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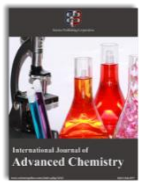

A comprehensive review on functional roles of cancerous immunoglobulins and potential applications in cancer immunodiagnostics and immunotherapy

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Abstract

In this research, poly (D, L-lactide-co-glycolide)-block-poly (ethylene glycol), (PLGA-PEG) nanoparticles (NPs) of less than 195 nm in diameter containing of Naringenin (NRG) a naturally flavonoid were synthesized. Encapsulated form NRG improves its medical properties and solubility. The therapeutic efficacy of the encapsulated naringenin (NRG-NPs) and NRG on human lung epithelial (A549) and mouse mammary (4T1) carcinoma cells proliferation was determined by MTT assays. The cytotoxicity potency was rated as follows: NRG-NPs > NRG. The antioxidant effects of the NRG and NRG-NPs were also determined by FRAP method. Our results show that NRG-NPs are cytotoxic compounds for cancer cells and anti-cancer effect can be attributed to the presence of Fe chelatory and antioxidant effects of NRG-NPs.

Keywords: *Cancerous Immunoglobulins; Cancer Immunodiagnostics; Cancer Immunotherapy.*

1. Introduction

Colon cancer is currently of high incidence and mortality rate. Identifying the factors influencing its prognosis can be very beneficial to its clinical treatment. Recent studies have shown that lymph nodes ratio can be considered as an important prognostic factor. The aim of the present study is to investigate the effect of this factor on the prognosis of the patients presenting with stage III colon cancer and to compare the result with the effect of lymph node stage on their prognosis [1-18]. This cross-sectional study was carried out on 66 patients of stage III colon cancer, who met the study inclusion criteria. Patients were categorized into four groups based on Kaplan-Meier plots: LNR1 0-12%, LNR2 13-40%, LNR3 41-84% and LNR4 85-100%. Survival was estimated by Kaplan-Meier method, and differences analyzed by Log-rank test [19-89]. A Cox proportional hazards model was used for multivariate analysis. Lymph nodes ratio was a significantly variable both in overall survival (P<0.0001) and in disease-free survival (P=0.009). Lymph node stage was significant in overall survival (P=0.008) but not in disease-free survival (P=0.05) [90-157]. Multivariable analysis of overall survival showed lymph nodes ratio as the only independent prognostic factor. Lymph node ratio is a more accurate prognostic factor than lymph node stage in overall survival and, in particular, in disease-free survival in patients with stage III colon cancer [158-208].
In this study, the honey bee mating optimization algorithm (HBMO) is proposed for optimizing drug schedules in cancer chemotherapy model with considering adjustable rest period. Cancer treatment with chemotherapy drugs have dangerous side effects on patient's body [209-273]. The design aims are traded-off between two opponent aims, eliminate of tumor cells and reducing of side effects after a predefined time. Moreover, there are clinical limitations in treatment administration such as drug concentration, drug toxicity and drug resistant [274-279]. So, drug schedules must be balanced between the reducing of tumor cells, drug concentration and drug toxicity during fixed period of treatment with no drug resistant. Two drug scheduling types are presented in this work, continuous and discontinuous [280-287]. HBMO that is a nature inspired algorithm which simulates the process of real honey-bees mating, is used to optimize the dose quantities with rest periods (periods of treatment that chemotherapy is stopped). Comparison of the results with previous works shows that in the case of discontinuous dose the number of remained cells decreased significantly, and in the case of continuous drug dosage the results are in the order of best previous results [288-356].

2. Biological and immunological studies of cancerous immunoglobulins and rp215

2.1. General comparison of normal and cancer immune systems

In this research, poly (D, L-lactide-co-glycolide)-block-poly (ethylene glycol), (PLGA-PEG) nanoparticles (NPs) of less than 195 nm in diameter containing of Naringenin (NRG) a naturally flavonoid were synthesized. Encapsulated form NRG improves its medical proper-

ties and solubility. The therapeutic efficacy of the encapsulated naringenin (NRG-NPs) and NRG on human lung epithelial (A549) and mouse mammary (4T1) carcinoma cells proliferation was determined by MTT assays. The cytotoxicity potency was rated as follows: NRG-NPs > NRG. The antioxidant effects of the NRG and NRG-NPs were also determined by FRAP method. Our results show that NRG-NPs are cytotoxic compounds for cancer cells and anti-cancer effect can be attributed to the presence of Fe chelatory and antioxidant effects of NRG-NPs.

2.2. Immunohistochemically studies with RP215 as a probe

This research has suggested a practical mathematical model by considering non-specific cell cycle for drug resistance in chemotherapy of the cancer. In this model, two models have taken into account to occupy the medicine elimination of the cancerous cells. This study aims to investigate the role of cancerous cells resistance to any of both types of medicines in development of the cancer and creation of populations' resistance to any medicine by using above-mentioned model. One of the main specifications of this model is displaying the development process of a unique cell and turning it into cancerous cells. By such a view, one could study the role of inherent resistance and or acquired resistance of cancerous cells comparing to chemotherapy in different stages of development and or inhibition of the cancer. Using exploratory searching methods, this thesis provided a methodology for optimizing the chemotherapy of cancer in a mathematical model with non-specific cell cycle. This study used two intelligent optimizing algorithms including bee algorithm and genetic algorithm as tools used in optimal control. The general objective of this study includes controlling the development of resistant cells by using minimum amount of medicine comprised from two different cytotoxic factors. Results indicate that modern exploratory optimization methods including above algorithms are considered as proper selection for optimizing the complex systems and provide effective solution for preparing a proper schedule for injecting the medicine to control the development of cancerous cells.

2.3. Functional effects of RP215 on cultured cancer cells

Breast cancer is the second diseases of death in women next to lung cancer. Recently, selecting highly specific mAbs, optimizing linker technology and improving cytostatic of linker and drug can improve level of producing for ADCs in breast cancer. In silico target is one of the most technologies that enable the prediction of biological target to protein on basis chemical structures. Similarity search and docking of structure of chemical compounds is helped to design and synthesis chemical linker compounds using for ADCs. In this study, ten compounds have been mentioned as similarity search for cytostatic cyclohexane 1,3,5-trione compound which are illustrated range of P active is 0,0335 also P inactive is 0.065 then using BRCA1 and Herceptin protein in Argus lab 4.01 for molecular computational docking. The 3D crystal structure of the protein was retrieved from protein data bank (PDB) and protein binding sites were identified for cytotoxic cyclohexane 1, 3, 5-trione as ligand. ARG 1649 amino acid in BRCA1 with -5.8410 Kcal/mol and ALA 810 amino acid in Herceptin with -5.9355 Kcal/mol have more significant value energy in Argus lab software when do dock between protein as mAb and chemical compound as linker in ADCs.

2.4. Other studies related to the roles of RP215 and cancerous immunoglobulins in cancer immunology

A large number of women with breast cancer experience psychological distress during the course of diagnosis and treatment. Forgiveness as well as Acceptance and Commitment Therapy (ACT) are two programs that appear to be relatively efficacious in reducing psychological problems of these patients. The aim of this study was to investigate the effect of incorporating forgiveness to acceptance-based strategies on psychological adjustment of breast cancer patients. The data of current study came from 29 patients suffered from breast cancer who randomly distributed into two groups of treatment and control. All the participants were in stage 0-II of breast cancer and completed their breast surgery. Moreover, they completed Bell Adjustment Inventory before and after the intervention. The treatment group received the therapy over a 12-week period. Based on the findings, the therapy included forgiveness and acceptance-based strategies could meditate social and emotional psychological problems of cancer patients significantly ($p<0.05$). The effect size of the intervention was in the moderate range. However, no significant difference was found in home adjustment. These preliminary findings suggested that incorporating forgiveness to acceptance-based strategies had a positive effect on psychological adjustment of breast cancer patients.

The present study was undertaken to investigate the chemotherapeutic activity of Ferula (F.) assa-foetida hydroalcoholic extract on colon cancer induced by 1,2 dimethylhydrazine (DMH) in rat. Rats were classified into 4 groups: a control group without DMH; a group with injected DMH and two groups receiving F. assa-foedita extracts after DMH injection as chemotherapeutic groups. The effects of the extracts were tested by estimating the detoxification enzymes (GST & CYP 450). In following, the colon tissues were collected for colonic β-catenin assessment and histopathological analysis. The results showed that the treatment of cancer group with F. assa-foedita indicated a significant decrease in the expression levels of β-catenin and CYP450 together with the elevation of GSTs (activity and protein). These data are in parallel with decreased ACF formations in histopathological biopsies in F. assa-foedita extract treated groups. Thus, the results obtained from the present study suggested the F. assa-foedita extracts as an effective chemotherapeutic agent on colon carcinogenesis induced by DMH.

The use of liposomal and biodegradable polymeric nanoparticles (NPs) to encapsulate and deliver therapeutic compounds has increased because of clinically demand. In this study, we focused on new hybrid carrier; poly (D, L-lactide-co-glycolide) (PLGA)–lecithin nanoparticles for controlled release of N-acetyl cysteine (NAC) to lung cancer cell line. These core–shell NPs consist of (i) a PLGA hydrophobic core, and (ii) a soybean lecithin mono-layer shell, and were synthesized by a nanoprecipitation combined with self-assembly method. Nanoparticles were characterized in terms of surface morphology, FTIR spectroscopy, size distribution, in vitro drug release by high performance liquid chromatography (HPLC) and differential scanning calorimetry (DSC). The results indicate that the hybrid NPs around hr to release of NAC versus hr for PLGA NPs. To evaluate the nanoparticles cytotoxicity, cell cytotoxicity test was carried out on the Cor L human epithelial lung cancer cell line and showed cell viability at NPS. Our data suggest that the PLGA–lipid core–shell NPs may be a useful new controlled release drug delivery system.

The study deals with the differentiation of mental health level between first stage and advance stages of cancer patients, including inpatients and outpatients of Bharat Cancer Hospital and Research Institute of Oncology, Mysore, India (2006). The aim of the study was to assess mental health among two stages of cancer patients. The data were collected from 30 first stage cancer patients and 30 fourth stages (advanced)of cancer patients and who included male and female, married and unmarried patients available. General Health Questionnaire (GHQ28) including four subscales (Somatic symptoms, Anxiety, Social dysfunction and Depression) was used to assess mental health. The results revealed that there was significant difference in all subscales between first stage and advanced stage of cancer patients. pre-

sent study establish that the cancer stage position can be influence of cancer patients' mental health, in other word the mental health of cancer patients depending to stage of cancer, can be alter.

The most common psychological effects of breast cancer patients are suffering from There is anxiety and depression. The present study was conducted to evaluate the effectiveness of group cognitive - behavioral therapy in reducing depression and anxiety in women with breast cancer. This was a trial study with pre-test, post-test control group. For this purpose, were selected among women with breast cancer who were referred to the American Institute for Cancer Research (AICR) in 2013. The selected sampling and sampling people 24And were replaced randomly divided into two groups of 12 as test and control groups. The data gathering was conducted through a questionnaire Beck Depression and Anxiety. Data obtained were analyzed using analysis of covariance and using the software SPSS. Findings showed that treatment led to a decrease in anxiety and depression in the experimental group compared with the control group significantly. Cognitive - behavioral therapy has an important role in reducing anxiety and depression in patients with breast cancer by reducing anxiety and depression, altered Finally, the cognitive intervention cognition and increasing their safety.

The cancer involves its infected people in all mental pressures; the pressures that affect their life, job and social relationships and if they are not solved, complicate the patient's status. Cognition therapy based on mindfulness is a method to reduce the distress. The objective of this study is to investigate the Effectiveness of cognitive-behavioral therapy and mindfulness-based cognitive therapy on reduction of distress of patients infected by breast cancer in Isfahan. Data collection tool: For this purpose, 45 women infected by breast cancer hospitalized in the American Institute for Cancer Research (AICR) were selected through convenient method and processed randomly in three groups of 15 subjects: Mindfulness-based cognitive therapy, cognitive-behavioral therapy and control. Before and after mindfulness and cognitive-behavioral therapy training, the groups were tested with respect to the distress level. Mindfulness and cognitive-behavioral therapy was trained to the test group during 8 sessions each 1 hour. The results were analyzed using analysis of variance. The summary of ANCOVA between three groups of distress scores of testers in both pretest and posttest stages indicated that training the mindfulness has been effective($p<0/05$) on reduction of distress scores of trained patients. practices and trainings based on mindfulness-based cognitive therapy and cognitive behavioral therapy were influential on cognitive system and information processing by escalating the participants` awareness of the present moment, through special techniques such as focusing on the breath and body and being aware of here and now. Therefore, considering the positive effect of these two types of practice and training in treating distress of patients infected by breast cancer, widespread usage of these ways is recommended and this intervention method may be used independently or along with other treatment methods such as pharmacotherapy to reduce the distress of these sufferers.

Endoplasmic reticulum has a critical role in the synthesis and folding of secretory and membrane proteins. High accumulation of proteins in ER activates the unfolded protein response and glucose regulated protein 78 or GPR78 plays an essential role in this pathway. Unfolded protein response is activated in cancerous cells due to their adverse condition to survive and it has been shown that GRP78 can be expressed in tumor cell membrane. Overexpression and localization of GRP78makes it a suitable target for the treatment of cancer. This review describes cellular localization, biological function, and role of GRP78 in cancer induction. Methods for tumor inhibition via GRP78 are also discussed.

Breast Cancer is the most widespread Cancer among women. Breast cancer is the second leading cause of cancer death in women. The number of new cases of breast cancer was 124.8 per 100,000 women per year. The number of deaths was 21.9 per 100,000 women per year. These rates are age-adjusted and based on 2008-2012 cases and deaths. This represents about 12% of all new cancer cases and 25% of all cancers in women. Conventional diagnosis methods of Breast Cancer include biopsy, mammography, thermography, and Ultrasound imaging. Among these methods, mammography is the most efficient method for the early diagnosis of Breast Cancer. Detecting Breast Cancer and classifying mammography images are the standard clinical procedures for the diagnosis of Breast Cancer. In order to classify mammography, is provided automated computer-based detection methods. In this study, Gray-Level Co-occurrence Matrix and Cumulative Histogram features were used. We also use a Decision Tree as a classifier system. Then we introduce a new algorithm that called Discrete Version of Imperialist Competitive Algorithm as a global optimization algorithm in discrete space, and we use this algorithm for finding the best features of the extracted features.

Microarray data have an important role in identification and classification of the cancer tissues. Having a few samples of microarrays in cancer researches is always one of the most concerns which lead to some problems in designing the classifiers. Therefore, gene selection techniques should be utilized before classification to remove the non-informative genes from the microarray data. In this work, a new method is proposed for gene selection based on hybrid Binary Particle Swarm Optimization (BPSO) and Bayesian Linear Discriminant Analysis (BLDA) in order to classify a large scale of microarray data. The proposed algorithm is applied on four cancer datasets and its results are compared with other existing methods. The results illustrate that the proposed algorithm has higher accuracy and validity in comparison to other existing methods and is able to select the small subset of informative genes in order to increase the classification accuracy.

Breast cancer is the most common type of cancer among women worldwide and affects American women at least one decade earlier than their counterparts in the developed countries. The aim of this study was to determine whether northeastern American breast cancer patients, who were either pre- or postmenopausal, had differences pertaining to their body mass index (BMI) and obesity incidence in comparison with controls. A case-controlled, cross-sectional study was performed to assess the BMI of 214 patients, who were either pre- or postmenopausal and had been diagnosed with breast cancer via excisional biopsy. Patients were compared to 463 healthy women. Regardless of their menstrual status, patients and controls exhibited a significant difference in the mean BMI (P-value = 0.04). When the menstrual status and BMI were analyzed, the obesity rate was higher among both premenopausal (P-value = 0.03) and postmenopausal women. Our results showed that there was an increased risk of breast cancer among obese.

Permanent change in the dynamic characteristics of a system, by exerting an input in a finite duration, is a very interesting and challenging topic in control engineering. We show that if an input effect on the parameters of the system instead of its states and change them, it can alter the dynamics of the system even after its elimination. Then, the application of this subject is used in cancer modeling and dynamic analysis. In this research, a novel mathematical model is developed for tumor–immune system with positive immune response, focusing on the role of external inputs in the progression of cancer which is not considered yet. We also conducted an investigation in to the effects of input on dynamic system, and provide a comprehensive discussion of how cancer has variable behavior patterns throughout the lives of patients. The behavior of the cancer (with inputs) is studied using the trajectory patterns and stability analysis. We show that Hope bifurcation may occur due to change in the normal rate of changing of ECs into the tumor site caused by external inputs. Therefore, the present analysis suggests that a proper treatment method should change the dynamics of the cancer instead of only reducing the population of cancer cells.

3. Conclusion

In this study, a new mathematical model is developed to represent the interaction between healthy and cancer cells in the human body, focusing on the role of input on the dynamics of the cancer. Therefore, the effect of input, acted in limited duration, on the dynamics of a system is investigated. It is shown that nonlinearity is a necessary condition for a system in order that its dynamical properties change due to a limited time acted input. Then, based on this new approach, the best radiotherapy protocol is extracted. For this purpose, three aspects of constant radiation are considered. In this study we display consequences for protocols applied, taking into account the sort of fractionation, the dose per fraction, treatment time and the total dose. The simulations were performed with the aim of determining which protocol has minor damage in patients exposed to radiation. In other words, which protocol has the lowest fraction of normal cell kill (FN) and shorter time for the tumor removal. According to the results, the accelerated fractionation is the best protocol. Also, after removing the radiotherapy the patient become healthy and the cancer do not relapse due to change in the dynamics of the cancer. So, the present analysis suggests that a proper treatment method should change the dynamics of the cancer instead of only reducing the population of cancer cells.

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