured using ELISA technique. Our results revealed that mRNA expression of CD133 was significantly elevated in HCV patients without complications while maximal CD44 mRNA expression and maximal circulating MMP-2 levels was noticed in HCC patients. **Conclusion:** These results suggests that, chronic HCV infection appear to predispose cells towards path of acquiring cancer stem cell traits by inducing CD133 and CD44 expression leads to their transformation into CSCs. In addition, HCV has important role in creating a microenvironmental change by enhancing MMP-2 release that increase invasion potential and facilitate tumor progression.

**Keywords:** CD133; CD44; Hepatocellular carcinoma (HCC); Hepatitis C virus (HCV); Matrix metalloproteinases-2

Editor-in-Chief: Prof. M.L. Salem, PhD - Article DOI: 10.21608/JCBR.2021.59361.1127

## Cytokine gene polymorphisms in lymphoma

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**Background:** Several cytokines are known to be involved in the pathogenesis of non-Hodgkin Lymphomas (NHL). **Aim:** Given the importance of understanding the genetic predisposition involved in the pathogenesis of NHL, this work was designed to study the impact of IL-10 (-1082 G/A; rs1800896 and -819 C/T; rs1800871), IL-6 (-174 G/C; rs1800795) and CD38 (184C/G; rs6449182) gene polymorphisms on the susceptibility of Egyptians to NHL. **Materials and Methods:** Both loci of IL10 were genotyped using polymerase chain reaction- sequence-specific primers (PCR-SSP), IL6 rs1800795 G/C was genotyped using mutagenically separated PCR (MS-PCR) and restriction fragment length polymorphism-PCR (RFLP-PCR) was used to genotype CD38 (rs6449182 C/G) in 100 Egyptian patients and 119 controls. Plasma levels of IL-6 and IL-10 were measured using enzyme-linked immunosorbent assay (ELISA). **Results:** An insignificant change in IL-10 (rs1800896 and rs1800871) genotypes were recorded. GT haplotype was significantly elevated. **Conclusion:** Lymphoma samples express a particular polymorphism.

**Keywords:** CD38; IL-10; IL-6; NHL; SNP

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Editor-in-Chief: Prof. M.L. Salem, PhD - Article DOI: 10.21608/JCBR.2021.60776.1159

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## Analysis of cytolytic capability of natural killer cells and cytotoxic T cells in the peripheral blood of cancer patients

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**Background:** Lung cancer is a one of the most cancer types speeded worldwide. In Egypt, lung cancer counted as the third cause of deaths among males after liver and bladder cancers. It is characterized with two type's SCLC represents about (10% to 15%) and NSCLCs which represents (80% to 85%). In NSCLCs, treatment only treat 15%–30% of patients due to the presence of tumor mediators which enhance tumor surveillance by secreting PGE<sub>2</sub>, TGF- $\beta$ . CD8+ and NK are the main cells to defeat and kill cancer cells. **Aim:** The aim of this study is to address the functionality of T-cells and NK cells from lung cancer patient's pre and post stimulation in-vitro. Lung cancer is a one of the most cancer types speeded worldwide. In Egypt, lung cancer counted as the third cause of deaths among males after liver and bladder cancers. Lung cancer characterized with two type's SCLC represents about (10% to 15%) and NSCLCs which represents (80% to 85%). In NSCLCs, treatment only treat 15%–30% of patients due to the presence of tumor mediators which enhance tumor surveillance by secreting PGE<sub>2</sub>, TGF- $\beta$ . CD8+ and NK are the main cells to defeat and kill cancer cells. The aim of this study is to address the functionality of T-cells and NK cells on lung cancer patient's pre and post stimulation in-vitro. Materials and methods.

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Editor-in-Chief: Prof. M.L. Salem, PhD - Article DOI: 10.21608/JCBR.2021.63951.1181

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## Investigating the role of Notch and related signaling pathways in Breast cancer patients

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**Background:** Breast cancer is the most common cancer in women worldwide. Cancer Stem Cells play an important role in the processes of drug resistance and metastasis. Studies showed that behavior and biology of B.C differ in different racial groups, emphasizing the importance of understanding the biology of the disease in each population separately. **Aim:** Here we investigated the differential expression of a number of CSCs regulating genes in Egyptian and British patients. we have studied the influence of cancer therapy on the expression levels of these genes. **Materials and Methods:** CSCs were isolated from a total of 24 B.C patients from Egypt and England, using Anoikis resistance assay. RNA was extracted, its concentration and quality were measured by nano drop, bioanalyzer and qPCR) and cDNA was then synthesized. qPCR arrays harboring primers specific for (Notch1, Notch4, Nanog, JAG1, PARP1, HIF1A, SP1, STAT1, NFKB1, DNMT1, DNMT3B) were designed. The differential gene expression between; Egyptian untreated vs British untreated, Egyptian treated vs British treated, Egyptian untreated vs Egyptian treated, and British untreated vs British treated was detected using  $\Delta\Delta C_t$  method. **Results:** We have detected which genes of the genes under study are differentially expressed between Egyptians and British patients. we determined which genes in both racial groups may be responsible for CSCs resistance to therapy. **Conclusion:** Our study strongly confirms the racial variation in B.C biology and is the first study to show that CSCs signaling pathways are behind this variation. More importantly, we detected which genes showed be targeted to sensitize CSCs to therapy in Egyptian patients.

**Keywords:** Breast cancer; NOTCH; PARP1; Stem cells

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Editor-in-Chief: Prof. M.L. Salem, PhD - Article DOI: 10.21608/IJCBR.2021.61818.1169

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## Analysis of the cellular expression of checkpoint molecules on immune cells in patients with breast cancer

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**Background:** Breast cancer is a heterogeneous malignant tumor that includes several types of cells. Among them, only breast cancer stem cells (BCSCs) have tumorigenic ability. In this study we tested the hypothesis that BCSCs are behind disparities in behavior and biology of breast cancer between different ethnic groups and it is very important to investigate signaling pathways regulating BCSCs in each population. Therefore, we investigated the role of WNT, HH and apoptosis signaling pathways together with ALDH1A1 and CD44 in BCSCs resistance to chemotherapy in tumor biopsies collected from Egyptian patients compared to British patients. **Aim:** We investigated the expression levels of specific members of Wnt, Hedgehog, and apoptosis signaling pathways in BCSCs isolated from treated Egyptian and British patients. The change in their expression levels between the two populations was detected. **Materials and Methods:** Breast Cancer tumors were collected from Egyptian and British patients, dissociated to a single cell suspension in collagenase IV containing buffer. CSCs were isolated using anoikis resistance assay from treated and untreated samples. RNA was extracted and cDNA was synthesized. Custom qPCR arrays were used to detect the gene expression of Wnt5A, CXCR4, LEF1, TCF4, SHH, GLI1, BCL2, XIAP, ALDH1A1 and CD44. Data were analyzed by  $\Delta\Delta C_t$  method. **Results:** Our data showed a number of genes with different expression levels in the treated Egyptian patients compared to the treated British patients. **Conclusion:** Molecular mechanisms that regulate BCSCs differ from a population to another. Moreover, the different treatment regimens in different countries may affect the way BCSCs resist therapy.

**Keywords:** Breast Cancer Stem Cells; Hedge Hog; Wnt

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Editor-in-Chief: Prof. M.L. Salem, PhD - Article DOI: 10.21608/IJCBR.2021.61799.1165

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## Analysis of the cellular expression of checkpoint molecules on immune cells in patients with breast cancer

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**Background:** Despite of the success of the breast cancer therapies, recurrence and metastasis still occur after treatment. These may be due to the immune cell suppression through immunoregulatory T cells (T reg) and immune checkpoint pathways such as programmed cell death protein 1 (PD-1) or programmed cell death ligand 1 (PDL-1) that expressed on circulatory tumor cells (CTCs). **Aim:** The present study aimed to analyze the phenotypic and the functions of immune T cells in the peripheral blood (PB) of breast cancer patients. Further to analyze the expression of checkpoint molecules (PD-1, PDL-1) on immune cells, also analyze the expression of PDL-1 on CTCs and cancer stem cells in (PB) of breast cancer patients, and correlated the results with clinical status of the patients compared to healthy woman. Blood samples were collected from breast cancer patients (n=28) at different stages (II, III, IV) before surgery compared to healthy individuals (n=10) to explore the significant role of T regulatory (Treg) cells, and the expression of PD-1 on immune T cells in (PB) of breast cancer patients. **Results:** The study showed the significant role of PDL-1 on circulatory tumor cells (CTCs) in peripheral blood of stages (III- IV) of breast cancer patients before and post chemotherapy. Our findings help us to understand the immunomodulatory nature of Treg, PD-1 expression on immune cells and PDL-1 expression on cancer cells. **Conclusion:** This study provides a better understanding of the nature of a recurrence and metastasis of breast cancer patients. Furthermore, recommended breast cancer patients need seriously to immunotherapy.

**Keywords:** Breast cancer; Circulatory tumor cells; Programmed cell death protein 1; Programmed cell death ligand 1; T regulatory cells

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Editor-in-Chief: Prof. M.L. Salem, PhD - Article DOI: 10.21608/IJCBR.2021.61808.1168

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## Comparative histological and immunological studies on young and aged inbred and outbred mice

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**Background:** Using of experimental animal as models to mimic human pathological conditions has facilitated understanding the mechanisms of different processes involved in these diseases. Among the experimental animals, mice are the mostly widely used animals in different experimental biology since it has a small size, easy breeding, low cost, high fertility rate, and the extensive knowledge of its genome. The differences in the immune cell complements between young and adult mice, however, have not been well investigated. **Aim:** The present study aimed to compare aging on the immune cell components in outbred and inbred mice as well as to evaluate the their responses to the inflammatory stimuli Polyinosinic:polycytidylic acid (poly(I:C)). **Results:** The study investigated whether the aging or the poly(I:C) has the more damaging effect on the cell histology of the thymus gland and spleen. This study confirms that the alteration in the histology of the spleen of aged mice as compared to young mice. Furthermore, poly(I:C) had more tendency to induce alteration in the architecture and cellular components in the thymus and spleen of old mice than those in young mice. **Conclusion:** Immune compartments in old mice are more susceptible to inflammation than those in young mice.

**Keywords:** Aging; Poly I:C; Spleen; Thymus gland

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Editor-in-Chief: Prof. M.L. Salem, PhD - Article DOI: 10.21608/JCBR.2021.61950.1172

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## Biochemical studies on the relation between tamoxifen, nano-nutrients and some bioactive components and gene expression in experimental breast cancer

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**Background:** Research encourages the use of nanotechnology to limit the development and spread of breast cancer and the inhibitory effect of them on development of toxic materials. **Aim:** To study converting drug (Tamoxifen), some nutrients (yeast) and bioactive compounds (Silymarin and Isoflavone) to nanoparticles and study their different effects in nano and normal scale on gene expression. **Materials and Methods:** To induce mammary tumor, mice were treated for 180 days with a single oral dose of (25 mg/kg) 7,12-dimethylbenz[a]anthracene (DMBA) in female rats. The body weight and food consumption will be examined. Upon the completion of the study, the histopathological studies on the breast tissues will be performed. The therapeutic and protective effects of these compounds in nano and normal scale were evaluated using the appropriate parameters to determine the level of several chemicals related to oxidative damage (8-OHdG, Lipid Peroxide, TAC), apoptosis, plasma estrogen and ErbB-2 in the blood samples. Also, the gene expression of ErbB-2 was investigated in the blood samples. All the experimental results evaluated, tabulated and statistically analyzed. **Results:** Tamoxifen in the form of nanoparticles increased apoptosis and the levels of lipid peroxidation while reduced the signs of breast cancer ErbB-2 and 8-OHdG and the level of estrogen as compared with the natural form of tamoxifen and. Although the nano silymarin group did not show activation of the apoptosis process, it showed lower levels of 8-OHdG, ErbB-2, and estrogen and also had the ability to inhibit the progression of breast cancer when administered at the late stage. **Conclusion,** Breast cancer is highly curable if diagnosed with nutrients or medications whether in their normal or nano particles form at an early stage.

**Keywords:** Bioactive Components; Breast Cancer; Experimental Rats; Gene Expression; Nanonutrients

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Editor-in-Chief: Prof. M.L. Salem, PhD - Article DOI: 10.21608/jcbr.2021.60060.1139

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## Impact of SOX2 and CD44 as Cancer Stem Cell Markers in Urinary Bladder Carcinoma

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**Background:** In Egypt, bladder cancer (BC) is the third common malignant tumor. The most important items of CSCs regulatory core are transcription factors like SOX2. The cell adhesion molecule CD44 has also been found as a cell surface marker with CSCs in multiple types of tumors, like BC. **Aim:** This study was conducted to detect the expression of SOX2 and CD44 and correlate their expression with the available pathological parameters. **Materials and Methods:** The study was done on 80 cases of BC (60 cases of transitional cell carcinoma, 17 cases of squamous cell carcinoma and three cases of adenocarcinoma), 20 specimens were collected by radical cystectomy and 60 specimens were collected by transurethral resection. The specimens were immunostained with SOX2 and CD44. **Results:** SOX2 was positive in 46 cases of urothelial carcinoma (76.7%), 11 cases of SCC (64.7%) and all adenocarcinoma cases. SOX2 immunostaining was significantly increased with muscular invasion, and high stage in urinary bladder carcinomas. CD44 was positive in 46/60 cases of urothelial carcinoma (76.7%) and all cases of squamous cell carcinoma. The basal cell layer of adjacent, apparently normal urothelium, was also expressed a positive reaction for CD44. There was significant inverse relation in statistics between CD44 and tumor grade. CD44 was also inversely correlated with muscle invasion. **Conclusion:** SOX2 overexpression could be used as a marker of poor progression in bladder carcinoma cases. It could be a target for an efficient therapeutic strategy of BC treatment, high grades and more liability for infiltration. BC is associated with low expression or complete loss of CD44 immune reactivity.

**Keywords:** Bladder cancer; Cancer stem cells; SOX2, CD44; Immunohistochemical markers

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Editor-in-Chief: Prof. M.L. Salem, PhD - Article DOI: 10.21608/jcbr.2021.63456.1178

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## Evaluation of the use of long noncoding RNAs as biomarkers for diagnosis of breast cancer

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**Background:** FAM83H antisense RNA 1 (FAM83H-AS1) and long noncoding RNA activated by TGF  $\beta$  (lncRNA-ATB) are two lncRNAs that have tumor promoting functions in breast cancer (BC). Matrix metalloproteinase-9 (MMP-9) is another tumor marker that exerts an oncogenic role in BC and facilitate cancer invasion and metastasis. **Aims:** Our study aimed to 1) analyze serum levels of FAM83H-AS1, lncRNA-ATB, and MMP-9 in BC patients, 2) compare their diagnostic role with that of CA15-3 in BC patients with different stages (I-II, III, and IV), and 3) correlate the levels of the measured lncRNAs, MMP-9, and CA15-3 with the clinicopathological features of BC. **Materials and Methods:** Serum FAM83H-AS1 and lncRNA-ATB levels were analyzed in 90 BC patients and 30 healthy controls using RT-PCR. While serum levels of MMP-9 and CA15-3 were measured in the same studied groups by ELISA. **Results:** FAM83H-AS1, lncRNA-ATB, MMP-9, and CA15-3 levels were significantly elevated in sera of BC patients. ROC curve analysis showed that lncRNA-ATB and MMP-9 had higher AUC values than CA15-3 in diagnosis of stage I-II patients (AUC: 0.844 and 0.898,  $p=0.000$  for lncRNA-ATB and MMP-9, respectively versus 0.738,  $p=0.002$  for CA15-3). FAM83H-AS1 level was significantly correlated with higher stage, larger tumor size, positive lymph node metastasis, and distant metastasis. FAM83H-AS1 level was also significantly increased in PR-negative and ki67-rich tumors. **Conclusion:** Our study demonstrated that circulating lncRNA-ATB and MMP-9 could be used as diagnostic biomarkers for early BC. FAM83H-AS1 could also be a potential candidate for staging BC and monitoring disease progression.

**Keywords:** Breast cancer diagnosis; FAM83H-AS1; lncRNA-ATB; Long non-coding RNA; MMP-9

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Editor-in-Chief: Prof. M.L. Salem, PhD - Article DOI: 10.21608/jcbr.2021.60072.1153

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## Circulating Cancer Cells with Relative Expression of miRNA and Cytotoxic T-cell Activities in Non-small cell Lung Cancer Patients

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**Background:** Lung cancer is the leading cause of cancer-related death worldwide with a substantially low survival rate. MiRNAs have been shown to regulate self-renewal and differentiation properties of CSCs, Here, MicroRNAs play a significant role in shaping immune response. **Aims:** the current study aims to analyze the numbers of helper CD4+ and cytotoxic CD8+ T lymphocytes, CD133+ and Epcam+ CSCs. also, measure the relative expression of miRNAs in Non-small cell lung cancer patients before and after treatment. **Materials and Methods:** The frequencies of Epcam+ and CD133+ cells and the numbers of helper CD4+ and cytotoxic CD8+ T lymphocytes were analyzed in the peripheral blood of NSCLC patients before (n= 10) and after (n= 10) chemotherapy using multiparametric flow cytometry. The gene expression of miRNAs was measured using microarray. **Results:** Early diagnosed patients before treatment showed high numbers of Epcam+ and CD113+ CSCs when compared to CTRL; where the numbers of these cells were decreased after treatment as compared to early diagnosed patients. A significant upregulation of miRNAs and downregulation of miRNAs were observed in the peripheral blood of NSCLC patients as compared to healthy control. The relative and absolute numbers of CD4+ and CD8+ T-cells were significantly elevated in the peripheral blood of NSCLC patients. **Conclusion:** This study opens a new avenue to investigate the mechanism mediating the emergence of these cells on larger number of NSCLC patients at different treatment stages. We also discuss the role of microRNAs in therapeutic resistance and as biomarkers.

**Keywords:** Non-small cell lung cancer (NSCLC); miRNA; Cancer stem cells (CSCs)

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Editor-in-Chief: Prof. M.L. Salem, PhD - Article DOI: 1010.21608/jcbr.2021.61161.1162

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# IJC CBR

INTERNATIONAL JOURNAL OF  
CANCER AND BIOMEDICAL RESEARCH

**SECTION 4**  
**Anti-Cancer**  
**Therapeutics**

## Assessment of the immune and antitumor effects of products from Sea hare inhabiting the Egyptian water using an experimental tumor mouse model

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**Background:** Although anticancer chemotherapy is effective, it has side effects. Novel agents with potent anti-tumor effects are needed, potential source could be extracted from marine animals since they possess products with anticancer effect. **Aim:** the aim of this study was to study the potential anti-tumor effect of egg extract and purple fluid in vitro. EAC cells were incubated with different concentrations of both extracts in vitro for 24 hours and then cell cycle, apoptosis was analyzed by flow cytometry and survival was analyzed by trypan blue exclusion and MTT assays. Incubation of EAC cells with both extracts resulting in significant decreasing in number of cells and increasing in apoptosis in a dose dependent manner. Untreated cells were negative control, cells treated with cisplatin were positive control. **Results:** Egg extract at (50 µg/ml, 100 µg/ml, 150 µg/ml, 200 µg/ml, 250 µg/ml) induced (68%, 60%, 55%, 48%, 42%) respectively in proliferation, and (6.3%, 6.4%, 7%, 7.1%, 7.2%) increases in apoptosis. Purple fluid at (0.5 µg/ml, 1 µg/ml, 1.5 µg/ml, 2 µg/ml) induced (55%, 50%, 45%, 35%) respectively in proliferation, and (5%, 7.1%, 7.2%, 11.5%) increases in apoptosis. **Conclusion:** both egg extract and purple fluid showed significant anti-tumor efficacy which, further studies required to evaluate the potential efficacy.

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Editor-in-Chief: Prof. M.L. Salem, PhD - Article DOI: 10.21608/IJCBR.2021.61856.1170

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## Effect of Buteyko Breathing Technique on Asthma Severity Control among School Age Children

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**Background:** Asthma is a complex condition that can impair the child's physical growth. It affect not only the child's physical status but also his optimal functional capacity and performance. Buteyko Breathing Technique is an exercise designed to regulate the breathing process. **Aim:** This study aimed to study the effect of Buteyko Breathing Technique (BBT) on asthma severity control among school age children. **Materials and Methods:** A quasi-experimental design (one group pre and posttest) was conducted on 33 asthmatic school age child who attended the sensitivity outpatient clinics at Mansoura University Children's Hospital (MUCH). Tools: Structured interview sheet for child and their parent, Childhood Asthma Control Test(C-ACT), Peak Expiratory Flow Rate (PEFR) and Control Pause Test (CP) are used to collect data. **Results:** The mean C-ACT pretest was significantly improved in the posttest with high mean percent of change of posttest than pretest, which was clinically and statically high significant. There was a statistical significant increase in the mean of PEFR and CP at the fourth week than the first one with a high significant mean percent of change. There was a significant positive decrease in the heart rate over the four weeks of follow up with high mean percent of change at fourth week than first one. **Conclusion:** This study support the effectiveness of BBT in improving respiratory outcome and promoting asthma control among school age children with bronchial asthma.

**Keywords:** Bronchial asthma; Buteyko breathing technique; Respiratory outcome; School age children

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Editor-in-Chief: Prof. M.L. Salem, PhD - Article DOI: 10.21608/jcbr.2021.59903.1135

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## In vitro survival of breast cancer cell lines following chemotherapy or radiotherapy in comparison with gold-mediated phototherapy

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**Background:** Breast cancer is a heterogeneous disease that mandate efficient therapeutics, lower drug toxicity, and overcoming drug resistance. Combination therapy was suggested as a future treatment to attain the required efficacy and tolerable side effects. **Aim:** The current study aimed to compare and evaluate the efficacy of single and combined treatments in the MCF-7 breast cancer cell line. **Materials and Methods:** The study included seven MCF-7 groups according to the treatment modality. Cell viability was evaluated by MTT assay at different doses and time course treatments. **Results:** When nanoparticles were used alone, the starting point of significant cell death was 100 µg, but when using a photothermal combination modality the loss of viability % was about 2-fold higher than nanoparticles alone especially in low concentrations and there was a significant difference between the 2 groups. There was a significant difference in cell viability between FAC + AuNPs group when compared to FAC only or control group ( $p \leq 0.05$ ). There was a significant difference in cell viability between Taxol + AuNPs when compared to control ( $p \leq 0.05$ ). there is a significant effect of radiation doses on cell viability within all subgroups ( $p < 0.001$  for R0, and  $p=0.001$  for R2 subgroup). there is a significant effect of the radiation doses on the cell viability within each subgroup as indicated by significant p values ( $p= 0.027$  for RN0, and  $p=0.001$  for RN2). **Conclusion:** Combined GNPs and FAC, paclitaxel, and Radiotherapy treatment modalities could improve breast cancer outcomes and prognosis.

**Keywords:** Breast cancer; Chemotherapy; MCF-7; Photothermal treatment; Radiosensitizers

Editor-in-Chief: Prof. M.L. Salem, PhD - Article DOI: 10.21608/JCBR.2021.60568.1150

## Enhancing the therapeutic chemosensitivity of hepatocellular carcinoma cells using alpha-solanine

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**Background:** Anti-cancer chemotherapy although effective it induces serious adverse effects. In addition, cancer cells can develop resistance to chemotherapy. **Aim:** The clinical application of cisplatin is limited by severe side effects associated with high applied doses. The synergistic effect of a combination treatment of a low dose of cisplatin with the natural alkaloid  $\alpha$ -solanine on human hepatocellular carcinoma cells was evaluated. **Materials and Methods:** HepG2 cells were exposed to low doses of  $\alpha$ -solanine and cisplatin, either independently or in combination. The efficiency of this treatment modality was evaluated by investigating cell growth inhibition, cell cycle arrest, and apoptosis enhancement. **Results:**  $\alpha$ -solanine synergistically potentiated the effect of cisplatin on cell growth inhibition and significantly induced apoptosis. This synergistic effect was mediated by inducing cell cycle arrest at the G2/M phase, enhancing DNA fragmentation and increasing apoptosis through the activation of caspase 3/7 and/or elevating the expression of the death receptors DR4 and DR5. The induced apoptosis from this combination treatment was also mediated by reducing the expression of anti-apoptotic mediators Bcl-2 and survivin, as well as by modulating miR-21 expression. **Conclusion:** Our study provides strong evidence that a combination treatment of low doses of  $\alpha$ -solanine and cisplatin exerts a synergistic anticancer effect and provides an effective treatment strategy against hepatocellular carcinoma.

**Keywords:** Cisplatin; Bcl-2; HepG2 cells; miR-21;  $\alpha$ -solanine

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Editor-in-Chief: Prof. M.L. Salem, PhD - Article DOI: 10.21608/IJCBR.2021.63663.1179

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## ***Achillea santolina* and *Raphanus sativus* extracts downregulated NOTCH1, SIX1 and WNT1 developmental gene expressions in breast and colon cancer cell lines**

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**Background:** Although anticancer treatment with chemotherapy is effective, cancer response occurs due mainly to reduction of cancer stem cells. The development of cancer stem cell is regulated by several genes including NOTCH1, SIX1 and WNT1. **Aim:** we have found recently that treatment of Caco2, HepG2 and MCF-7 with *Achillea santolina* or *Raphanus sativus* results antitumor effect. In this study we aimed to evaluate the effect of these natural product on the gene expressions NOTCH1, SIX1 and WNT1 in Caco2 and MCF-7. **Materials and Methods:** Colon adenocarcinoma cell line (Caco2) and Breast cancer cell line (MCF-7) as well as normal amniotic cell line (WISH) were treated with 110 IC50 concentration of *Achillea santolina* and *Raphanus sativus* extracts to compared to 110 IC50 of cisplatin as a reference chemotherapy drug. Total RNA was extracted after 72 hours of treatment and incubation then cDNA was prepared for reverse transcriptase PCR for NOTCH1, WNT1, and SIX1. **Results:** *R. sativus* treatment highly decreased NOTCH1 expression in MCF7 and Caco2 cell lines, while decreased SIX1 gene expression in Caco2 cell line and WNT1 in MCF7 cell line. On the other hand, *A. santolina* observably decreased the WNT1 gene expression in MCF7 cell line. **Conclusion:** The crude extracts of *R. sativus* decreased the developmental gene expression of NOTCH1, SIX1 in Caco2 cell line as same as on NOTCH1 and WNT1 in MCF-7 cell line more than cisplatin chemotherapy. While the *A. santolina* crude extract decrease the expression of WNT1 in MCF-7 cell line more than cisplatin chemotherapy.

**Keywords:** *A. santolina*; NOTCH1; *R. sativus*; SIX1; WNT1

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Editor-in-Chief: Prof. M.L. Salem, PhD - Article DOI: 10.21608/IJCBR.2021.62094.1175

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## Biochemical studies of the effect of arsenic trioxide on Ehrlich ascites tumor

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**Background:** Hexokinase 2 enzyme catalyzes the rate-limiting step in glycolysis. It is overexpressed in several carcinomas including breast cancer to sustain energy for rapidly dividing cells and associates with chemoresistance. However, impact of chemo drugs alone or in combination on hexokinase activity and autophagic cell death is unclear. Arsenic trioxide (As<sub>2</sub>O<sub>3</sub>) (ATO) is a metalloid with potent antineoplastic effects in several types of cancer especially acute promyelocytic leukemia and breast cancer. Due to the cytotoxicity and low efficacy of ATO when it is used alone, a combination of ATO with other chemotherapeutic drugs may provide a rational basis for novel therapeutic combinations. **Aim:** Examine the specific cellular events that account for differential effects of ATO on cancer cell viability and the possible therapeutic combinations remain to be well-defined. **Materials and Methods:** In this report, we used an in vivo murine adenocarcinoma model to validate the effects of As<sub>2</sub>O<sub>3</sub> and cisplatin on hexokinase activity and autophagic cancer cell death. **Results:** We found that the two drugs inhibit hexokinase activity and induce autophagic marker, beclin 1 expression. Interestingly, combining As<sub>2</sub>O<sub>3</sub> with cisplatin synergistically enhanced these effects and alleviated oxidative stress often encountered in As<sub>2</sub>O<sub>3</sub> treatment. Altogether, our data provide direct evidence that inhibition of hexokinase activity and induction of autophagic cell death are mediating the antineoplastic effects of As<sub>2</sub>O<sub>3</sub> and cisplatin. **Conclusion:** findings raise the potential of combining As<sub>2</sub>O<sub>3</sub> with cisplatin as an approach to augment cisplatin-induced cell death and combat cisplatin chemo-resistance in cancer.

**Keywords:** Arsenic Trioxide; Autophagy; Beclin 1; Cisplatin; Hexokinase

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Editor-in-Chief: Prof. M.L. Salem, PhD - Article DOI: 10.21608/JCBR.2021.60584.1152

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## Evaluation of the antitumor effect of trehalose in experimental models

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**Background:** Cancer continues to represent the main cause of mortality in the world, the second leading cause of death worldwide next to cardiovascular disease. Therefore, it is important to find effective non-toxic, inexpensive, and suitable neoadjuvant therapy with methotrexate (MTX) to decrease its dosage without lowering its chemotherapeutic efficacy. **Aim:** This study aimed to investigate the antitumor effect of trehalose (TRE) on mice bearing Ehrlich ascites carcinoma (EAC) and to test whether it can enhance the anticancer potential of MTX. **Materials and Methods:** In this experiment, mice were assigned into 8 groups were used for assessment of antitumor activity of TRE. The antitumor activity of TRE was assessed by measuring the survival time, counting tumor cells, monitoring autophagic activity at the cellular level by flow cytometry, monitoring autophagic and apoptotic regulated genes (Caspase 3, Bec1, and Bcl2 genes) by real-time PCR, as well as the biochemical parameters, oxidative stress markers in liver homogenate, complete blood picture (CBC) and histological studies of all groups. **Results:** Treatment of EAC mice with TRE or MTX alone or in combination resulted in a significant decrease in total, viable, and non-viable tumor cells count as well as the tumor volume in comparison with EAC mice. Treatment with TRE alone or in combination MTX induced a significant increase in the hepatic antioxidant status, a significant upregulation in the gene expression of caspase 3, with the highest expression in the combined group, as compared to the non-treated EAC group. On the other hand, the same treatments resulted in a significant downregulation of Bcl2 and Bec1 genes, with the lowest expression in the combined group. These results showed a significant decrease in autophagic activities in both TRE- and TRE+MTX -treated groups as compared to the non-treated EAC group. Histopathological examination revealed normal lobular architecture with central vein and radiating hepatic cell cords in normal control mice. **Conclusion:** TRE is considered as an autophagic inhibitor for cancer cells which could be used as a potential neoadjuvant for the antitumor drug, MTX, and probably other chemotherapeutic compounds. This new role of TRE coupled with its apoptotic induction property on tumor cells and lack of toxicity on normal cells increases the efficacy of an antitumor drug for treating a spectrum of cancers. (This Ph.D. thesis was approved by the Faculty of Science, Tanta University, Egypt by March 31, 2018).

**Keywords:** Apoptosis; Autophagy; Ehrlich ascites carcinoma; Methotrexate; Trehalose

Editor-in-Chief: Prof. M.L. Salem, PhD - Article DOI: 10.21608/JCBR.2021.57676.1116

## Impact of the treatment with praziquantel and cisplatin on some biochemical parameters after *Schistosoma mansoni* infection and Ehrlich ascetic carcinoma in mouse model

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**Background:** Infections with *Schistosoma mansoni* considers a potential factor for developing cancers in different parts of the human body. **Aim:** This study evaluates the efficacy of cisplatin and its possible role as a complementary medicine with the anti-schistosomal drug; PZQ. **Materials and Methods:** Mice were infected with (40-50) *S. mansoni* cercariae then, after 35 days of infection, mice were (i.p.) injected with 1x10<sup>6</sup> cells/mouse of EAC cells. Mice groups were divided as following; GP I (control), GP II (*S. mansoni* infected alone), GP III (inoculated EAC alone), GP IV (*S. mansoni*/EAC alone), GP V (*S. mansoni*/EAC treated with PZQ), GP VI (*S. mansoni*/EAC treated with cisplatin 10 $\mu$ g), GP VII (*S. mansoni*/EAC treated with cisplatin 40 $\mu$ g), GP VIII (*S. mansoni*/EAC treated with PZQ with cisplatin 10 $\mu$ g) and GP IX (*S. mansoni*/EAC treated with PZQ with cisplatin 40 $\mu$ g). Worm burden, eggs were counted. Also, tumor volume, total tumor cell counts were measured. We assessed liver and kidney function tests, otherwise we evaluate oxidative and antioxidant parameters. **Results:** Our data showed worm burden and egg counts were decreased in single cisplatin treated groups and the tumor cell counts in cotreated groups. Also, Hepatic GSH, GST were improved in co treated groups with PZQ than single ones, while hepatic toxicity parameters were decreased. Overall, we concluded that cisplatin even at low doses has anti-schistosomal effects. Also, PZQ co-administration with cisplatin doses ameliorated the level of GSH, it involves the maintenance of antioxidant capacity in protecting the hepatic tissue against oxidative stress by scavenging the very reactive hydroxyl and peroxy radicals. **Conclusion:** Treatment with praziquantel and cisplatin alters biochemical parameters after *Schistosoma mansoni* infection.

**Keywords:** Antioxidant; Cisplatin; Ehrlich's ascites carcinoma; Praziquantel; Schistosomiasis

Editor-in-Chief: Prof. M.L. Salem, PhD - Article DOI: 10.21608/IJCBR.2021.61969.1173

## Role of metformin in oxaliplatin-induced peripheral neuropathy in colorectal cancer patients

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**Background:** Metformin, an anti-diabetic drug, has been found in recent studies to have multifactorial effects in different clinical settings. **Aim:** Peripheral sensory neuropathy is the most prominently reported adverse effect of oxaliplatin. This study was conducted to evaluate metformin role in oxaliplatin-induced neuropathy. **Patients and Methods:** From November 2014 to May 2016, 40 patients with stage III colorectal cancer were enrolled and randomly allocated to a control group, received 12 cycles of FOLFOX-4 regimen, and a metformin group, received the same regimen plus metformin 500 mg three times daily. The metformin efficacy was evaluated using the brief pain inventory short form "worst pain" item, National Cancer Institute Common Terminology Criteria for Adverse Events (NCI-CTCAE version 4.0) and a 12-item neurotoxicity questionnaire (Ntx-12) from the validated Functional Assessment of Cancer Therapy/Gynecologic Oncology Group. In addition to malondialdehyde, interleukin-6 and neurotensin serum levels assessment. **Results:** At the end of the 12th cycle, the mean pain score in metformin group was significantly lower than those of control group, (6.7 versus 7.3,  $P = 0.005$ ). On the other hand, 95% of patients in control group experienced grade 2 and 3 neuropathy while only 60% experienced grade 2 and 3 neuropathy. Furthermore, metformin group showed significantly higher total scores of Ntx-12 questionnaire than control group (24.0 versus 19.2,  $P < 0.001$ ). Mean serum levels of malondialdehyde and neurotensin were significantly lower in metformin group after the 6th and the 12th cycles. **Conclusion:** Metformin may be a promising drug in protecting colorectal cancer patients against oxaliplatin-induced chronic peripheral sensory neuropathy.

**Keywords:** Colorectal cancer; Metformin; Peripheral neuropathy; Oxaliplatin

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Editor-in-Chief: Prof. M.L. Salem, PhD - Article DOI: 10.21608/IJCBR.2021.57231.1112

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# IJC CBR

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**SECTION 5**

**Drug Discovery**

## Biological role of phlorotannis extracted from brown algae and its activity in the diabetic treatment

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■■■

**Background:** Diabetes mellitus is characterized by hyperglycemia, which is associated with failure of various organs. **Aim:** This study aimed to investigate biological activity including the antioxidant, antibacterial and antidiabetic activities of polyphenolic compound "phlorotannis" derived from Egyptian brown seaweed *Cystoseira compressa* and *Sargassum linifolium*. **Materials and Methods:** Phlorotannis were extracted and confirmed by different chemical and physical tests. The seaweed extracts exhibited higher antioxidant properties. Phlorotannis extracts showed antibacterial activity evaluated against species [*Staphylococcus aureus*, *Escherichia coli*, and *Bacillus cereus*]. In in vivo study, fifty white male albino rats were divided into six equal groups. The first three groups of rats are control normal, control *C. compressa* extract and control *S. linifolium* extract groups, the last three groups which are diabetic by intraperitoneal injection of streptozotocin had one diabetic control and diabetic that got 60 mg/kg of *C. compressa* phlorotannis extract and diabetic that got 60 mg/kg of *S. linifolium* after four weeks of diabetes induction. **Results:** Phlorotannis extracts decrease serum glucose,  $\alpha$ -amylase, glucosidase activity and liver malondialdehyde. However, serum insulin, hepatic glutathione and total antioxidant capacity "TAC" were significantly increased compared with diabetic non-treated groups. Also, phlorotannis make activation of AMPK $\alpha$ 2 expression in skeletal muscle in treated group as compared to diabetic group. The histopathological results supported that phlorotannis extracts markedly reduce damage in  $\beta$  cells of pancreas. **Conclusion:** This study confirmed that phlorotannis extract from *C. compressa* and *S. linifolium* algae have the capacity to act as antioxidant and antidiabetic agents. These results point phlorotannins extracts as potential pharmaceutical resources for human health.

**Keywords:** Antidiabetic; Antioxidant; Brown seaweed; Phlorotannis

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Editor-in-Chief: Prof. M.L. Salem, PhD - Article DOI: 10.21608/JCBR.2021.59486.1131

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## A Biochemical study on the effect of some treatments on bone resorption and formation in osteoporotic rats

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**Background:** Osteoporosis thins bones, weakening them and making them more susceptible to fractures. It may be related to withdrawal of sex hormones by ageing. **Aim:** The present study was conducted to evaluate the bone protective effects of raloxifene, risedronate, and their combination on osteoporotic male and female rats. **Materials and Methods:** Osteoporosis was induced by orchidectomy (ORX) of 35 male Wistar rats and ovariectomy (OVX) of 50 female Wistar rats. Four weeks post-surgery, each of ORX and OVX rats were randomized into 4 groups: control, Raloxifene (RAL), Risedronate (RIS) and Raloxifene+Risedronate (RAL+RIS). RAL dose was 3 mg/kg given orally 3 times/week. RIS dose was 5µg/kg given by s.c. injection, twice weekly. After 6 weeks of treatment, alkaline (ALP) and acid phosphatase (ACP) activities, bone mineral density (BMD), histochemical localization of ALP, gene expression of osteoprotegerin (OPG) and bone morphogenetic protein-2(BMP-2) were examined. **Results:** The OVX and ORX rats showed a significant increase in plasma ALP and ACP activities and histochemical activity of ALP in ORX rats and OVX rats as compared with sham, and attenuated by treatment with RAL and RIS. BMD of femur didn't change after gonadectomy. In OVX-RAL and ORX-RIS, BMD was improved compared to untreated rats. Gene expression of OPG and BMP-2 was down regulated in OVX rats versus sham, but was up-regulated by RAL and RIS treatments. In ORX rats, OPG gene expression was up-regulated versus sham, but was down-regulated by RIS treatment. **Conclusions:** Both RAL and RIS reduced bone turnover and maintained BMD in osteoporotic rats.

**Keywords:** Osteoporosis; osteoprotegerin; Raloxifene; Risedronate

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Editor-in-Chief: Prof. M.L. Salem, PhD - Article DOI: 10.21608/JCBR.2021.59559.1132

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## Molecular and immunological investigation of neuroinflammation induced by mycotoxines

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**Background:** Neuroinflammation represents the coordinated cellular response to tissue damage. Mycotoxins are low-molecular-weight natural products produced as secondary metabolites by filamentous fungi. The toxic effect of mycotoxins on animal and human health is referred to as mycotoxicosis, *Fusarium* species are the main pathogenic fungi causing maize ear and kernel rot worldwide, mainly produce fumonisin B (FB) that contaminate grains and grain products. **Aim:** To test the antifungal effects of corn seed extracts. **Materials and Methods:** In this study, fungi were isolated from corn seeds and ethanolic natural product crude extracts were used as antifungal compounds. Antifungal effects of three extracts were assessed in vitro on toxin production and different toxin concentrations (in vitro study). A newly identified sequence was registered to our study group and was given a new accession number by GenBank. The inhibitory effect for the production of fumonisin B1 was for *Cinnamum zeilanicum* followed by *Berberis vulgaris* and finally *Calluna vulgaris*. Gene expression by Real time PCR the fold change calculated values for the assessment of IL-1 $\beta$ , COX II, iNOS and TNF- $\alpha$  gene expressions showed decreased values. **Conclusion:** Corn seed extracts showed immunological anti-inflammatory effects on neuroinflammation induced by mycotoxines.

**Keywords:** Cinnamon zeilanicum; *Fusarium sporotrichioides*; mycotoxins; natural product; neuro-inflammatory

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Editor-in-Chief: Prof. M.L. Salem, PhD - Article DOI: 10.21608/IJCBR.2021.61334.1161

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## Lactobacillus acidophilus and bifidobacterium bifidum reduce chronic HCV progression

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**Background:** Hepatitis C virus (HCV) is a major leading cause of pathogenesis of liver disease which was treated with IFN-based therapy and recently with Sovaldi®. There is a challenge to explore new drugs. Probiotics are the most common natural therapeutic that can ameliorate liver dysfunction. Aim: study the antiviral and antibacterial responses of the probiotics in patients with chronic (HCV). **Materials and Methods:** patients were treated with IFN/ribavirin, or both IFN and probiotics capsule that was containing L. acidophilus and Bifidobacterium spp. and administered as one capsule per day for a month. Blood and urine samples were collected before and after treatment strategies and were processed for quantitative determination of HCV PCR assay, identification of bacteria by VITEK2 system and 16S r RNA gene sequencing, estimation of probiotics antibacterial activity, as well as counts of leukocytes and CD3+ T cells and CD56+ natural killer cells. **Results:** Treatment of patients with L. acidophilus and Bifidobacteria spp. enhanced the responses of the patients to IFN- $\alpha$  and ribavirin treatment, as shown by the viral titter of HCV PCR assay that clarified the antiviral activity and also the antibacterial activity against the most common bacterial infections in patients with chronic HCV. Additionally, it increased the numbers of CD3+ and CD56+, **Conclusions:** Treatment with probiotics before IFN- $\alpha$  and ribavirin therapy can act as a supportive supplement with antiviral, positive immune response and antibacterial activities.

**Keywords:** Bifidobacterium befidum; Lactobacillus acidophilus; HCV infection, Probiotics

Editor-in-Chief: Prof. M.L. Salem, PhD - Article DOI: 10.21608/JCBR.2021.63823.1180

## Antioxidant and antimicrobial effects of Geranium extracts as flavoring agents in some prepared foods

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■■■

**Background:** Essential oils and their fragrance compounds are a very important part of industry. Geranium extracts are used in numerous health disorders and medical conditions and has been validated as commercial exploitation in many industrial branches. **Aim:** Test the effect of geranium extract against spoilage and pathogenic bacteria, and test if it can be used for the development of novel systems for food preservation. **Materials and Methods:** Geranium steam extract and geranium n-Butanol extract were used as a natural flavor in food products. **Results:** The selected Geranium extracts were used as natural sanitizers to reduce and control pathogen contamination or the growth of native microflora. The inclusion of geranium extracts altered the antioxidant properties of the ice cream and jelly candy samples. Due to some limitations of the extract impacting on texture and color of the product, the extract was recommended to use at the lowest level. **Conclusion:** Geranium was found to be a good source of alternative for the future flavors of ice cream and jelly candy.

**Keywords:** Key words: Antioxidant; Antimicrobial; Hydro distillation; Pelargonium graveolens; Supercritical CO<sub>2</sub>

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Editor-in-Chief: Prof. M.L. Salem, PhD - Article DOI: 10.21608/JCBR.2021.56898.1111

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## Metformin: An AMPK-dependent antidiabetic drug with novel medical applications

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■■■

**Background:** Metformin (MET) is a well-known antidiabetic drug for type 2 diabetes mellitus (T2DM) treatment. **Aim:** To test the therapeutic effects of MET coming from its ability to decrease both the production of hepatic glucose and its absorption via the intestine and improves insulin hormone sensitivity. **Materials and Methods:** MET is used in pre-clinical trials to treat cancer and slow proliferation rate, emerging from its hypoglycemic effect and antioxidant activity. **Results:** MET enhanced the functions of immune T-cells and reduced the proinflammatory mediators in macrophages. Based on the pre-clinical studies, its effect on the reproductive system is confirmed; however, the effect on the sperm number and motility is still in debate. Treatment with MET also showed some beneficial effects on bone health, and its administration led to a deficiency in vitamin B12. Furthermore, MET enhances anaerobic pathways and increases lactic acid levels. **Conclusion:** This study demonstrated clearly the novel uses of MET in different clinical settings with explained mechanisms of actions.

**Keywords:** Anti-diabetic; Anticancer; Antioxidant; Metformin; Obesity

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Editor-in-Chief: Prof. M.L. Salem, PhD - Article DOI:

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## Beneficial prophylactic effects of poly(I:C) and zymosan against *Schistosoma mansoni* infection

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**Background:** The use of vaccination in the control of schistosomiasis at a population level induced low cure rates and also resistance to drugs has been recently recorded in Egyptian patients. For these reasons, a search for new drugs with adjuvant and anti-schistosomal activity is urgently needed. **Aim:** The study focused on newly synthesized ligands that play a central role as inducers of innate and adaptive immune responses and are therefore considered as potential targets for vaccine adjuvants. These ligands include Polyinosinic: polycytidylic acid (Poly (I:C) (TLR3L) and zymosan (TLR2L) which have displayed an impressive array of biological activities including antitumor and antiviral effects. The present study investigated their adjuvant and anti-schistosomal effects in *S. mansoni*-infected mice. **Materials and Methods:** The study was divided into two experimental settings including the vaccination and treatment settings. In the vaccination settings, the mice were assigned into 8 groups. Mice were vaccinated with the ligands 2 times at 2 weeks intervals, then infected with *S. mansoni*. Five weeks post-infection, the mice were euthanized for analysis. In the non-vaccination settings, the mice were assigned into 8 groups. The determination of worm burden, tissue eggs count, assessment of liver function tests, and parameters of oxidative stress were done. **Results:** Vaccination and treatment by Poly (I:C) and Zymosan increased the counts of platelets, segmented neutrophils, eosinophils, and monocytes while decreases the lymphocytes count, indicating to the immunological effect of these ligands. The current study showed that Poly (I:C) and Zymosan displayed an adjuvant with soluble worm antigen protein (SWAP) antigen that associated anti-schistosomal activity and with improvement in the liver enzymes and oxidative stress as compared to the vaccination with SWAP antigen alone. These ligands also showed an apparent effect on the granuloma volume. These TLR ligands had no side effects on normal healthy mice and reduced the adverse effects caused by *S. mansoni* through the improvement of liver enzymes, oxidative stress, reduction of worm burden, and ova count. **Conclusion:** This study is the first study that assesses TLR ligands as adjuvants and treatment for *S. mansoni* infection. Our recommendation is to use vaccination and increase the treatment time of both ligands for significant reduction of worm and ova to preserve normal liver function parameters.

**Keywords:** Poly(I: C); Zymosan; SWAP antigen; Adjuvant; *S. mansoni*

Editor-in-Chief: Prof. M.L. Salem, PhD - Article DOI: 10.21608/JCBR.2021.57652.1115

## Physiological studies on the role of cyanobacteria in ameliorating the toxic effects of copper in trigonella *Foenum gracum*

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**Background:** Cyanobacteria has been found to possess anti-toxic effects. **Aim:** To evaluate the ameliorating effects of *Foenum gracum* on the toxic effects of copper in a greenhouse experiment. **Materials and Methods:** The growth and some metabolic activities of *Trigonella foenum gracum* at 30, 60 days of growth was assessed after treatment with *Nostoc muscorum* (2 g/ kg soil fresh pellets). The yield under different concentrations of CuSO<sub>4</sub> was assessed. **Results:** Application of *Nostoc* in a mixture with Cu significantly increased all growth parameters, photosynthetic pigments and activity, soluble and insoluble nitrogen at 30 and 60 days of growth when compared with their counterparts of Cu treatment. In addition, the content of K<sup>+</sup>, Ca<sup>2+</sup>, P<sup>3+</sup> and iron were increased except for a decrease in Cu level at 60 days of growth. On the other hand, the content of starch and peptides were significantly decreased at 30 and 60 days of growth. Moreover, the activity of both POD and SOD were reduced by applying *Nostoc* to the soil having different concentrations of Cu. Biochemical analysis of the yielded seeds of *Trigonella* revealed that the content of total carbohydrate, total soluble protein and total lipids were significantly increased, whereas total alkaloids and phenolics were significantly decreased. Mixing *Nostoc* with Cu increased the percentage of unsaturated fatty acids when compared with control and Cu singly. Scanning SDS-PAGE gel indicated de novo synthesis of two polypeptides with molecular weight of 44 and 67 KDa. **Conclusion:** Isozyme profile of POD and  $\alpha$  and  $\beta$ -esterase of yielded seeds showed 3 isoforms of POD and  $\alpha$  esterase and two isoforms of  $\beta$ -esterase varied in their intensity and thickening in response to different treatments.

**Keywords:** Amelioration; Biochemical changes; Copper; *Nostoc muscorum*; *Trigonella foenum gracum*

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Editor-in-Chief: Prof. M.L. Salem, PhD - Article DOI: 10.21608/IJCBR.2021.60441.1144

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## A Phytochemical and Biological Investigation of Some Plants Belong to Cycadales Order Cultivated in Egypt

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**Background:** Gymnosperms are naked seed-producing plants and still a dark area in scientific researches although they considered as a rare gift of the nature. Cycads are one of the largest groups of living Gymnosperms. The three extant families of Cycadales are Cycadaceae, Stangeriaceae, and Zamiaceae. According to review of literature, availability of the plants in Egypt, preliminary phytochemical screening of leaves of some plants of gymnosperms belong to Cycadals order, and the results of biological screening, six plants were chosen to be our target of this study. These plants were *Cycas pectinata* and *Cycas thoursaii* (Family Cycadaceae), *Dioon spinulosum*, *Dioon mejiae*, *Dioon merolae* and *Encephalartous laurantianous* (Family Zamiaceae). **Aim:** The study has been classified into two parts: 1) Preliminary biological and phytochemical screening of leaves of the six plants. 2) Biological activities and phytochemical investigation of the leaves of *Dioon spinulosum*, the most active plant. Biological investigation of six plants belonging to Cycadals order cultivated in Egypt. **Materials and Methods:** Antioxidant activity was investigated using different methods: a) Bleomycin-dependent DNA damage, b) ABTS method, c) Assay for erythrocyte hemolysis. For antimicrobial activity, all the plants extracts were individually evaluated for in vitro antibacterial activity against Gram-positive bacteria (*Staphylococcus aureus* and *Bacillus subtilis*) and Gram-negative bacteria (*Escherichia coli* and *Pseudomonas aeruginosa*). The anti-fungal activity was tested against two fungi (*Candida albicans* and *Aspergillus flavus*). For biological investigation of *D. spinulosum* leaves extract. Activity of *D. spinulosum* total methanol extract, pet-ether, methylene chloride, ethyl acetate and n-butanol fractions were investigated. For biological investigation of pure isolated compounds from *D. spinulosum*, nine compounds were subjected to further investigation for antioxidant and cytotoxic activities. **Results:** *Dioon spinulosum* showed significant activity among investigated compounds. Phytochemical investigation of *D. spinulosum* leaves resulted in isolation of two new flavonoids, apigenin 7-O-a-D-glucopyranoside and amentoflavone 7- O- $\alpha$ -L-rhamnopyranoside, in addition to fifteen known compounds: phytone, trans-phytol  $\beta$ -sitosterol, stigmasterol, oliveriflavone, 7,7'',4',4''' tetra-O-methyl amentoflavone, 7,7'',4' tri-O-methyl amentoflavone, scaidopitysin, bilobetin, isoginkgetin, aromadendrin, sotusflavone, engeletin, and eriocitrin for the first time together with amentoflavone. Secondary metabolites isolated from *D. spinulosum* displayed the highest protective activity against DNA damage, higher than the positive control. A promising future may await *D. spinulosum* in drug discovery. **Conclusion:** Results from this study clearly demonstrated that *D. spinulosum* total methanol extract offered an evident for its improvement in the hepatocyte structural changes.

**Keywords:** Apigenin 7-O-a-D-glucopyranoside; Amentoflavone 7- O- $\alpha$ -L-rhamnopyranoside; Biflavonoids; Cycas; *Dioon spinulosum*

Editor-in-Chief: Prof. M.L. Salem, PhD - Article DOI: 10.21608/jcbr.2021.57862.1119

## Antioxidant and antidiabetic activities of some algal species

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**Background:** Algae are known to have active ingredients that have anti-oxidant activities that might have biological importance. **Aim:** Antioxidant and antidiabetic activities of some algal species. **Materials and Methods:** In this study different crude extracts of two microalgae *Spirulina platensis*, *Chlorella vulgaris* and six seaweeds *Turbinaria decurrens*, *Padina pavonica*, *Sargassum muticum* and *Sargassum acinarium*; *Ulva lactuca* as well as *Pterocladia capillacea* were tested to evaluate their antioxidant properties and in vitro antidiabetic potential on  $\alpha$ -amylase and  $\alpha$ -glucosidase enzymes. **Results:** The phytochemical screening of these extracts showed the presence of bioactive compounds that responsible for the antioxidant and antidiabetic activities. In addition, all analyzed extracts exhibited antioxidant activity using DPPH, reducing power and total antioxidant capacity assays in addition to antidiabetic activity. Among these extracts, *S. platensis* methanolic extract and *T. decurrens* acetone extract exhibited the highest antioxidant activity and inhibitory effects on  $\alpha$ -amylase and  $\alpha$ -glucosidase; which was related with its total phenolic content. Both extracts showed no toxicity on normal cell lines using MTT assay. GC-MS analysis of the *S. platensis* ME and the *T. decurrens* AE revealed the presence of different bioactive compounds. Concerning the in vivo study, both *S. platensis* ME and *T. decurrens* AE at different doses caused anti-hyperglycaemic activity by reducing the blood glucose level. A remarkable decrease in different liver and kidney functions and hyperlipidemia related to diabetes. The algal extracts treatment also showed enhancement of body weight loss and improvement of the total protein, albumin and hemoglobin levels. Furthermore, treatment of diabetic rats with the extracts caused improvement of the histopathological changes of the liver and pancreas tissues related to diabetes. **Conclusion:** The investigated compounds may be acted synergistically and responsible for its antioxidant and antidiabetic activities.

**Keywords:** Algae; Antioxidant; Antidiabetic; Gas Chromatography; Mass Spectroscopy; Phytochemical

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Editor-in-Chief: Prof. M.L. Salem, PhD - Article DOI: 10.21608/jcbr.2021.59328.1125

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## Investigative study of *Withania somnifera* family Solanaceae cultivated in Egypt to be used for pharmaceutical industry

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**Background:** An investigative study of Egyptian *W. somnifera* revealed that the plant belongs to chemotype uiolll and having 20-hydroxywithanolides with  $\alpha$ -oriented side chain. **Aim:** Test whether *Withania somnifera* family *Solanaceae* cultivated in Egypt can be used for pharmaceutical industry. **Materials and Methods:** An accurate TLC method was developed and is introduced for the evaluation of this chemotype. Cell viability assay showed that the ethanolic extracts of leaves produce significant anticancer effect in liver and breast cancer cell lines. **Results:** Withanolides E and C had the highest effects against liver cancer. Moreover, withanolide C is pointed out as a lead anticancer agent targeting both breast and liver cancer cell lines. Ripe fruit extract showed the best inhibitory activity towards AChE as well as moderate antioxidant and nitric-oxide scavenging activities which explain the therapeutic potential of this extract in treatment of Alzheimer's. Withanolide S; a major constituent in the Egyptian plant that was also found in the leaves of the Italian and Israelian plant, could be regarded as an interesting drug candidate for treatment of Alzheimer's disease based on its strong (AChE) inhibitory activity. **Conclusion:** All together it can be concluded that unlike the Indian plant that is reputed for the medicinal use of its roots, both the fruits and leaves of Egyptian plant have better biological activities than the roots. Towards improving the extraction efficiency of withanolides, we suggest the use of soxhlet extraction as the optimum extraction method for industrial application using 70% ethanol for extraction of dried powdered leaves.

**Keywords:** Alzheimer's; Anticancer; Withanolides; *Withania somnifera*

Editor-in-Chief: Prof. M.L. Salem, PhD - Article DOI: 10.21608/jcbr.2021.58552.1124

# IJC CBR

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CANCER AND BIOMEDICAL RESEARCH

SECTION 6

**Biological Applications  
of Biochemicals**

## Chemical studies on some chromone derivatives with anticipated pharmaceutical applications

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**Background:** Heterocyclic are known to have multiple applications in particular biomedical settings. **Aim:** The present study reports a convenient protocol for the design and synthesis of new heterocyclic compounds incorporating 1- hydroxy-naphthyl and new angular chromones bearing allylnaphthyl fragments. **Materials and Methods:** The versatile precursor 2-acetyl-4- allyl-1-hydroxy naphthalene was subjected to Claisen-Schmidt condensation but the precursor 6-allyl-3-formyl-4H-benzo[h]chromone was prepared via Vilsmeier–Haack reaction of 4-allyl-1- hydroxy-2-acetonaphthone. **Results:** Some new compounds are considered as promising leads with dual biological activity as antibacterial and antioxidant. The isoalloxazine ring of the cofactor FAD is essential to the recognition of the compound that has proper antioxidant activity. Benzocoumarin ring is essential for the recognition of the amino acid residues. Allyl chain improves the p stacking interaction while the n-propyl chain attenuates the overall interaction. Naphthyl ring needs to be substituted with a short bridge to avoid the ring extended away from the pocket. The antimicrobial and anti-quorum-sensing activities of the newly synthesized compounds showed that many compounds have good and promising activities in comparison with the reference drugs. **Conclusion:** Based on the computational prediction of pharmacokinetics, drug-likeness properties, biological activity, and molecular docking suggested that formyl chromone and tetracarbonyl may be potent antimicrobial drugs.

**Keywords:** Antimicrobial activity; Antiquorum-sensing; Docking

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Editor-in-Chief: Prof. M.L. Salem, PhD - Article DOI: 10.21608/JCBR.2021.60308.1142

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## Some efficient synthetic approaches to construct heterocyclic systems

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**Background:** Heterocyclic compounds containing nitrogen, oxygen and sulfur atoms possess various interesting biological activities. Among these compounds, 1,3-oxathiolan-5-one and its diverse derivatives which are literature documented ones of the most potent core structures in drug design and pharmaceutical industry. **Aim:** This thesis describes the utility of 1,3-oxathiolan-5-one in the synthesis of pyridinonethiol and their annulated systems through multicomponent reaction of 2-methyl-2-phenyl-1,3-oxathiolan-5-one (1), aniline and  $\alpha,\beta$ -unsaturated carbonyl compounds. **Materials and Methods:** Different bioactive heterocyclic systems such as thiophene, furo-oxathiolone, mercapto-diphenylcyclopenta-2,4-dien-one, triazole and thiadiazine were efficiently synthesized via tandem reactions of 1,3-oxathiolan-5-one 1 with different nucleophilic reagents. **Results:** The structures of newly synthesized compounds were confirmed by spectral data, elemental analyses and mechanically discussed. Also, in vitro antioxidant and antitumor activities of these compounds were evaluated. In addition, the synthesized compounds were screened against hepatic cancer cell line HepG-2, as the optimistic results exhibited that compounds 29, 33 and 34 have excellent antioxidant and anti HepG-2 activities. **Conclusion:** The synthesized heterocyclic compounds possess significant anti-bacterial and anti-cancer capabilities.

**Keywords:** Antitumor; Antioxidant; Heterocyclization; Oxathiolanone; Pyridinonethiol

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Editor-in-Chief: Prof. M.L. Salem, PhD - Article DOI: 10.21608/JCBR.2021.60610.1151

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## Quinones as synthon for construction of heterocyclic systems with anticipated bioactivity

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**Background:** Lawsone (2-hydroxynaphthalene-1,4-dione) is a natural product that shows significant biological activity. The National Cancer Institute (NIH, United State) disclosed the lawsone skeleton that contains the quinone moiety as a precursor for clinically cytotoxic activity. **Aim:** Lawsone has interesting pharmacological performance, particularly as antitumor, antimicrobial, anti-parasite (*Trypanosoma cruzi*), and Leishmanicidal activity, anti-lung cancer. **Materials and Methods:** Three different approaches were taken in the synthetic approach. The first approach was based on the synthesis of naphthoquinone annulation that was synthesized from the reaction of 2 with different bi-nucleophilic reagents via Michael addition followed by intramolecular condensation. The second approach was based on the synthesis of new  $\alpha$ -lapachone analogs during the cyclo-condensation reaction of 1 with  $\alpha,\beta$ -unsaturated ketones. The third approach was based on the synthesis of novel spiro lawsone-ring skeletons, which focuses on the synthesis of spiro lawsone ring skeletons by Claisen-Schmidt condensation of 1 with some selected advanced reagents. **Results:** Pharmacological studies of the synthetic compounds provided an indication of biological activities, including effects against hepatocellular carcinoma (HePG-7) and mammary gland breast cancer (MCF-7). The molecular structures of some molecules were examined by using DFT calculations. **Conclusion:** The synthetic compounds possess significant anti-tumor capabilities.

**Keywords:** Alpha Lapachone; Anti-Oxidant; Anti-Tumor; Geometrical optimization; Lawsone

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Editor-in-Chief: Prof. M.L. Salem, PhD - Article DOI: 10.21608/JCBR.2021.60637.1155

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## Synthesis of some heterocyclic of expected bioactivity via reactions of thiazine derivatives

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**Background:** 2-acetylphenothiazine plays an important role in organic chemistry. The behavior of 2-acetylphenothiazine towards various reagents was carried out. **Aim:** The aim of the present work is to design and synthesize some of heterocyclic nuclei through the reaction of phenothiazine derivatives as scaffold moiety with different reagents. **Materials and Methods:**  $\alpha,\beta$ -Unsaturated ketones containing phenothiazine moiety 4, 5, 7 were synthesized by condensation of 2-acetylphenothiazine with different aryl aldehydes 2, 3, and (DMFDMA). Pyrazole skeletons were also synthesized by 1,3-dipolar cycloaddition reactions of  $\alpha,\beta$ -unsaturated ketones with different nucleophilic reagents. Formylpyrazole derivative 36 was synthesized through the Vilsmeier-Haack reaction of phenylhydrazone 35b. **Results:** Azines derivatives of phenothiazines were synthetically constructed from one-pot multicomponent reactions of 1-(4a, 10a-dihydro-10H-phenothiazine-2-yl) ethan-1-one with various reagents. Newly synthesized compounds were screened as antioxidant agents. The sequence of these reactions that adopted for the synthesis of the designed compounds in this thesis is summarized into two sections. **Conclusion:** studying of the biological activity of the newly synthesized compounds as antioxidants properties were performed.

**Keywords:** Anti-oxidant; 2-acetylphenothiazine; Aminonicotinonitriles; Pyrazoles; Pyridine

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Editor-in-Chief: Prof. M.L. Salem, PhD - Article DOI: 10.21608/JCBR.2021.60773.1158

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## Utility of benzopyrones as building blocks to synthesize new heterocycles

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**Background:** Coumarin compounds are one of the most active classes of heterocyclic compounds. They play active roles in medicine due to their biological activity. These compounds are found in many natural products. **Materials and Methods:** The aim of the present work is to design and synthesize fused bicyclic and polycyclic ring systems via enamino derivatives incorporating benzopyrone moiety (coumarin structure). **Results:** Hydroxylochocarpin (a), lonchocarpin (b) and lonchocarpene (c) are used as anticancer reagents. Moracin D (d) used as an antifungal while cromakalim (e) produces anti-hypertensive effects and SD-8381(f) produces anti-inflammatory effects as a new cyclooxygenase inhibitor. Catechin (g) and epigallocatechin gallate [EGCG] (h) both represent antiallergic and anticancer effects, while KRH-102140 (i) is identified as a5-lipoxygenase (5-LO) inhibitor. Seseline (j) and xanthylein (k) exhibit anticancer activities. Rotenone (l) used as an anti-anaphylactic agent for treating asthma. Also dronabinol [ $\Delta^9$ -THC] (m) and other cannabinoids used for treating symptoms of cancer. Suksdorfin (n) inhibits the human immunodeficiency virus (HIV) while daleformis (o) inhibits the endothelin-converting enzyme. **Conclusion:** The synthesized bicyclic and polycyclic ring systems with coumarin structure possess significant biological activities.

**Keywords:** Anti-oxidants; Anti-tumor; Benzopyrones; Coumarin

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Editor-in-Chief: Prof. M.L. Salem, PhD - Article DOI: 10.21608/JCBR.2021.60822.1160

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## Chemical studies of some fused heterocyclic compounds containing oxygen with anticipated biological interests

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**Background:** Coumarin compounds are one of the most active classes of heterocyclic compounds. They play active roles in medicine due to their biological activity. These compounds are found in many natural products. **Aim:** This study aimed to synthesize some new compounds containing oxygen and nitrogen. The newly prepared compounds are evaluated biologically as antituberculosis, anti-inflammatory, and anti-tumors. Also, some computational measurement studies were carried out as docking, drug prediction, and modeling. **Materials and Methods:** The present work divided into three parts: Part 1: Unorthodox synthesis, biological activity, and DFT studies of novel and multi functionalized naphthoxocine derivatives Part 2: Synthesis of some novel heterocyclic compounds derived from naphthopyranone-3-carboxaldehyde and 3-carbonitrile. **Results:** The first pathway concern with the effect of mononucleophiles such as 4-amino antipyrine and 2-amino benzothiazole. The second pathway promotes the effect of 1,2-N, N-nucleophiles such as hydrazine hydrate. The third pathway study the effect of 1,3-C, N-nucleophiles such as cyanoacetamide and N-(aryl or hetero aryl) derivatives to building up the nicotinonitrile derivatives. The fourth direction the reactivity towards a variety of 1,4-N, N-(or N, S-) binucleophiles. Part 3: Computational and biological evaluation the newly prepared compounds are evaluated pharmaceutically as antituberculosis, anti-inflammatory, and anti-tumors. Also, computational measurement studies were carried out as docking, drug prediction, and modeling. **Conclusion:** The studies fused heterocyclic compounds containing oxygen showed appreciated biological activities.

**Keywords:** Antituberculosis; DFT studies; Naphthoxocine

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Editor-in-Chief: Prof. M.L. Salem, PhD - Article DOI: 10.21608/JCBR.2021.59452.1141

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## Current nursing practices for managing children with burn injuries

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**Background:** Triazines represent a promising scaffold for cancer treatment due to their similarity to the biologically active purine and pyrimidine systems. Besides, triazines and annulated compounds exist in the skeleton of numerous natural and synthetic chemotherapeutic agents such as Azanucleosides (6-azacytosine and 6-azauracil). Also, triazine derivatives proved to display antiviral, anti-inflammatory, antimicrobial and antifungal activities. Moreover, it was found that triazine derivatives display significant wide spectrum anticancer activities against lymphoblastic lung adenocarcinoma A549, leukemia CEM and myeloid leukemia K562 cancer cell lines. **Aim:** Test the antimicrobial and antitumor activities of nitrogenous precursors in a fused or binary heterocyclic system. **Materials and Methods:** Newly series of triazine-based thiadiazol, thiadiazine, thiadiazepine, pyrazole tetrazepino[b]indol-one, triazolotriazine, tetrazolotriazine, triazinotetrazine, and triazinotetrazepinoindole moieties were synthesized, spectrally discussed and mechanistically discussed. On the other hand, the synthesized compounds were evaluated against different types of biological bioassays (Antitumor, Antioxidant and Antimicrobial). Also, compounds 33c and 37 were evaluated against three human cancer cell lines (HepG-2, HCT-116, and MCF-7) for their in-vitro anticancer activities. **Results:** The results declared that all compounds had a potent anticancer activity with IC50 values ranging between 10.8 and 23.4  $\mu$ M. **Conclusion:** Th synthesized nitrogenous precursors in a fused or binary heterocyclic system expressed antimicrobial and antitumor activities.

**Keywords:** Anti-tumor; Anti-oxidant; 1,2,4-Triazine

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Editor-in-Chief: Prof. M.L. Salem, PhD - Article DOI: 10.21608/JCBR.2021.60293.1148

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## Antibacterial Activity of Seaweeds against Urinary Tract Infection with Special Reference to the Virulence Genes

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**Background:** Seeking natural and safe sources for the treatment of multidrug resistance bacteria (MDR) has become a global need. This study showed the ability of some common Egyptian seaweeds as promising treatment bases for human urinary tract infection (UTI) diseases and as new antibacterial agents to replace synthetic antibacterial drugs. **Aim:** To evaluate the effect of seasonal variation on the antibacterial activity of some seaweeds against the bacterial isolates causing urinary tract infection (UTI) diseases and investigated its virulence genes factors in order to genetically compare the virulence activities of the affected UTI strains after seaweed extracts treatment. **Material and Methods:** Pathogenic UTI bacterial isolates were collected from urinary tract infected patients at Tanta University hospitals, Department of Urology. After morphological and biochemical investigations, the bacterial isolates were classified into 3 groups of Gram-negative species of *Escherichia* sp., *Klebsiella* sp. and *Proteus* sp., which were the main cause of the UTI infection and were identified using Vitek system 2 technique. Different seaweeds (macroalgae) belonging to different divisions viz. *Enteromorpha intestinalis* and *Ulva lactuca* (Chlorophyta), *Petalonia fascia* and *Sargassum vulgare* (Phaeophyta), *Gelidium spinosum* and *Jania rubens* (Rhodophyta) were collected seasonally during 2015-2016 from Abu-Qir Bay, Alexandria, Egypt. In order to extract the antimicrobial material, diverse polar solvents (85%) of acetone, chloroform, diethyl ether, ethanol, hexane, methanol, and water were used. PCR was used to investigate the virulence genes responsible for multidrug resistance of the UTI bacterial strains. **Results:** The highest antibacterial activity was recorded for the screened green algal species in spring season followed by winter, summer and finally autumn seasons. The red algal species reached its maximum antibacterial activity in summer season followed by autumn, winter, and spring seasons. The brown algal species were detected only in spring season and showed the lowest antibacterial activity. Collectively, the strongest antibacterial activity was recorded for the ethanolic extract (85 %) of *Ulva lactuca* green seaweed in spring season. The UV absorption of these 5 fractions showed the same absorption peaks at 245, 401 and 666 nm, respectively by using UV spectrophotometer (UV 2101/pc). Therefore, these 5 fractions were pooled together to obtain the active compound of *Ulva lactuca* ethanolic extract. The phytochemical screening of this active compound indicated the presence of phenolic, flavonoid, saponins, alkaloids and glycosides secondary metabolites. FTIR analysis indicated the presence of u OH group, u CH aliphatic (CH, CH<sub>2</sub> and CH<sub>3</sub>), u C=O, u C=C, u C-O, u aromatic phenyl ring (CH, CH<sub>2</sub> and CH<sub>3</sub>). All the strains contained ureC genes in a rate of 96.66%. The PCR amplicons of hpmA gene was detected in the three bacterial strains. **Conclusion:** Seaweed derived compounds proved their ability as new natural and safe source for antibacterial agents, which could reduce the virulence genes activity and prevent the resistance and pathogenicity of these kind of pathogenic bacteria

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Editor-in-Chief: Prof. M.L. Salem, PhD - Article DOI: 10.21608/jcbr.2021.57971.1121

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## Investigating the Efficacy of Biocides Used in Tanta University Hospitals on Antibiotic Susceptibility and Virulence of Bacterial Isolates

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**Background:** Bacterial resistance to antibiotic is a serious challenge. There is a need to study the impact of biocides on the emergence of this resistance. **Materials and Methods:** A total of 1000 samples including 600 clinical samples comprising urine (58), blood (166), sputum (247), stool (36), and wound pus (93) plus 400 environmental samples were collected from different departments of Tanta University Hospitals, Egypt. All samples were cultured on nutrient agar, then stained by Gram stain and examined microscopically. Gram negative (n=485) and Gram-positive bacteria (n=115) were subjected to biochemical identification and then confirmed by culture on Hi chrome agar medium. The susceptibility of all the recovered bacterial isolates (n=600) to different antibiotics and different biocides (BAC, TCS, phenol, hydrogen peroxide, chlorohexidine and citric acid) was performed using agar dilution and broth dilution methods, respectively. **Results:** The increase in antibiotics MICs was relatively more pronounced in *Escherichia coli* (n=78), *Klebsiella pneumoniae* (n=50), *Proteus mirabilis* (n=31) and *Pseudomonas aeruginosa* (n=43) isolates after adaptation to benzalkonium chloride (BAC) and triclosan (TCS). After adaptation, multiple observations were recorded: 1) BAC and TCS significantly increased ( $p < 0.05$ ) efflux activity in *E. coli* and *K. pneumoniae* isolates, respectively; 2) marked increases in the expression of the efflux pump genes *acrB* and *yihV*, *mdfA*; and *norE* genes; 3) significant decreases in the membrane integrity and permeability; 4) morphological modifications ranged from deformed cells, with individual bumps, grooves, ridges, and cavities, to overall cell surface wrinkling; 5) increases in the average adhesion index; and 6) increases in the HI and in *intI* and *intII* genes were detected in the tested isolates. **Conclusion:** There is a potential of certain biocides to contribute in the emergence of antibiotic resistance in bacteria. This might have a role in the detection of the relatively high percentage of the multidrug resistant bacterial isolates in the present work.

**Keywords:** Adaptation; Antibiotics; Biocides; Efflux; Membrane; Resistance

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Editor-in-Chief: Prof. M.L. Salem, PhD - Article DOI: 10.21608/jcbr.2021.57805.1117

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**International Journal of Cancer & Biomedical Research**  
**(IJCBR) Online ISSN 2682-2628**

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