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Poster Session Abstracts

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Bioaccumulation and Removal of Pb and Cr from Aqueous Solutions by Two Aquatic Macrophytes

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Pollution by toxic heavy metal in water and soil is a major environmental problem, and most conventional remediation approaches do not provide acceptable solutions. Wetland plants are being used successfully for the phytoremediation of trace elements in natural and constructed wetlands. Under the present investigation effectiveness of two aquatic macrophytes Ceratophyllum demersum (Rigid Hornwort) and Lemna gibba (duckweed) were tested for the removal of two toxic metals (Pb and Cr). These plants were grown at four different concentrations (2.0, 4.0, 10.0 and 15.0 mg/L) in single metal solution of the two metals and were separately harvested after 2, 4, 6, 9 and 12 days in laboratory experiment. These plants have performed extremely well in removing the Cr and Pb from their solution and were capable of removing up to 95% of lead and 84% of chromium during 12 days incubation period. Highest removal was observed on 12th day of experiment. Results revealed Lemna gibba as the most efficient for the removal of selected heavy metals followed by Ceratophyllum demersum. Results from analysis confirmed the accumulation of Pb and Cr within the plant and a corresponding decrease of these metals in the water. Significant correlations between metal concentration in final water and macrophytes were obtained. Plants have accumulated heavy metals in its body without the production of any toxicity or reduction in growth. Selected plants shown a wide range of tolerance to the selected metals and therefore can be used for large scale removal of heavy metals from waste water.

Factors Affecting Cyst Formation of Azotobacter Chroococcum for its Application as a Biofertilizer

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Beneficial free living soil bacteria especially Azotobacter chroococcum are widely spreading in Egyptian soil and usually referred to as plant growth promoting rhizobacteria (PGPR). Azotobacter sp. were isolated from different locations in Egypt and identified as Azotobacter chroococcum as their morphological and physiological properties according to Bergey's Manual of Systematic Bacteriology. Species of Azotobacter are known to form heat and desiccation-resistance cysts that have a long life. Encystment in A.chroococcum can be induced by different methods i.e., butanol and ethyl alcohol as a sole carbon source. The cyst formation was detected by accumulation of poly-β-hydroxybutyrate, alginate formation, the morphology of vegetative and cyst forms were examined by cyst's stain and electron transmission microscope. The resistance of cyst against different stress factors was investigated as the effect of heat resistance, pH range, NaCl tolerance and desiccation-resistance. Physiological characteristics of A.chroococcum such as acetylene reduction activity (nitrogenase enzyme) and production of some plant growth promoting substances such as Indole acetic acid (IAA), hydrogen cyanide (HCN) and sidrophores production were

also studied. Analysis with Random Amplified polymorphic DNA-Polymerase Chain Reaction (RAPD-PCR) was used to compare between the similarity pattern of the selected Azotobacter isolates and the reference strain and used as an identification tool of polymorphism. SDS-polyaclyramid gel electrophoresis (SDS-PAGE) has been used to give the total protein pattern as a direct reflection of the gene expression of Azotobacter chroococcum under vegetative and cyst condition. Preservation and survival of vegetative and cyst forms of A.chroococcum in the liquid and carrier based inoculants through different periods was estimated. Evaluation of the effect of Azotobacter chroococcum under vegetative and preserved cyst liquid based inoculants as a biofertilizer on the growth of maize plants was studied.

Saffron Attenuates D-Galactosamine/Lipopolysaccharide-Induced Liver Injury in Rats

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Background & Aims: Crocus sativus L., commonly known as saffron, is a perennial stemless herb of the Iridaceae family. It is one of the oldest and most expensive spices, bears importance to many cultures besides being a popular colouring and flavouring agent in culinary purposes. This study aimed to evaluate the modulating capacity of C.sativus on hepatocellular apoptosis induced by D-GalN/LPS in rat; in comparison to a hepatoprotective agent, pentoxiphylline. Method: C.sativus ethanolic extract was orally given to rats pre- and post- hepatotoxicity induction using D-GalN/LPS (300mg/kg/30µg/kg, i.p. respectively). Assessment of some serum biochemical parameters, as well as, histopathological, immunohistochemical examinations and DNA damage evaluation of liver sections were also done. Results: Both pre- and post-treatment of hepatotoxic rats; reversed the altered biochemical, histopathological and immunohistochemical findings nearly to normal values. In conclusion: C.sativus resulted in alleviation of liver histopathological injury, attenuation of cell apoptosis and reduction in DNA damage of murine liver injury; supporting its use as hepatoprotective and heptotherapeutic natural remedy.

Design and Synthesis of Novel Tetra-Hydro-ß-Carbolines as Kinesin EG5 Inhibitors

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Inhibitors of kinesin spindle protein (KSP) are a promising class of anticancer agents that cause mitotic arrest in cells through blocking of the formation of the bipolar mitotic spindles. In this proposal, we explain the design and synthesis of a novel series of tetrahydro-ß-carboline analogs based on the structure of the known KSP inhibitor HR22C16. Two main approaches will be adopted namely keeping the tetrahydro-beta-

carboline scaffold but varying both the C5 substituents and the N-substituents of the hydantoin ring, another appraoch would be the replacement of the hydantoin ring with a final basic alkyl amino group, the effect of these changes together with the manipulation of the diffrent stereoismoers on activity is studied. The synthesized compounds will be tested for their kinesin EG5 inhibitory effect together with their ability to inhibit growth of two cancer cell lines in vitro.

Toxinogenic Fungi and Human Health: Tea Powders, Bottled Water and Canned Beans in Egypt

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The main objective of this study was to analyse the occurrence of fungi in bottled water, tea powders and canned beans in Egypt and to examine their potentiality to produce Aflatoxin B1 (AFB1). Seventy-five samples of five different brands collected randomly from Suez Canal governorates in 2011. Isolation and identification media were Czapek's yeast extract agar, malt extract agar, Aspergillus flavus/parasiticus agar and yeast extract sucrose broth. It was possible to encounter as many as 25 fungal species (3 Zygomycota, 1 teleomorphic Ascomycota and 21 anamorphic Ascomycota) belonged to fourteen genera from Suez Canal governorates. 40 Wistar male rats were used to investigate the effect of dominated toxinogenic fungi in all sources under investigation. Rats divided into 4 groups (10 of each) in which: the first was fed standard diet, the second was fed diet with Aspergillus ochraceous, the third was fed diet with A. flavus, and the last were fed diet with A. parasiticus respectively. Blood, liver and kidney samples were collected after 2, 4 and 8 weeks from start date of the experiment. Results showed significant elevation of alanine aminotransferase (ALT) and aspartate aminotransferase (AST) in groups 2, 3, and 4. Moreover, alkaline phosphatase, urea, and creatinine were significantly elevated in groups 2 and 4. These elevations were more prominent at the 8th week. High histopathological lesions recorded in liver of the fourth group and in kidney of the second group in the 8th week. We conclude that mycological analyses of all examined brands reveal that these substrates were contaminated with fungi some of which are mycotoxin producers. Hence, extreme precautions must be taken in the manufacture, handling, transport and storage to avoid mycotoxicosis of human in Egypt. In addition, urgent cooperation between Ministry of Health and Agriculture in Egypt to control this situation is required.

Polymannuronic Acid, a Microbial Polymer of Great Medicinal Application

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Alginate is a collective term for a family of polysaccharides produced by brown algae and bacteria. Species of Pseudomonas and Azotobacter are the only prokaryotic sources for this algal like-polymer. Polymannuronic acid (PM) together with polyguluronic acid (PG) constitute the structure of alginate. In the last few years, polymannuronic acid has

gained much more attention due to its diverse pharmaceutical and medicinal applications. Polymannuronic acid rich polymers and high-quality alginates of extreme purity, used in the pharmaceutical field, are sold for up to U.S. $ 40,000 kg–1. Capsules of these polymers are of particular practical interest for cell transplantation. Immobilising insulin-producing cells within pure alginate capsules was established to treat type I diabetes. Therefore, the main goal of our study was to produce alginate with high amount of mannuronic acid (polymannuronic acid- rich polymer) by a Pseudomonas aeruginosa and to investigate the physical and chemical parameters that may influence the polymer production in controlled bioreactors. Our study focused on investigating the effect of different aeration rates and other medium components on the PM-rich polymer production. Intermediate aeration rate of 0.467 vvm appeared to favour the maximum amount of polymer production (1.36 g l-1 after about 45.5 h). Lower or higher aeration rate (0.167, or 0,833 vvm) resulted in a lower polymer concentrations. At the optimal conditions, a yield of 0.587 g g-1 from the produced biomass (Ypx) was achieved, compared to 0.26 g g-1, and 0,178 g g-1 at aeration rate of 0,167 and 0,833 vvm, respectively. The results obtained in this study show that controlling the oxygen supply is considered as importance factor for the production of such a polymer.

Biotransformation of Glucerol to 1,3-Propanediol by L.Reuteri ATCC 20016 in Aqueous System

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Biotransformation of glycerol to 1,3-Propanediol (PD) by resting cells of Lactobacillus reuteri ATCC 20016 in water was investigated. The production of 1,3PD was maximum (240 mM) with the addition of 250Mm 1,2PD as an inducer during the cultivation of cells, less activity was detected when using similar concentration of glycerol as inducer or when using lower concentrations of 1,2PD and in absence of an inducer no cell activity was detected. Resting cells produced under anaerobic conditions were able to yield more 1,3PD during biotransformation of glycerol (400 mM) under optimized reaction conditions compared to cells produced under aerobic and micro-aerobic conditions. The different factors affecting the biotransformation process such as cell density, glycerol concentration, temperature and PH were also investigated. The optimum PH was 7, cells showed highest activity at temperature 37, a linear relationship was observed between the 1,3PD production and cell density and 20 mg cells were able to convert up to 280 mM glycerol. This is the first report on the ability of using resting cells of L.reurei for production of 1,3PD in aqueous system, the metabolic pathway for production of 1,3PD is also discussed.

Contribution of Grain Size Trend to Sedimentary Study of Microtidale Beach: Case of the Tunis Gulf

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Beach sediment collected from the swash zone and the coastline slope at the beach of Tunis gulf, between Cape Gammarth and Cape Ferina, are used to (1) establish the grain size pattern(2) assess the effect of entropic and natural structures (port, rivers) and (3) understanding the complex interactions between sedimentology, morphology and hydrodynamics process in the nearshore.

Generally the swash zone sediment of the Tunis gulf beach have an average mean diameter of 1,50 Φ to 3,56 Φ while those from the coastline average at 2,01 Φ. The most of the sample are unimodal, finest with a good sorting, negatively skewed with leptokurtic distribution. The grain size tends to coarsen to the slope of the nearshore as a result of action of cross shore current.

In the other hand, the trend nearshore increase in the mean grain size is locally distorted at the river mouths, lagoon and harbour structures. The characteristic of the totality of sediment (90%) in this part show finer size to silt, negatively skewed and with a leptokurtic distribution.

Although the shoreline has been modified by human activity, the gulf of Tunisia bay has retained its natural configuration. To understand the variability at the nearshore-coastline interface, we characterised the morpho-hydro dynamic of sediment. The prevailing north east and eastern wave, lead to a NNW/SSE longshore drift intercepted by local sedimentary cell; which seems to be the factor of the bimodality and mixing of different grain population observed at the nearshore of Tunis gulf.

Interchangeability of a Brand and Generic Atenolol Products Marketed in Egypt

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The affordability and sustainability of healthcare in Egypt is based on locally manufactured generics. However, reliability and interchangeability of generics has always been questioned by clinicians and patients. The aim of this study was to assess the clinical efficacy and tolerability of a generic and brand tablet products of atenolol, a widely prescribed antihypertensive drug. The pharmaceutical quality of the two study products was ensured in-vitro prior to clinical testing. Then, a prospective clinical study was carried out according to a randomized controlled double-blind parallel design. The trial was conducted at the Alexandria Clinical Research Center in accordance with Good Clinical Practice (GCP) after approval of Research Ethics Committee of Faculty of Medicine and obtaining an informed consent from research subjects. A hundred patients aged 18-60 years with essential hypertension (systolic blood pressure (SBP) 140-179 mm Hg, and diastolic blood pressure (DBP) 90-109 mm Hg), were selected based on inclusion and exclusion criteria. Following clinical examination, clinical laboratory testing and patient counseling and education, patients were administered a 100mg tablet of either products once daily in the morning for 28 days and were followed-up at days 14 and 28 for SBP, DBP, heart rate and adverse effects. Both atenolol tablets resulted in a statistically significant lowering in mean values of SBP, DBP and heart rate ($p<0.001$).

Patients on brand tablets showed earlier control of BP evidenced by a larger mean SBP difference, -10.9 ± 18.8 versus -7.9 ± 9.8 at 14 days) although difference was not statistically significant ($p<0.05$). Common adverse events including rashes, gastrointestinal complaints, dizziness and uncontrolled blood pressure were reported for both products with no statistical difference. In conclusion, both brand and generic atenolol study products can be considered therapeutically equivalent and interchangeable. This would enhance confidence of the clinical community in locally manufactured generic drug products.

Microbiological Activities and Phytochemical Screening of Three Mistletoes Commonly Used in Folk Medicine

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Mistletoe is the name designated for obligate hemi-parasitic plants, which grow attached to and within the branches of a tree or shrub. Three mistletoe named Plicosepalus acacia, Plicosepalus curviflorus and Phragmanthera austro arabica were collected from Saudi Arabia. Those plants have been traditionally used in folk medicine to treat smallpox, diarrhea and respiratory tract infections. This work aims at phytochemical screening and determining the effectiveness of these plants as medicinal herbs. Phytochemical screening revealed their accumulation of flavonoids, anthraquinones, steroids and/or terpenoids. The methanolic extracts were tested for their antimicrobial activities using disc diffusion method and the minimum inhibitory concentration (MIC) determination. At a concentration of 500/20 µl (disc load) all the tested extracts were active only against the tested gram positive microorganisms. The inhibitory activity was about 1/3-1/4 the strength of the reference antibiotics gentamycin and ciprofloxaxcin. Increasing the concentration to 1000 µg/20µl resulted in higher activity. Plicosepalus curviflorus and Plicosepalus acacia demonstrated the highest activities against the tested Gram positive Staphylococcus aureus. The gram negative microorganisms, Pseudomonas aeruginosa was affected by all the tested samples, while both Salmonella typhi and E.coli were susceptible only to Plicosepalus curviflorus and Plicosepalus acacia. Plicosepalus curviflorus demonstrated the highest activity against E.coli, which is higher than half the activity of gentamycin. None of the examined extracts showed antifungal activity against Candida albicans up to a concentration of 1000 µg/20µl. Reasonable MIC values, which confirmed the results of the disk diffusion test, were recorded. The most important human pathogens, Pseudomonas aeruginosa and Staphylococcus aureus, had lower MIC values for all tested extracts, compared to other tested microorganisms. This study supports the potential use of these three plants as medicinal herbs.

Computer-Aided Discovery of New Cruzipain Reversible Inhibitors for the Treatment of Chagas' Disease

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Chagas disease is an endemic Latin American parasitosis associated to poverty and rural populations. It is estimated that about 15 million people in Latin America are infected with Chagas' disease; current chemotherapy for Chagas is effective only in the initial, acute phase of the disease[1]. The progressive increase in the knowledge of the molecular biology of the causal agent (Trypanosoma cruzi) has facilitated the rational development of specific chemotherapies to treat Chagas. The cysteine protease cathepsin L-type named cruzipain stands out among the most promising novel molecular targets to develop innovative antichagasic medications. Cruzipain is the major protease of T. cruzi and it is active in all stages of the parasite life-cycle; thus, cruzipain inhibitors may prove effective in all stages of Chagas[2].
Virtual screening consists in applying computational models to seek drug candidates throughout large virtual chemical repositories in an efficient manner.
We present the development of a new model based on molecular topology and capable of predicting whether a given drug candidate is or is not a cruzipain reversible inhibitor. For modeling purposes, 163 cruzipain reversible inhibitors and non-inhibitors were compiled from literature; this dataset was partitioned into representative training and test sets by application of a 2-step clustering analysis based on a hierarchical approach (maximal common substructure) and subsequent k-means clustering. Afterwards, Linear Discriminant Analysis was conducted to derive a binary classificator based on topological descriptors from Dragon Software (Milano Chemometrics). The topological model showed good predictive capability, with an area under the ROC curve of 0.878 for the test set. The obtained topological model may be used to efficiently detect novel antichagasic drugs through large chemical databases.

[1]World Health Organization on behalf of the Special Programme for Research and Training in Tropical Diseases (2007).
[2]Cazzulo et al; Curr. Pharm. Design. 2001.

Computer-Assisted Early Identification of PGP-Substrates and Non-Substrates as a Strategy for the Design of New Drugs for the Treatment of Refractory Epilepsy

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P-glycoprotein (Pgp) is one of the major efflux transporters associated to multi-drug resistance issues (i.e. inability of a wide-range of unrelated drugs to control disease progression and/or symptoms) in a number of health conditions, such as epilepsy, cancer and HIV. Therefore, early recognition of Pgp substrates is an important step in the drug design process in order to develop novel therapies capable of overcoming Pgp-mediated multi-drug resistance issues [1,2]. In our case, we are interested in the development of novel anticonvulsant treatments capable of controlling refractory (or intractable) epilepsy, which affects around one third of the antiepileptic patients [3].
We have developed a highly specific ensemble of topological models capable of differentiating a Pgp-substrate from a non-substrate [4]. This ensemble has been applied to select drug candidates for the treatment of refractory epilepsy from a large virtual

repository of small organic drug-like molecules (ZINC database). We have selected a first series of six candidates that are being pharmacologically tested in preclinical animal models of epilepsy. Two of them hydroxycycloheptane-1-carboxylic acid and 7,7 dimethylbicyclo [2.2.1] heptane-1-carboxamide have already shown to be effective to protect from seizures in an animal model of epilepsy: the Maximal Electroshock test, at the minimal doses stipulated by the NIH Anticonvulsant Drug Development Program.

The Potentiality of Grape Seed Extract (GSE) as a Novel Anti-Hepatitis C Virus (HCV) Agent

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HCV frequently leads to chronic hepatitis and cirrhosis, in addition to being associated with the development of hepatocellular carcinoma. In spite the highly vigorous and extensive research in this field, a protective vaccine and effective treatment are not yet available. The mains tay of anti-HCV therapy, interferon (IFN-α) along with ribvirin leads, at best, to viral clearance for about 40-50% of patients infected with HCV. Therefore, exploration for new anti-HCV principles is urgently needed.
In this study, the effect of GSE and its major constituents (Gallic acid, catechin & epicatechin) on HCV replication into HepG2 cell line was analyzed. Cytotoxicity assay was used to determine the non-toxic concentrations to the culture cells. The HepG2 cells were incubated with GSE and each constituent respectively, and then infected with HCV. Inhibition of viral replication was detected by the amplification of viral RNA using the RT-PCR technique. Both the whole GSE and its constituents were considered active upon inhibiting the viral replication into HepG2 cells, as evidenced by the disappearance of the (+) and/or (-) strands of viral RNA- amplified products detected by RT-PCR (compared with the positive control). A quantitative analysis was then done by real time-qPCR.
In order to test ability of the tested treatment to scavenge the free radicals, the Flow Cytometer assay was used on which, the scavenging HCV-induced free radical in HepG2 cell line was measured.
Our quantitative analysis by real time-qPCR revealed that all treatments have the ability to inhibit the HCV with priority to epicatechin (50.4%), in addition, the free radical scavenging reached up to 87.74%. This study suggests that all treatments possess anti-viral and anti-oxidative properties, which are associated with their direct free radical scavenging abilities. Further studies of the mechanism underlying epicatechin-mediated HCV inhibition may open new ways to design novel anti-HCV drugs.

Sequence Analysis of VdThnr Gene in Highly and Weakly Aggressive Isolates of Verticillium Dahlia

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Verticillium dahliae (Kleb.) is a soilborne deuteromycete that causes vascular wilt in hundreds of annual, perennial and woody plants worldwide and affects yield and quality of infected plants. Understanding pathogenesis mechanisms of the pathogen is essential to control the disease. Melanin pigment has been known as an important component in

appressorium maturation, facilitation of penetration, pathogenesis, and survival of many fungal pathogens including V. dahliae. In this study, the full length of tetrahydroxynaphthalene reductase (VdThnr) gene, a key enzyme in melanin biosynthesis pathway, was isolated, amplified from two V. dahliae (Vd1396-9, highly-, and Vs06-14, weakly-aggressive) isolates by PCR. The gene was cloned into the plasmid pGEM®-T Easy vector, then, three clones of the gene were sequenced. Comparative sequence analysis of the gene from the two isolates and VdLs.17 V. dahliae isolate (The Broad Institute, reference isolate) revealed many variations. In total, 15 differences were observed in the two isolates as compared to the reference isolate. One insertion/deletion mutation was found in isolate Vs06-14, which caused a frame shift of the open reading frame that resulted in a different sequence of the deduced amino acid in this isolate while, the deduced amino acids in both VdLs.17 and Vd1396-9 were identical. The insertion/deletion frame shift mutation seems to be linked to the differential morphological appearance and expression of this gene that was observed in the proteomics analysis of Vd1396-9 and Vs06-14 isolates. These differences in DNA sequences may explain the differential level of the pathogenicity of the two V. dahliae isolates. Molecular analysis of the pathogen will provide information for the development of more efficient management strategies for Verticillium wit disease.

Over-Expression of a DEAD-Box Helicase, PDH45, Confers Both Seedling and Reproductive Stage Salinity

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To improve the salinity tolerance of rice, a DEAD-box helicase gene isolated from pea with a CaMV35S promoter was transformed into the Bangladeshi rice variety Binnatoa through Agrobacterium-mediated transformation. The transgenic seedlings showed significantly higher chlorophyll content, but decreased root length compared to wild type (WT) under normal physiological conditions. Their status was confirmed by polymerase chain reaction (PCR), semi-quantitative reverse-transcription PCR and Southern blot hybridization for positive integration of the transgene. The T2 progenies from three independent transformation events were characterized for salinity tolerance both at seedling and reproductive stages. Compared to the WT plants, the average decrease in chlorophyll content and dry weight of seedling leaves was lower by 20 and 12% respectively at 12 deciSiemens per meter (dS/m) NaCl stress in hydroponics. A higher leaf K+/Na+ ratio of 0.346 was maintained by the transgenic lines compared to the WT ratio of 0.157, which indicated induced ion homeostasis. At the reproductive stage, transgenic rice plants expressing PDH45 showed better fertility and produced higher grain yield by 16% compared to WT plants under continuous stress of 6 dS/m from 30 days till maturity. One of the transformed lines, PDH45-P3, outperformed the others, and replicated data in reproductive stage soil stress of 12 dS/m NaCl showed its enhanced fertility and yield by 46 and 29% over WT, respectively.

Stability-Indicating HPTLC Determination of Amlexanox in Bulk Drug and Pharmaceutical Dosage Form

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A sensitive, selective, and stability-indicating high-performance thin layer chromatography (HPTLC) method for analysis of amlexanox both as a bulk drug and in formulation was developed and validated. The method employed TLC aluminium plates precoated with silica gel 60F-254 as the stationary phase. The solvent system consisted of methylene chloride/absolute ethanol/acetic acid (9.36:0.44:0.2, v/v/v). Densitometric analysis of amlexanox was carried out in the absorbance mode at 350nm. This system was found to give compact spots for amlexanox (Rf value of 0.40 ± 0.02, for six replicates). Amlexanox was subjected to acid and alkali hydrolysis, oxidation, dry and wet heat treatment, and photo degradation. The degradation products were adequately resolved from the pure drug with obviously different Rf values. Amlexanox was determined over a concentration range of 10–800 ng/spot with a satisfactory correlation coefficient (r = 0.9999). The LOD and LOQ were 3.26 and 9.9 ng/spot, respectively. Statistical analysis proves that the method is repeatable and specific for the estimation of the studied drug.
Keywords: Amlexanox, HPTLC, Stability-indicating, Degradation

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Effect of Nigella Sativa and Wheat Germ Oils on Scopolamine-Induced Behavioral Alterations in Rats

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Memory enhancing effects of Nigella sativa oil (NSO) and wheat germ oil (WGO) were evaluated in scopolamine-induced memory impairment in rats by using T maze alternation task and object recognition test. Two groups of male Wistar rats received single doses of saline and scopolamine (16 mg/kg, i. p.) and served as normal and control groups, respectively. The other three groups were pretreated with single doses of NSO (1ml/kg, p. o.), WGO (170 mg/kg, p. o.) and donepezil (10mg/kg, p. o.) used as a reference drug 30 min prior scopolamine injection. Scopolamine injection- induced impaired performance in the T maze alternation task and deficits in the object recognition paradigm. Administration of NSO, WGO and donepezil significantly reversed scopolamine-induced deficit of spatial and non spatial working memory in the T maze alternation task and object recognition test, respectively. Furthermore, NSO and WGO may possess anti-amnesic activity that may hold significant therapeutic value in alleviating certain memory impairments observed in Alzheimer's disease.

Improving Yeast Protein Function Prediction Using Weighted Protein-Protein Interactions

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Bioinformatics can be used to predict protein function, leading to an understanding of cellular activities. In the past, Biologists tried to determine protein functions from the structure of the protein. Possible roles of similarity between the protein and its homologies; from other organisms; are investigated to predict protein functions. Because of the diverse groups of homologous, these methods were found to be exhaustive and non-certain. Other techniques have been used to predict the protein functions as analyzing gene expression patterns, protein sequences, protein domains, and integrated multi sources. But these technologies suffer from high error rates because of their inherent limitations. The computational approach is adopted to solve this problem by using information gained from physical and genetic interaction maps to predict protein functions. Recently, the researchers introduced different techniques to determine the protein function prediction using the information extracted from PPI. Although these trials are promising, they lack addressing effective problems such as network topology and strength of interaction. Network topology represents the interaction between proteins and how they are connected. Usually, equally-weighted (PPI) are used to predict the protein functions. The present study provides a new weighting strategy for PPI to improve the prediction of protein functions. The weights are dependent on the local and global network topologies furthermore the number of experimental verification methods. The proposed methods were applied to the yeast proteome. The results revealed improvement in the sensitivity and specificity of prediction in terms of cellular role and cellular locations.

Successful Morphological Changes on HeLa Cells during Adaptation to the Production Serum-Free Media

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Serum content of culture medium has important effect on HeLa-S3 cell morphology. Increasing the serum concentration from 5% to 20% in Ham's F12 medium increased the cell volume. Larger cell sizes were obtained in high serum concentration from 10% to 20%. On the other hand, cell size decreased gradually by decreasing serum concentration. Serum deprivation leads to dramatic changes in cell morphology from flattened or triangular shape to spindle shape accompanied by the loss of cell adhering ability. However, these changes do not affect cell activities and metabolism (published previous). Adaptation of cells to be able to grow in serum-free medium is usually accompanied by morphological changes. Cell size usually decreases after the adaptation steps as well as the shape of the cells become spindle and round. These rounded cells used in large scale production bioreactor.

Structures of Phenytoin- and Trimethadione- Analogs with Anticonvulsant Activity

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The lack of efficacy and the large number of adverse effects of AEDs available today justify the search for new anticonvulsant agents.
In this work we present the biological evaluation of anticonvulsant activity of heterocyclic phenytoin- and trimethadione- analogs designed and synthesized for this purpose.
Phenytoin is a widely used drug in the treatment of epilepsy. It achieves control of different types of crisis, but it also causes a wide-range of side reactions such as drowsiness, digestive disorders, gingival hyperplasia, lupus erythematosus, cutaneous, agranulocytosis, hepatotoxicity and osteomalacia among others[(1)]. Trimethadione is effective in absence seizures but is no longer a drug of choice due to the high incidence of teratogenic effects that occurs among other undesirable effects[(2)].
We relied on these structures, on which we performed bioisosteric replacements in order to preserve or enhance the biological activity and achieve a reduction in adverse effects.
We present the results of pharmacological evaluation of rigid 5-member heterocyclic compounds with 3 different heteroatoms (N-1, 2, 3-oxatiazolidin-4-one-2, 2-dioxides). We have also studied the activity of some synthesis intermediates α-hydroxy amides. The tests were performed according to stage I of the Antiepileptic Drug Development (ADD) Program from the National Institute of Health (NIH) (USA)[(3)] using MES and PTZ test for the evaluation of anticonvulsant activity and rotorod test for the evaluation of neurotoxic effects. All the compounds tested were classified as Class I of NIH ADD Program, i.e. they present anticonvulsant activity at doses less than or equal to 100 mg / kg with no evidence of neurotoxic effects at the same dose.

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Molecular Topology Applied to the Recognition of Substrates of Breast Cancer Resistance Protein

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Breast Cancer Resistance Protein (BCRP) is an ATP-dependent efflux transporter protein belonging to ABC transporters superfamily. This protein, together with other family members such as Pgp, reduces the bioavailability of drugs, so they are associated with multidrug resistance in many diseases. The objective of this work is the development of computational models based on topological molecular descriptors for early recognition of BCRP substrates.
To this purpose, we first generated a dataset of 156 substrates and 106 non-substrates of human wild type BCRP from literature. This dataset presents wide structural diversity, ensuring that the models that may be derived from it would present a broad applicability domain. This dataset was partitioned into training and test sets through a two-step clustering process, based on hierarchical approach followed by k-means clustering.

The resulting representative training set was composed of 164 compounds (85 substrates and 79 non-substrates) while the test set of 98 compounds (71 substrates and 27 non-substrates). We then proceeded to obtain models able to discriminate between BCRP-substrates and non-substrates, using linear discriminant analysis and Dragon's (Milano Chemometrics) topological molecular descriptors.
The best model we obtained allowed a correct classification of around 98% BCRP-substrates and 55% of non-substrates. The model was validated through standard methodologies (cross-validation, Fisher's randomization test and external validation) in order to assess its robustness and predictive ability. ROC (Receiver Operating Characteristic) curves were built in order to increase specificity (reduce false positives rate) through an adequate selection of the cutoff value to discriminate substrates from non-substrates. The area under the ROC curve for this model was 0.859 (1 representing a perfect classificatory model).
This model it can be applied for design of drugs that are not recognized for BCRP transporter and for the prediction of potential drug reactions due to competition of two drugs for this transporter.

ATF4 Sustains the Mammalian Circadian Oscillators

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Circadian clocks endow organisms with a survival advantage as they enable them to anticipate environmental changes, thereby adapting their behavior and physiology to the appropriate time of the day. Many of these changes are controlled by endogenous circadian clocks that control events such as cell signaling, gene expression, hormone production, neuronal activity, and many aspects of behavior. CLOCK and BMAL1 heterodimers activate transcription of the components of the central clock; period (Per) and cryptochrome (Cry) genes, through a conserved E-box element. The resultant transcriptional activation of these genes is subsequently repressed by their protein products, resulting in the negative feedback loop making up a portion of the central clock mechanism. Beside thier role in the central oscillator, CLOCK and BMAL1 have also been reported to activate clock-controlled genes regulating the expression of of clock-controlled output genes. Another transcriptional pathway that has been implicated in rhythmic regulation is the cyclic AMP response element (CRE)-binding protein (CREB) pathway. CREB family are stimulus-induced transcription factors that can be activated by a large number of environmental changes. and also suggested to be responsible for sustaining the the core oscillation loop. However the sustainable mechanism remains to be fully understood. In this study, we are trying to provide the molecular link between the central components of the clock oscillation machinery and the cAMP-dependent signaling pathway. We proved that the central components directly control CREB2/ATF4 transcription. We also invistigated the functional involvment of ATF4 in the circadian regulation of the circadian regulation of CRE-mediated transcription. These results may give one of the molecular mechansims regulating the many intracellular pathways such as energy metabolism, aminoacid transport and osteogenesis.

Investigation of Multiple Cytoprotective Potential of Sulforaphane in Primary Cultured Rat Hepatocyt

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There is an increasing demand for promising phytochemical candidates that can interact with multiple cytoprotective targets. This will eliminates the need to combination therapy, eliminating both risks for drug-drug interctaion and toxicity [1]. The present study aimed to investigate the potential of sulforaphane (SF, a chemopreventive isothiocyanate from broccoli sprouts) to induce multiple members of cytoprotective proteins including some with antioxidant functions (quinone reductase NQO1, thioredoxin reductase TRXR-1, haemoxygenase HO-1 and glutathione reductase GR) and selected proteins of the heat shock family (HSP70, HSP90, GRP58 and GRP94) in primary cultured rat hepatocytes [2]. 24 h post treatment, cell lysates of vehicle or SF-treated hepatocytes were analysed for the levels of expression of the above cytoprotective proteins with quantitative Western blotting. A concentration-dependent upregulation of the NQO1 protein expression was detected in SF-treated hepatocytes reaching 3 fold induction of this protein at maximum non toxic SF concentration of 25 μM, as compared to the DMSO control. SF also produced a significant 5.8 fold increase in the protein expression of the anti-apoptotic HSP70 over control at 25μM. To the best of our knowledge, this is the first report of the induction of HSP70 by sulforaphane in primary cultured rat hepatocyte model. Under the experimental conditions, no significant induction of the rest of the studied cellular proteins was observed. Taken together, the findings of the present study have revealed the possibility of coordinate induction of HSP70 and NQO1 protein expression by SF in primary rat hepatocytes as members of the cytoprotective proteome.

Keywords: Sulforaphane, Cytoprotection, Phytochemicals, primary hepatocytes
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Hepatoprotective Activity Screening of Inula Crithmoides L.Extracts

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In traditional medicine a number of herbal extracts were used for the treatment of liver complains. Family Asteraceae is known for its hepatoprototective constituents such as those reported in Globe artichoke and the seeds of the milk thistle (Silybum marianum). Hepatoprotective mechanisms are mostly linked to antioxidant, as demonstrated by a number of studied herbal extracts. One of the most common examples of hepatoprotective agents is silymarin, which protects against liver damage due to its antioxidant properties. While, artichoke with its main constituents of dicaffeoylquinic acid derivatives are intended to improve liver function and for treatment of gall bladder stones.

Some Inula species have recently appeared to possess a unique hepatoprotective activity as I. britannica, I. heterolepsis and I. racemosa.
The present study was undertaken to evaluate the hepatoprotective effect of herbal extracts of Inula crithmoides L. against experimentally induced liver injury in rats. Silymarin was used as the reference hepatoprotective agent.
Treatment of rats with hepatotoxic carbon tetrachloride resulted in a severe damage of hepatocytes as indicated by the significant increase of serum transaminases (SGOT and SGPT) and alkaline phosphate levels (ALP). Severe jaundice and hepatic cell injury were indicated by increased level of serum bilirubin.
The effect of the investigated extracts was assessed on the basis of the aforementioned biochemical markers in blood.
A comparative study for the hepatoprotective activity of aerial parts and roots was performed. The most active extract was subjected to biologically guided fractionation. Accordingly, further phytochemical investigation was performed on the active fractions, resulted in the isolation of 2 new caffeoyl derivatives in addition to 1,5-dicaffeoylquinic acid aiming to find out new sources of natural hepatoprotective drugs.

Guanethidine and Propranolol Modulate the Effect of Sildenafil

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Aim: This study aims to further elucidate the role of adrenergic transmission in erection and to highlight whether adrenergic transmission in the penis modulates sildenafil' action. Methods: measurement of intracavernosal pressure in the anesthetized rat model. Results: Guanethidine (3 and 6 mg/kg) potentiated intracavernosal pressure/mean arterial pressure (ICP/MAP) rises in response to cavernous nerve stimulation by 4.375±0.425 and 18.375±1.085% respectively. Propranolol did the opposite. In presence of guanethidine, sildenafil (0.01, 0.1 and 1 mg/kg) potentiated ICP/MAP responses by 81.571±4.918%, 147.83±10.864% and 279.285±23.053% at 1 Hz compared to 22.277±2.139%, 123.571±8.443% and 186.25±13.542% respectively in the absence of guanethidine. Propranolol inhibited the effect sildenafil at all frequencies of stimulation. Verapamil exhibited a pro-erectile action and potentiated the effect of sildenafil (0.01, 0.1 and 1 mg/kg) on erectile responses corresponding to 85.25±6.716%, 146±11.288% and 221.571±19.032% respectively compared to 26.011±1.911%, 87.142±8.73% and 182.2±16.921% in its absence. Conclusions: This study provides functional evidence that inhibition of sympathetic tone peripherally results in enhancement of erectile function. β-adrenergic receptors seem to play an important role in erection. The combination of sildenafil and guanethidine or verapamil could have a potential advantage on erectile function but propranolol may mask the effect of sildenafil on erectile function.
Keywords: erection, sildenafil, adrenergic transmission, guanethidine, propranolol, verapamil.

Terlipressin as a Novel Inducer of Experimental Rat-Models of Acute and Chronic Hyponatremia

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Hyponatremia (HN) is associated with mortality and morbidity risks due to development of encephalopathy and neurogenic pulmonary edema. When serum sodium concentration falls rapidly over a period of hours (< 48 h), acute HN, in which a more severe degree of cerebral edema for a given serum sodium level, results. Conversely, in chronic HN (≥ 48 h), brain swelling is minimized due to a slower process of adaptation of the brain cells. HN is frequently thought to be associated with elevated secretion of antidiuretic hormone, also called arginine vasopressin (AVP). Induction of HN as an experimental model was usually performed by multiple AVP administrations over the day or continuous infusion via an implanted osmotic mini pump. Terlipressin (TP, tricyllysine-vasopressin) is a synthetic, long-acting analogue of AVP, emerging as a potentially major advance in the treatment of septic shock. The present study has been constructed to investigate the possible capability of using one bolus of TP and one bolus of TP/day for 3 days, to induce severe acute and chronic HN in rats, respectively.
Serum sodium level was measured 2h following TP administration in the acute model and 24h following the last TP administration in the chronic model. Other parameters chosen to assess complications of HN included changes in locomotor activity, pain reflex and some lung function parameters. Histopathological examination of brain tissues was also carried out. It was found that proposed models in the present study produced acute and chronic HN that were coupled by the main neuropathological and histopathological features of human HN manifested by decreased locomotor activity, delayed pain reflex, impaired lung function as well as development of cerebral edema. However, these features were more severe in the acute model. These findings introduce TP administration as a novel experimental model for induction of HN in rats.

Manufacturing of Antioxidant Packaging Na-Caseinate Edible Films

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In the present work, we succeed to product an antioxidant packaging films of sodium caseinate by interrupting a model of antioxidants (Tannic Acid (TA) or Catechin (CAT) with these films. Films had a high antioxidant activity after the manufacture and during the storage at different storage conditions. The Radical Scavenging Activity (RSA) of sodium caseinate (NaCAS) films with 0 to 30% of casein (CAS) and antioxidants was measured. Tannic Acid (TA) and Catechin (CAT) were added in the film as model antioxidants. ABTS and DPPH methods gave similar results for RSA measurement. Film casein content led to most changes in initial RSA, increase of casein resulted in an apparent decrease of RSA due to quenching. During storage, a good stability of global RSA was then observed. A classical decrease of surface RSA occurred during 20 first days of storage, followed by a surprising result of strong surface RSA increase during

the continuation of the 90-day storage, especially at high relative humidity. This phenomenon was due to NaCAS plasticizing with a possible network alteration for long storage time.

Assessment of Physicochemical and Invasive Pathogens in Shanomi Creek in the Niger Delta, Nigeria

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The physicochemical and microbial qualities of the Shanomi Creeks were assessed between May and September 2011 in Niger Delta, Nigeria. The temperature across all sampling stations ranged between 16 and 34oC, while pH varied from 5.52 to 7.52. Turbidity of the samples was in the range of 2.9 – 395.3 NTU and conductivity ranged between 55.7 and 1035.0 µS/cm. The concentrations of other physicochemical are as follows: chemical oxygen demand [COD] (8.75 – 176 mg/L); ammonia (0.93 - 85.9 mg/L); nitrate (0.89 – 76 mg/L); nitrite (0.78 - 68.9 mg/L); orthophosphate (1.8 – 57.6 mg/L). The differences in the values of most water quality parameters at the sites were significant ($P < 0.05$). The microbial quality of the water bodies did not comply with the limits set by the World Health Organization guidelines in respect of pathogens such as Escherichia coli, Salmonella, Shigella, Faecal coliform and Total coliform. The study has revealed that there was an undesirable impact on the physicochemical and microbial characteristics of the water bodies as a result of the discharge of untreated municipal and domestic waste entering into the watershed. This poses a health risk to several rural communities which rely on the water bodies primarily as their sources of domestic and recreational waters. We conclude that these water bodies are potentially hazardous to public health and that proper river quality monitoring are necessary towards the protection of public health and vulnerable water resources.

Role of Rest in Stemness of Neural Stem Cells and Glioma Derived Stem Cells

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Glioblastoma multiforme (GBM) is the most aggressive form of brain cancer associated with poor prognosis. Recently the initiation and growth of GBM has been linked to tumor stem like cells which share some features with neural stem cells (NSCs). REST (Repressor element1 silencing transcription factor), a neuronal transcription repressor, was shown to control NSCs and embryonic stem cells self renewal. However, the role of REST in NSCs and GBM stem-like cells (GSCs) is still unclear. NSCs were isolated from the cortices of E12 mice embryos of day 12 (E12) from both wild type (E12WT) transgenic mice where eGFP is expressed under REST promoter (E12-eGFP). In E12-eGFP, REST coexpress with GFP and neural stem cell markers Sox-2 and Nestin under proliferation conditions. Upon differentiation, expression of REST, Sox2 and Nestin goes down with concomitant expression of the three lineages differentiation markers, Tuj-1, MBP and GFAP. Sorted E12-eGFP cells (E12-GFP+ve), have NSCs

characteristics as they self-renew and undergo both symmetric and asymmetric divisions. Knock down of REST decreased the self renewal potential in E12NSCs. Moreover, we found that GSCs have varying expression levels of REST, some with relative high REST expression (HR-GSCs) and others with relative low REST expression (LR-GSCs). Stable knock down of REST in HR-GSCs resulted in decreasing both self renewal capacity in vitro and tumorigenicity when these cells were injected in brain of nude mice. On the other hand, forced expression of REST in LR-GSCs showed increased self renewal and tumorigenic potential. Thus, these results indicate that REST regulates the tumorigenicity of GSCs through maintaining self renewal in these cells, which may suggest REST as a potential therapeutic target for GBM.

Nampt and Vaspin: New Adipokines Correlated with Various Parameters in Type 2 Diabetes Mellitus

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Type 2 diabetes mellitus (T2DM) is a complex metabolic disorder. Its prevalence is expected to increase exponentially around the world, particularly in developing countries. Insulin resistance, inflammation and dysregulation of adipokines play a major role in the pathogenesis of T2DM. Among the huge growing adipose secretome, nicotinamide phosphoribosyl transferase (Nampt) and vaspin emerged as novel interesting adipokines having insulin-mimetic and sensitizing effects, respectively. However, their role in T2DM is still controversial. Accordingly, this study was designed to investigate their levels in T2DM patients compared to healthy control subjects, and to study the correlation between these two novel adipokines and the correlation between each of them with anthropometric parameters, insulin resistance, hyperglycemia, dyslipidemia, and also the inflammatory marker interleukin-6 (IL-6). The levels of these two novel adipokines and other parameters were measured in non-obese and obese T2DM patients together with matched healthy non-diabetic control subjects. The Nampt, vaspin and IL-6 levels were measured by ELISA while insulin levels by chemiluminescence technique. The Nampt and vaspin levels were found to be significantly elevated in non-obese (25.9 ± 3.4 ng/ml and 1.6 ± 0.2 ng/ml, respectively) and obese T2DM patients (45.4 ± 4.6 ng/ml and 2.8 ± 0.4 ng/ml, respectively) compared to control subjects (9.4 ± 2.0 ng/ml and 0.4 ± 0.05 ng/ml, respectively) at $p<0.01$. Furthermore, Nampt as well as vaspin were found to be significantly correlated with one another and with various metabolic parameters. In conclusion, Nampt and vaspin are potential candidates to play important role in the development and progression of T2DM.

Stability-Indicating HPTLC Method for the Determination of Lamotrigine

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The International Conference on Harmonisation (ICH) guidelines Q1A emphasize on the stability testing of new drug substances and products. That aims at examining the features that are susceptible to change during the storage of drug products and thus

affecting safety, efficacy and quality of the drug. In this work, a simple, sensitive and stability-indicating High Performance Thin Layer Chromatographic method (HPTLC) for the determination of lamotrigine is presented. According to ICH guidelines Q1A, lamotrigine was exposed to a variety of stress conditions; these include heating in acidic, basic and neutral media. Its stability towards oxidative stress, humidity, high temperature and direct sunlight was also examined. Separation of the drug from its forced degradation impurities was achieved using TLC aluminum plates precoated with silica gel 60F-254 as stationary phase and a mobile phase composed of ethyl acetate: methanol: ammonia [17: 2: 1, v/v/]. Densitometric analysis of the obtained spots was carried out at 310 nm. The linear regression analysis of the data obtained for the correlation plots showed good linearity (r = 0.9998) over the concentration range 10-300 ng/spot. With respect to the forced degradation studies, lamotrigine is liable to degradation under acidic, basic, neutral and oxidative conditions. In order to assess the purity and stability of the drug in tablet formulations, the developed method was applied to the analysis of commercially available tablets. In all cases, there was no interference from the excipients commonly present in the tablet matrix. Moreover, the detection of a single spot corresponding to lamotrigine can indicate that the degradation of the drug has not occurred in the marketed formulations that were analyzed by this method.

F-Protein Coding Gene as a Species-Specific Nucleotide Sequence may Acquired from GP64-Laked Baculoviral Host Genome

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Viral envelope fusion proteins are important structural proteins that mediate viral entry and may affect or determine the host range of a virus. The acquisition, exchange, and evo-lution of such envelope proteins may dramatically affect the success and evolutionary di-vergence of viruses. In the family Baculoviridae, two very different envelope fusion pro-teins have been identified. Budded virions of group I nucleopolyhedroviruses (NPVs) contain the essential GP64 envelope fusion protein. In contrast group II NPVs and granu-loviruses have no gp64 gene but instead encode a different envelope protein called F. This study is focusing on the relation of F protein-coding sequence with the type of viral host basing on two types of insect hosts, the first one Spodoptera littoralis which is suscepti-ble for infection by both nucleopolyhedrovirus (SlNPV) and granulovirus (SlGV), the second Phthorimaea operculella which is susceptible for infection by granulovirus (PopGV). The results reflect that fusion protein (F) gene is host–dependent gene. Therefore, may dra-matically acquired from the viral host genome, which proved by that changing in viral host resulting in change in the nucleotide sequence in the F-protein coding region, furthermore the Phylogenetic interrelationships study among six species of gp64-lacked baculoviruses which resulted from ClustalW multiple sequence alignment performed on the same re-gion, indicating that SlGV is more evolutionary related to SlNPV than other granuloviruses genera due to both of them infect the same host larvae (Spodoptera littoralis) however, are derived from different baculovirdae genus. By utilizing of the verity of gap content in the performed F-gene alignment mentioned above, PCR primers designed able to amplify species-specific amplicon size which is useful for distinguishing among gp64-lacked bacu-loviruses.

Pollution of Groundwater: Burden, Scientific and Awareness Strategies for Control

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Groundwater pollution is a worldwide phenomenon with potentially disastrous consequences. The aim of the present investigation was to: (1) Raise the national awareness on the significance of the groundwater pollution in South Sinai being the sole water resource in the area, (2) investigate the physico-chemical and microbiological properties of groundwater, (3) explore the diversity and distribution of algal and fungal taxa in groundwater, (4) detect the efficiency of some local microbes to biosorbe radionuclides and heavy metals of polluted groundwater, and (5) consider the possible effect of the fungal taxa on water quality and human health. 1620 samples of groundwater from 27 wells were analyzed from June (2008) to May (2009). Microbiological analyses included bacteria (total viable, total coliform) and fungi. Temperature, pH, total dissolved salts, electric conductivity, NaCl %, heavy metals, total phosphate, nitrate, nitrite, ammonia, fluoride, uranium and thorium were determined. Fifteen aquatic-derived and eight aquatic zoosporic fungi were recovered, while a total of fifty algal taxa were recorded. 24 awareness campaigns, water education and competitions for 1200 local Bedouins and school students were complemented to teach the importance of safe drinking and water conservation. We were able, based on our awareness campaign, to get two hundred devices of ecoBETA© water-efficient products donated and installed to safe groundwater for the Bedouins. Total coliform count, heavy metals (Pb, Mn and Cu), nitrates, nitrites, fluorides and uranium contents of the majority of studied sites exceed the permissible level concentration for drinking water standards recommended by WHO and Egyptian Standards. Aspergillus niger and Spirogyra varians were considered as new Egyptian biosorbents for removal of radionuclides (Uranium and Thorium) within all screened species based on their potentiality. Finally it's important that fungal content of water should be considered when the microbiological safety and quality of Egyptian drinking water are assessed.

RAPD and ISSR Markers Associated with Flag Leaf Senescence under Waterstressed Conditions in Wheat

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Time of flag leaf senescence is an important determinant of yield under stress and optimal environments. A segregating population from a cross between drought sensitive genotype (Variant-1) and drought tolerant genotype (Veery), was made to identify molecular markers linked to flag leaf senescence gene in wheat under water-stressed conditions as indicator for drought tolerance. Thirty eight RAPD and twenty-five ISSR primers were tested for polymorphism among parental genotypes and F2 population. The present study indicated that four RAPD and two ISSR markers linked to the flag leaf senescence gene in wheat. QTLs for flag leaf senescence were associated with RAPD markers (Pr11230bp, Pr19240bp, OPU06340bp and OPH13450bp) and explained 7.0%, 50.0%, 24.0% and 13.0% of the phenotypic variation, respectively. QTLs for flag leaf senescence were also associated with ISSR markers (M11100bp and

AD2300bp.) and explained 25% and 34% of the phenotypic variation, respectively. The RAPD markers (Pr11230bp, Pr19240bp, OPU06340bp and OPH13450bp) have genetic distance of 15.6, 15.0, 13.2 and 17.4 cM from flag leaf senescence gene, respectively. The ISSR markers (M11100bp and AD2300bp) also showed the genetic distance of 12.5 and 10.2 cM from flag leaf senescence gene, respectively. Therefore, these four RAPD and the two ISSR markers were linked to the QTL for the flag leaf senescence gene as indicator of drought tolerance. These markers can be used in wheat breeding programs, as a selection tool in early generations.

Co-Production of Thermostable Cellulase and Xylanase using Statistical Experiment Design

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Cellulosic resources such as paper, cardboard, wood, agricultural residues and other fibrous plant material are in general very widespread and abundant and are considered a renewable source of energy. The biomass feedstock most commonly considered for conversion are agricultural wastes, energy crops (perennial grasses and trees), and forest waste. The fermentable fractions of these feedstocks include cellulose (1,4-linked glucose) and hemicellulose, a substantial heterogeneous fraction composed of xylose and minor five- and six-carbon sugars. Although it is an abundant biopolymer, cellulose is unique because it is highly crystalline, water insoluble, and highly resistant to depolymerization. The definitive enzymatic degradation of cellulose to glucose, probably the most desirable fermentation feedstock, is generally accomplished by the synergistic action of distinct classes of enzymes.
In this study, a thermotolerant Bacillus sp. isolated from Saudi Arabian soil producing thermostable extracellular xylanase and cellulase was characterized and identified based on 16sr RNA sequencing. A phylogenetic analysis then revealed its closeness to Bacillus subtilis. To evaluate the effect of culture conditions on the co-production of both enzymes by Bacillus subtilis 276NS, a Plackett-Burman factorial design was applied to determine the impact of fifteen variables. Among the tested variables, xylan induced the production of both enzymes. Incubation temperature and time were found to be the most significant for encouraging the production of both enzymes. D-sucrose was found to promote xylanase production. Yeast-extract and ammonium sulfate produced a high positive significant effect on cellulase production. On the other hand pH produced a high positive significant effect on xylanase production. Based on a statistical analysis, a pre-optimized medium attained the maximum production of xylanase and cellulase 165 ul/ml/min and 186 u/ml/m, respectively.

Production and Optimization of Surfactin from Two Bacillus Strains Isolated from Environmental Waste

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Twenty one bacterial isolates were isolated from soil contaminated oil, oil waste and sea water with oil spills. Bacterial isolates were screened for their ability to produce biosurfactants. The most two potent biosurfactants-producing isolates were identified as

Bacillus sp.biotech1 (JN836728) and Bacillus sp.biotech2 (JN836729) according to morphological characteristics, biochemical tests and 16srRNA/DNA technique.
To maximize the production of biosurfactants by these two isolates several production media were used and Mckeen medium was the best production medium. Kerosene was the best carbon source. A mixture of sodium glutamate 1% (w/v) and yeast extract 0.2 % (w/v) was found to be the best nitrogen source concerning biosurfactants production. K2HPO4 0.1% (w/v) and MgSO4.7H2O 0.1% (w/v) increased biosurfactants production. On the other hand, the optimum conditions for biosurfactants production using the above two isolates were 37 0C, 150 rpm, 3%(v/v) inoculume size (CFU= 3.6 x 106), pH7 and incubation time 8-9 days.
Plackett-Burman design was used to screen for the most significant factors that affect biosurfactants production. In case of Bacillus sp. biotech1 all factors were highly significant, except FeSO4 and sodium glutamate were significant, while agitation rate and MgSO4.7H2O were not significant. When Bacillus sp. biotech2 was used all factors were highly significant, except incubation time was significant, while sodium glutamate and yeast extract were not significant. The experimental responses over the predicted values were 98.5-99.84%.
The produced biosurfactants from both isolates were characterized as a Surfactin using MALDI-TOF MS technique. Interestingly, the Surfactin of Bacillus sp. Biotech1 was produced constitutively, while Surfactin of Bacillus sp. Biotech2 was inducible upon using kerosene.
Data above would encourage the use of these two environmental friendly bacterial strains for the commercial production of biosurfactants on large scale using environmental wastes.

Marine Derived Fungi through Drug Discover and Application in Neurological Disorder

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Fungi derived from marine sources are considered to represent a huge reservoir of secondary metabolites, many of which are biologically active and are produced. Marine fungi are highly potent producers of bioactive substances with antifungal, anti-cancer, anti-inflammatory and antioxidant activity, which are major role in treatment of Neurological disorder. tyrosine kinase inhibition and antioxidant and anti-inflammatory effect in addition to the inhibitory effect of fungal extract to acetyl cholinesterase indicate the powerful effect of fungal extract as a protective against many neurological disorder such as Alzheimer's disease (AD), Parkinson's disease (PD) and Huntington's disease (HD). Our result recorded highly inhibition ratio by 91.98%, 91.09%, 93.55% of tyrosine kinase, in-vitro lipid per oxidation (TBARS inhibition assay) and acetylcholinestrase inhibition respectively.

Optimization of Lysate Activity of Lactobacillus Bulgaricus 761N Extracellular Extract

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This investigation is concerned with subcellular fractionation of cell lysate of Lactobacillus bulgaricus 761 N for obtaining three fluids involving lysozyme fluid, osmotic fluid and cytoplasmic fluid representing the desired cell fractions which are extracellular, intracellular and intercellular subcellular fractions respectively. Extracellular extract of L. bulgaricus 761N was observed to possess the highest proteolytic activity reaching 63.1 U/ml/min. The proteolytic activity was found to be affected by a number of factors including incubation period, temperature,pH,salinity, casein content, and metal ions concentration. The proteolytic activity of casein-derived media leads to production of bioactive peptides in the culture filtrate termed as bacteriocins. Bacteriocins were found to possess high antibacterial activity reaching 89% inhibition for the tested pathogens.
Key words:
Subcellular fractionation, Optimization, Proteolytic activity, Bacteriocins, Antibacterial.

Multiple Antibiotic Resistance Profiles of Some Pseudomonas spp Isolated in South Africa

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Pseudomonas species are ubiquitous group of bacterial in soil, plant root and rhizosphere microbiota milieu whose species are of great environmental interest. Seasonal distribution of isolates was revealed as; summer (70.59%), winter (20.59%), autumn (6.86 %) and spring (1.96%). In summer, the highest number of Pseudomonas isolates was recovered from plant rhizosphere (95.83%), followed by plant root (2.77%) and cultivated soil 1.38%. Pseudomonas putida was revealed as the most prevalent of Pseudomonas species among all samples collected and distributed profile as follows; 95% plant rhizosphere, 41.2% plant root and 20% cultivated soil. The antibiotic susceptibility pattern of Pseudomonas isolates reveals 100% resistance against clinamycins, trimethoprim, vancomycin and oxacillin across all samples. Gentamicin had the highest susceptibility among Pseudomonas isolates across all samples; plant root (92.86%), cultivated soil (75%) and plant rhizosphere (85%). Ofloxacin showed susceptibility against Pseudomonas isolates from plant root (78.57%), cultivated soil (75%) and plant rhizosphere (55%). Ciprofloxacin was also susceptible among Pseudomonas isolates and revealed as cultivated soil (75%), plant root (64.29%) and plant rhizosphere (63.75%). Among the antibiotic resistant genes determined, integron gene was detected in 29.76% of P.putida 100% P.aeruginosa and 6.25% of other Pseudomonas species. The study reveals the presence of multidrug resistance Pseudomonas species in the studied microenvironment. The presence of integron gene in some Pseudomonas strains is of immense environmental and public health concern because they are potential disseminator of antibiotic resistance genes in the environment.

Anaerobic waste water as active biocatalyst in microbial fuel cell

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Microbial fuel cells (MFCs) are a biochemical-catalyzed system; electricity was produced by oxidizing biodegradable organic matter in the presence of either fermentative bacteria or enzyme. Our study was aimed to investigate the influence of different mediators and oxygen acceptors in cathode chamber with an activated sludge as biocatalyst in anode compartment. In this way, a two chambered MFC with glucose, 30g.l-1, as substrate was inoculated with anaerobic sludge from a lab-scale waste water treatment setup. The anodic compartment was stirred gently during the operation. Constant voltage was reached after 2 days of operation time and was 360 mV. Aeration in cathode chamber was started in three different rates. Maximum power and current density at optimized rate of aeration were 1.8 mW.m-2 and 8.9 mA.m-2, respectively. By fixing the optimized rate of aeration, iron, ferricyanide, potassium permanganate were used as electron acceptor. Polarization curves were obtained with several concentration of the mentions materials (100, 200, 300 and400 µM). The maximum power and current density, 68.459 mW.m-2 and 187.615 mA.m-2, occurred at 300 µM potassium permanganate concentration. Adding Neutral red and thiamine, at 100 and 200 µM concentrations, as mediators in anode, had no remarkable effects on the obtained results.

Evaluation of the Effect of Losartan on Methotrexate Treatment in Adjuvant-Induced Arthritis in Rats

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Angiotensin II (Ang II) is classically known as a cardiovascular mediator, with a primary role in the control of blood pressure. However, there is increasing body of evidence documenting the involvement of Ang II in inflammatory diseases and implicating it in the up-regulation of proinflammatory cytokines. The previously described up-regulation of Angiotensin II Type 1 (AT1) receptors in synovium samples obtained from Rheumatoid Arthritis (RA) patients raises the possibility that their blockade, by a specific inhibitor such as losartan, may present a novel and effective therapeutic target in the treatment of RA. The aim of the present study was to investigate the anti-inflammatory effect of losartan and to compare the efficacy of methotrexate, the most effective Disease Modifying Anti-Rheumatic Drug (DMARD), alone and in combination with losartan on some inflammatory and arthritic markers, as well as on extra-articular manifestations, involving the hepatic system, in adjuvant-induced arthritis in rats.

The PharmacoMicrobiomics Portal: A database for Drug-Microbiome Interactions

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The Human Genome Project provided insight into genetic variations among humans; yet, such information has not sufficiently accounted for all phenotypic differences between individuals. Thus, the Human Microbiome Project was launched to investigate the microbial involvement in human variations. As they outnumber the human cells (10^14 vs. 10^13), microbial communities residing in the human body are an integral part of the human gene pool, and various studies have investigated the relationship between resident microbiota and human health and disease. However, very little information is available on the effect of the microbial gene pool on drug fate and action in the human body.
Here, we present the PharmacoMicrobiomics database, which aims to collect, classify, and cross-reference all known drug-microbiome interactions through manual literature mining, curation and classification of interactions according to body site, microbial taxonomic classification, drug chemical and pharmacological classifications, and biochemical pathways. The database is integrated in a web portal including a search engine through which students and scholars can locate drug-microbiome interaction of interest, linked to and compiled from public literature and drug databases, such as: PubMed, PubChem, NCBI Taxonomy Browser, Comparative Toxicogenomics, and SEED.
The PharmacoMicrobiomics database and web portal were designed and created by the use of open-source technologies. MySQL was used as a database management system, and Django, a Python-based framework, was used for the creation of the relational database to store drug-microbiome interactions and classifications.
Currently, the database contains drug-microbiome relations for 12 drugs curated from over 100 research papers. Further developments may include the automation of data updating using BioPython libraries for Entrez Programming Utilities, and the participation of the community into data analysis, curation and database design.
Database URL: http://www.pharmacomicrobiomics.org

Laccase Producing Fungi in Egypt and Future Application for the Society

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Laccase enzyme (EC 1.10.3.2) is a benzenediol, a multi-copper enzyme, and one of the three main ligninases that differs from the others in its ability to catalyze the oxidation of lignin components. It is widely distributed in fungi and because of its importance in bioremediation; the search for fungal laccases with different properties and potential applications is still on-going. In view of its importance in large scale application, the present endeavor is to search for highly efficient laccase producing fungi from different environmental habitats in Egypt. Cultural conditions such as temperatures, pH, carbon sources and nitrogen sources were optimized for the production of high extracellular laccase activity. By screening sources under investigation namely: soil, wood, seaweeds, sponge, ascidia, drifted decaying wood, plants and miscellaneous materials it was possible to encounter as many as 60 species belonging to 33 genera. Zygomycota

represented by six species (10.16% of the total species number), teleomorphic Ascomycota (9 species, 15.25%), anamorphic Ascomycota (44 species, 74.57%) and Basidiomycota (1 species, 1.69%). Soil showed the highest Simpson's species diversity index of 0.83 while contaminated wax samples and *Adiantum capillus*-veneris showed the lowest value (0). All isolated taxa were tested for laccase production using a qualitative plate assay method by using guaiacol as color indicator. Sixteen isolates showed positive reaction indicating a lignin-degrading potentiality and out of them eight measured the highest zone diameter with high oxidation scale. The most promising taxa were endophytic namely: Chaetomium globosum, Phoma exigua, Thanatephorus cucumeris and Sordaria fimicola. pH 7, incubation temperature 30^{o}C, 1% maltose and 0.3% peptone supported the highest biomass and laccase production for Chaetomium globosum.

Optimization Strategy Design & Stability Study of Self-Nanoemulsifying Antihyperlipidimic Preconcentrates

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The aim of this study was to develop, optimize and characterize solid preconcentrates (SPC) for improving the dissolution rate of simvastatin giving better chance for oral bioavailability and to evaluate its stability. Suitable compositions of Self NanoEmulsifying Formulation (SNEF) were screened via solubility studies and compatibility tests. Response surface methodology and desirability approach were applied to optimize SNEF containing minimum amount of surfactant, maximum amount of lipid, and possess the smallest globule size with highest emulsification and dissolution rates. As part of the optimization process, the main effect, interaction effects and quadratic effects of amounts of lipid, surfactant/co-surfactant ratio on % transmittance, globule size, emulsification time and drug release were investigated. The optimized formulation consisting of 45% Capryol, 40.15% Chremophor RH 40 and 14.85 % Transcutol possessing globule size of 130 nm was mixed with Aerosil 200 to get uniform free flowing granules which were characterized for solid-state characteristics, surface and powder properties. The self- nanoemulsifying preconcentates filled into hard gelatin capsules showed 3 and 4 folds increase in simvastatin released compared to conventional tablet and pure drug respectively. The shelf life was found to be 458 days at 25 oC. Our study illustrated that the developed SPCs held great potential as a possible alternative to traditional oral formulations of simvastatin. They represent alternative candidate which can be commercialized due to their superior dissolution properties and comparable stability profile with respect to the commercially available oral dosage form.

Computer-Guided Drug Repurposing in the Search of Novel Antiepileptic Medications: The Sweetener Hypothesis

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Epilepsy is the most common central nervous system chronic disorder, affecting about 50 million worldwide, 90% of which come from developing countries [1]. Current antiepileptic chemotherapy fails to protect against seizures in around 30% of the

patients, a condition known as refractory or intractable epilepsy. What is more, current antiepileptic medications elicit a number of side effects that justify the continuous search of novel treatments.
Drug repurposing implies finding second (or further) medical uses to known medications. It is an interesting concept, since known drugs have already undergone extensive safety studies, which may facilitate the approval of new therapeutic uses. Although historically most second medical uses have been found by serendipity, a number of authors have recently pointed out the possibilities of knowledge-based drug repurposing (using computer models, bioinformatics and high-throughput literature searching to propose new medical indications for already known chemicals).
We have previously reported a computational model to identify antiepileptic agents [1-2]. Recently, application of that model in virtual screening indicated that several artificial sweeteners, such as acesulfame, saccharin and cyclamate, might have anticonvulsant activity. Pharmacological testing in the Maximal Electroshock test has confirmed these predictions, which led us to propose what we have called "the sweetener hypothesis", i.e. the existence of a structural link between the receptor that mediates the sweet response in the mouth and sodium channels in the brain. This hypothesis might explain why a number of artificial sweeteners manifest anticonvulsant activity in the MES test. Our results serve as proof-of-concept of the possibilities of computer-assisted drug repurposing.
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Purification, Characterization and Crystallization of an L-Amino Acid Oxidase from Bothrops Jararacu

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Snake venom is complex mixture of proteins, enzymes and peptides. Snake venom L-amino acid oxidases (SV-LAAOs) trigger a wide range of local and systematic effects including the inhibition of platelet aggregation, cytotoxicity, hemolysis, apoptosis and hemorrhage. These effects are mainly due to the uncontrolled release of hydrogen peroxide which is produced by the redox reaction involving L-amino acids catalyzed by these flavoenzymes. They have been tested for anti cancer, anti HIV and antibacterial activities. They kill leishmania spp. Besides their clinical relevance, few SV-LAAOs have been structurally characterized and the structural determinants responsible for their broad direct and indirect pharmacological activities are unknown. In this work, we purified, characterized and crystallized this enzyme from Bothrops jararacussu venom (Bj-LAAO). Functional assays showed that Bj-LAAO has a marked preference for hydrophobic and aromatic L-amino acids. Bj-LAAO crystals belong to the space group P21 with cell constants of a=66.38, b=72.19, c=101.53 Å (β = 90.9º). The asymmetric unit contains two molecules and the structure was determined and partially refined at 3.0Å.

Incredible Utilization of Polymer/Clay Nanocomposites for Removing Pesticides from Waste Water

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Exfoliated poly (methylmethacrylate) PMMA/CTA-MMT nanocomposites were prepared via in-situ emulsion polymerization. The CTA-MMT form was used as hosts for the preparation of poly (methylmethacrylate) nanocomposites after the basal space from 11.48 Ao to 19.49 Ao. Moreover, exfoliated nanocomposites was obtained after polymerization process take place and characterized by x-ray diffraction (XRD), transmission electron microscope (TEM), thermal gravimetric analysis (TGA), and differential scanning calorimetry (DSC). The fashioned nanocomposites exhibited better thermal stability than pure polymethymethacrylate. Furthermore, the prepared nanocomposite reveals tremendous affinity for removing pesticides. The data obtained from GC liquid chromatography illustrated that the removal efficiency of PMMA/CTA-MMT nanocomposites for organchlorine Pesticides (OCPs) varied from 32.81 to 99.36%.

Impacts of Climate Changes and Environmental Pollution on the Egyptian Museum

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The Egyptian Museum became an improbable backdrop to Egypt's ongoing revolution and witnessed changes not only in realm of politics but also in that of environmental and climatic factors. The Egyptian Museum is located at El-Tahrir Square, and is characterized by a high concentration of air-pollutants. This study examines –case study for one year- the internal and external conditions of the museum building and its collectable archaeological treasures, by taking into account the micro climatic conditions of the region. The physical, mineralogical and geochemical properties of the building's structural deteriorations were assessed by using Scanning Electron Micrograph (SEM), X-ray, meteorological data, monitoring. The air toxic emissions of vehicles e.g. Co2, No and So2, are among the main causative agents of decay on the ornamental calcareous stones, through sulfation or black-crust formation. Soot and metallic particles, bearing Fe, Cr, Ni, Cu, Mn, act in catalytic oxidation, which increase the superficial erosion of the artifacts. Vibrations generated from the underground metro, seepage of groundwater from capillary action, with salt crystallizations and dissolutions, biological contamination threaten our cultural heritage. Over 6500 visitors per day, who release heat, vapor and Co2. The natural ventilation allows dust, pollution, gases and non-filtered light that come from the diffused glass panels on the ceiling and from the windows to enter into the museum. A new renovation plan has been suggested, There should be increased pressure from the government to control building environments in a globally sustainable manner. Correctly installed and maintained mechanical ventilation should allocate air quality. Air purifying plants are recommended for removing gaseous pollutants from indoor air. An oxygen free environment could be applied on important objects as a preventive conservation to save our heritage for the successive generations. Serious environmental preservation plans should be considered for the square area outside in order to protect the museum.

Triple Trouble: The Effect of Combining Mechanical Stress, PBMCs and Cisplatin on HepG2 Cells

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In an attempt to increase the effectiveness of drugs to tumor cells, new models are suggested. A mathematical model (Klika V. and Marsik F., 2009) suggests that several factors drive one another and hence increase cancer cell death more than that caused by each factor alone. In this work, in vitro experiments using three stress factors (mechanical stress, cisplatin- a cytotoxic drug and PBMCs- Peripheral Blood Mononuclear Cells) are suggested to be necessary for higher cytotoxic effect against HepG2 (human hepatocellular carcinoma cell line) tumor cells. Each factor by itself has a certain effect in killing HepG2 cells and we explored the effect upon simultaneously combining all three parameters. The extent of cell death was assayed by MTT and the expression levels of some apoptosis related genes such as XIAP (inhibitor of apoptosis), BAX (apoptosis trigger) and HSP70 (a cyto-protective gene). MTT-assay results indicated a greater number of dead HepG2 cells after exposure to cisplatin and PBMCs simultaneously, than those that died after exposure to either cisplatin or PBMCs alone. RNA analyses demonstrated the up-regulation of BAX and HSP70 and the down-regulation of XIAP genes' expression in HepG2 cells that were treated with Cisplatin and/ or co-cultured with PBMCs. Thus compared to the effect of either cisplatin alone or PBMCs alone, simultaneous exposure to both resulted in increased death of HepG2 cells.