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ABSTRACT 1

Agricultural benefits of *Moringa Oleifera*: From animal model to improvement of human muscle health

Miri Cohen Zinder

ABSTRACT

Moringa oleifera is a rich source of antioxidants and a promising superfood / feed for human and livestock, due to significant amounts of protein, vitamins, carotenoids and polyphenols, and negligible amounts of anti-nutritional factors. In ruminants, a growing number of studies have tested its effects on production performance and quality characteristics, most of them, however, used dried leaves, harvested manually. Although drying of *Moringa oleifera* leaves preserves its nutritive value, our findings demonstrate the effectiveness of ensiling in preserving its antioxidative capacity. The beneficial effect of ensiled *Moringa oleifera*, provided as a supplement in the diet of growing lambs, on their muscle characteristics and its health index profile, will be highlighted in the current presentation. Specifically, changes were detected in sarcomere length (SL) which was significantly higher ($P<0.01$) in the muscles (*LD*, *BF*, and *SM*) of Moringa-fed lambs, in comparison to their counterparts, fed supplementary wheat silage. Moreover, the intra-muscular fat (IMF) of Moringa-fed lambs, exhibited lower content ($P<0.05$) and their muscle health index was improved, as reflected by its increased vitamin E levels ($P<0.01$) and decreased malondialdehyde (MDA) concentrations ($P<0.01$; positively correlates with lipid peroxidation process). Muscle transcriptome analysis exposed Moringa-derived differential expression of genes subjected to different metabolic and health associated pathways involving fiber and sarcomere organization, energy metabolism, mitochondrial biogenesis and stress of the endoplasmic-reticulum (ER-stress).

Keywords: *Moringa oleifera*, Muscle health, Super food

Presented by: Miri Cohen Zinder

Model Farm for Sustainable Agriculture, NeweYa'ar Research Center, Agricultural Research Organization – Volcani Center, Israel

Email: mirico@volcani.agri.gov.il



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ABSTRACT 2

Ameliorative effect of *Harrisoniaabyssinica* leaves extract on neurobehavioral, histological and biochemical changes in the hippocampus of rats with aluminum chloride-induced Alzheimer's disease

Hend Mohamed Anwar, Gehan S. Georgy, Sherin Ramadan Hamad, Wafaa K. Badr, Mohamed A. El Raey, Mohamed A.O. Abdelfattah, Michael Wink, Mansour Sobeh

ABSTRACT

Aluminium (Al) is an omnipresent element in the environment. The brain is a central goal of Al toxicity being more susceptible to oxidative damage. Therefore, recognition of drugs or natural products that guard against Al-mediated neuronal cell death is a powerful strategy for prevention and treatment of neurodegenerative disorders. This work aimed to explore the potential of *Harrisoniaabyssinica* leaf extract to modulate the neurobehavioral, biochemical, and histopathological 27 toxic actions induced experimentally by Al in vivo. Rats subjected to Al displayed decline in learn-28 ing and memory performance in passive avoidance test accompanied by reduction in the hippo-29 campal monoamines levels in addition to suppression of Bcl2 expression. Moreover, malondialde-30-hyde (MDA), inflammatory markers (TNF- α , IL-1 β), apoptotic markers (caspase-3, and expression 31 of Bax), and extracellular regulated kinase (ERK1/2) levels were elevated along with acetylcholin-32 esterase (AChE) activity, passive histological changes, and marked deposition of amyloid β plaques 33 in the hippocampus region of the brain tissues from Al treated animals. Concomitant administration 34 of the high dose of *H. abyssinica* (200 mg/kg b.w.) restored nearly normal levels of all parameters 35 measured rather than the low dose (100 mg/kg b.w.), an effect that was comparable to the reference 36 drug (rivastigmine). Molecular docking revealed the appropriate potential of the extract compo-37 nents to block the active sites of AChE and ERK2 enzymes. In conclusion, *H. abyssinica* leaf extract 38 conferred neuroprotection against Al induced neurotoxic effects, most likely due to its high phe-39 nolic and flavonoids content.

Keywords: *Harrisoniaabyssinica*; Hippocampus; Alzheimer; Polyphenols; ChE; ERK; BCl₂

Presented by: Mansour Sobeh

AgroBioSciences, Mohammed VI Polytechnic University, Lot 660–Hay Moulay Rachid, 43150 Ben-Guerir, 20 Morocco 21

Email: mansour.sobeh@um6p.ma



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ABSTRACT 3

Analysis of endoplasmic reticulum proteins of mulberry leaves under UV-B and dark stress using Tandem Mass Tag-based proteomics

Eman Shawky, Shengzhi Liu, Yuting Ou, Yaohan Li, Kaisa Sulaiman, Minglei Tao, Jingkui Tian, Wei Zhu

ABSTRACT

Mulberry leaves have been utilised in traditional medicine for centuries because of their antioxidant, anti-diabetic, and anti-hyperlipidemic effects. A prior study found that UVB radiation followed by dark incubation improved the concentration of active compounds including moracin N and chalmoracin in mulberry leaves. The endoplasmic reticulum (ER) is a protein quality control centre and a site for protein synthesis in plants, and it plays a role in their response to environmental stress. On mulberry leaves, ER proteomics was performed to study the processes in response to UVB radiation followed by dark incubation (UV + D). GRP78 and calnexin (CNX), two ER protein indicators, were considerably higher in the ER fraction than in the total protein fraction, indicating that the ER had been purified. Protein disulfide isomerase, UDPglucose glycoprotein glucosyltransferase, CNX, and calreticulin protein abundance decreased under stress compared to the control, but heat shock related protein abundance increased. Proteins associated to the P450 enzyme system and ribosomal proteins both increased significantly. These findings imply that, in response to UV + D stress, mulberry leaves triggered the cell redox and ER quality control systems, increasing protein synthesis while weakening N-glycan biosynthesis in the ER.

Keywords: Mulberry leaves, endoplasmic reticulum proteins, UVB and dark stress, TMT based proteomics

Presented by: *Eman* Shawky

Department of Pharmacognosy, Faculty of Pharmacy, Alexandria University, Alexandria, Egypt

Email: shawkyeman@yahoo.com

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ABSTRACT 4

Assessment and analysis of outpatient medication errors related to pediatric prescriptions

Marwa Kamal

ABSTRACT

Medication errors are the errors that impact the efficacy and safety of the therapy. The impact of medication errors is higher for certain subjects, such as pediatrics, who require more attention. Hence, the current study aimed to investigate the types and frequency of outpatient medication errors of pediatric subjects related to different prescription types.

Materials and Methods: A cross-sectional study was carried in several community pharmacies to record the medication errors found in outpatient pediatric prescriptions by gathering data from the outpatient prescriptions besides direct counseling with the subjects and their parents. Many medical resources (disease and drug-related) were used for checking the different aspects of medication errors. The data collection process included a preprepared sheet containing several items representing the medication errors in addition to a counseling session. Data were expressed as percentages and compared through the Chi-square test for results of handwritten and computerized prescriptions.

Results: 752 outpatient pediatric prescriptions were recruited in the study as they involve medication errors. Among the highest percentage of medication errors was the absence of essential data in the prescription, such as diagnosis, age, and weight. The duration of the therapy and contraindication for some of the prescribed medications were among the highest recorded errors. Among the critical errors were the drug interaction and drug duplication that directly affect the drug's efficacy and safety. There was a significant difference between computerized and handwritten prescriptions regarding the number of medication errors related to each type.

Conclusions: Medication errors related to outpatient pediatric prescriptions vary from one to another prescription with predominant errors that influence the therapy's safety or efficacy. The role of patient counseling and prescription checking is critical for improving patient therapy.

Keywords: Medication error, antibiotic misuse, pediatric, prescribed medication, counseling

Presented by: Marwa Kamal

Clinical Pharmacy Department, Faculty of Pharmacy, Fayoum University, Fayoum, Egypt

Email: marwahassan181@yahoo.com



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ABSTRACT 5

Beta-carotene attenuates cognitive and hepatic impairment in thioacetamide-induced rat model of hepatic encephalopathy via mitigation of MAPK/NF- κ B signaling pathway

Marawan Abd Elbaset Mohamed, Hanan A. Ogaly, Rehab F. Abdel-Rahman, Ahmed-Farid O.A., Marwa S. Khattab, Reham M. Abd-Elsalam

ABSTRACT

Liver fibrosis is a severe worldwide health concern due to various chronic liver disorders. Hepatic encephalopathy (HE) is one of its most common complications affecting liver and brain cognitive function. Beta-Carotene (B-Car) is an organic, strongly colored red-orange pigment abundant in fungi, plants, and fruits. The study attempted to know B-Car neuroprotective potential against thioacetamide (TAA)-induced neurotoxicity and cognitive decline in HE in rats. Hepatic encephalopathy was induced by TAA (100 mg/kg, i.p.) three times per week for two weeks. B-Car was given orally (10 or 20 mg/kg) daily for two weeks after TAA injections. Organ body weight ratio, Serum transaminase activities, liver's antioxidant parameters, ammonia, and liver histopathology were assessed. Also, the brain's mitogen-activated protein kinase (MAPK), nuclear factor kappa B (NF- κ B), antioxidant parameters, adenosine triphosphate (ATP), adenosine monophosphate (AMP), norepinephrine (NE), dopamine (DA), serotonin (5-HT), 5-hydroxyindoleacetic acid (5-HIAA) cAMP response element-binding protein (CREB) expression and B-cell lymphoma 2 (Bcl-2) expression were measured. The brain's cognitive functions (Spontaneous locomotor activity, Rotarod performance test, Object recognition test) were assessed. B-Car prevented alteration of the brain's cognitive function in a dose-dependent manner. The histopathological outcomes supported these biochemical evidences. Based on these results, it could be established that B-Car could be assigned to treat the brain's neurotoxicity consequences of HE via down regulation of MAPK/NF- κ B signaling pathways.

Keywords: Beta-carotene; liver injury; MAPK; NF- κ B; rat; thioacetamide.

Presented by: Marawan Abd Elbaset Mohamed

Department of Pharmacology, Medical Research and Clinical Studies Institute, National Research Center, Dokki, Giza, Egypt.

Email: dr.marawan@gmail.com



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ABSTRACT 6

Bioguided isolation of Hep-G2 cytotoxic constituents from *Laurus nobilis* Linn. cultivated in Egypt

Nesma Nagah, Islam Mostafa, Gamal Dora, Zeinab El-Sayed, Abdel-Monem Ateya

ABSTRACT

The air-dried leaves of *Laurus nobilis* cultivated in Egypt were successively extracted by petroleum ether followed by methylene chloride, ethyl acetate and finally methanol. The preliminary cytotoxic screening of these extracts against Hep-G2 using vinblastine sulfate (IC₅₀= 2.93 µg/ml) as standard showed that petroleum ether, methylene chloride and ethyl acetate extracts showed strong cytotoxic activity (IC₅₀= 10.6, 5.96 and 3.80 µg/ml, respectively) while the methanolic extract showed moderate activity (IC₅₀= 23.2 µg/ml). The extracts that exhibited strong cytotoxic activity were subjected to further investigation and bio-guided chromatographic isolation resulting in isolation of five compounds. The isolated compounds were identified as 1-tricosanol, reynosin, protocatechuic acid, vincetoxicoside B and vitexin and the chemical structures have been established on the basis of physical, chemical and spectroscopic methods, in addition to comparison with literature data. Among the isolated compounds, reynosin showed the most potent cytotoxic activity against Hep-G2 (IC₅₀= 4.98 µg/ml), while vitexin showed the lowest activity (IC₅₀= 219 µg/ml). Other compounds showed moderate to weak activity. The isolated compounds were docked to caspase3 to reveal their possible cytotoxic mechanism of action on the enzymatic level.

Keywords: *Laurus nobilis*, cytotoxicity, Hep-G2, reynosin, molecular modeling

Presented by: Nesma Nagah

Department of Pharmacognosy, Faculty of Pharmacy, Fayoum University, Fayoum, Egypt

Email: nesmanagah.b@gmail.com



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ABSTRACT 7

Characterization of the microbial community structure in Nile River water and sediment along the Greater Cairo area

Walaa A. Eraqi, Marwa T. El Rakaiby, Salwa A. Megahed, Noha H. Yousef, Mostafa S. Elshahed, Aymen S. Yassin

ABSTRACT

Identification and characterization of the microbial community structure and its diversity is a valuable tool for monitoring the influence of urbanization and industrial impact particularly in vast metropolitan areas. Here, we characterize the Nile River microbial composition in water and sediments in summer and winter at five locations along the natural flow of the Nile River through the Cairo metropolis. 16S rRNA gene datasets were analyzed to identify the role played by sample type, season and location in microbial community composition. In addition, attempts were made to functionally predict the potential of the Nile River microbiome. Sampling type played the major role in shaping microbial community structure, while seasonal effects were only observed in water samples. The differences observed among the locations did not represent a significant factor in shaping the community in either summer or winter seasons. Proteobacteria was the most abundant phylum in both water and sediment samples, with the order Betaproteobacteriales being the abundant one. Chloroflexi and Bacteroidetes were also prevalent in sediment samples, while Cyanobacteria, and Actinobacteria were abundant in water samples. Linear discriminative analysis Effect Size (LEfSe) identified the cyanobacterial genus *Cyanobium* PCC-6307 as the main variable between summer and winter water. Sequences representing human and animal potential pathogens, as well as toxin-producing Cyanobacteria were identified in low abundance within the Nile microbiome. Functional predicted metabolic pathways identified the presence of antibiotic biosynthesis, as well as aerobic xenobiotic degradation pathways. The results pave the way to fully understand the microbial diversity along the Nile River and its impact on the population living around it.

Keywords: Nile River, 16S rRNA gene sequencing, microbiome, freshwater, Sediment

Presented by: Aymen S. Yassin

Department of Microbiology and Immunology, Faculty of Pharmacy, Cairo University, Cairo, 11562, Egypt

Email: aymen.yassin@pharma.cu.edu.eg



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ABSTRACT 8

Comparative metabolomic profiling, phytochemical, and biological studies of three *Cycas* species growing in Egypt

Ahmed Ismail, Abeer S. Moawad, Hossam M. Hassan, Mohamed M. Radwan, Mona H. Hetta

ABSTRACT

Comparative analytical, phytochemical and biological studies of the crude extracts of the aerial parts of three *Cycas* species; *Cycas armstrongii* Miq., *Cycas circinalis* L. and *Cycas revoluta* Thunb., growing in Egypt were performed. The metabolomics profiling was done using Liquid chromatography-high resolution electrospray ionization mass spectrometry (LC-HRESI-MS). The in vivo biological studies included determination of LD50, studying the ameliorative role of *Cycas* species extract on γ -radiation toxicity using biochemical analysis of liver and kidney functions, glucose and insulin levels, partial restoring platelet count assay, partial restoring white blood cell count assays, IL-18, amyloid A, oxidative stress parameters, detection of brain Injury (NFkb, Cox2, MCP-1, GFAP), detection of pancreatic Injury (Amylase, Lipase, microRNA216a) and finally histopathological examination of brain and pancreatic tissue of albino rats. All these studies were carried out in a comparative manner with the aim to select the most bioactive species. *Cycas armstrongii* Miq. was selected based on the prevalence of its particular significance in many biological activities beside the rare reports on its chemical composition and biological effects. A detailed phytochemical study of the fractions of the selected *C. armstrongii* led to isolation of nineteen chemical compounds of different classes as first report in this species; β -sitosterol, stigmasterol, naringenin, kaempferol, dihydroamentoflavone, dihydrohinokiflavone, amentoflavone, β -sitosterol glucoside, isoginkgetin, pruinin, vitexin, naringin, vitexin-2''-rhamnoside, vanillic acid, p-coumaric acid, caffeine, catechin, epicatechin and epigallo-catechin 3- gallate. For caffeine, this is the first report in family Cycadaceae.

Keywords: *Cycas*, metabolomics, ionizing radiation, brain, pancreas, histopathology

Presented by: Mona H. Hetta

Pharmacognosy Department, Faculty of Pharmacy, Fayoum University, 63514, Egypt

Email: monahetta1@gmail.com



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ABSTRACT 9

Contribution of the phytotherapy in the control of viral infections

Abeer, A.H. Boseila

ABSTRACT

In the last two decades of the twenty-first century, there have been more than ten major viral disease outbreaks in human populations, caused by Coronavirus, Alphavirus, Myxovirus, Filovirus, Norovirus and Flavivirus family members. In addition, small sporadic outbreaks have originated from Henipaviruses, Bunyaviruses, Arenaviruses and other zoonotic RNA viruses. The common pathways of pathogen evolution in pandemic out breaks. Several factors contribute to the adaptive evolution of infectious agents to spread into different ecological populations, adapt to new hosts, escape from host defense mechanisms, and spread globally. They are broadly categorized in three major factors: host factors, microbial factors, and environmental factors. Eradication and control of viral infections include methods of diagnosis, treatment using antiviral agents, prophylaxis using vaccines and virucidal agents to destroy the infectious viral particles as in disinfectants and antiseptics. Plants started being used as a biopharmaceutical's platform for the manufacturing of diagnostic reagents and therapeutic proteins immediately after the first successful expression of recombinant antibody in a plant. Plants offer huge advantages compared with platforms based on traditional mammalian cell cultures. Moreover, Phytotherapy has many active constituents which have direct activity on the viral replication cycle including polyphenols, flavonoids, tannins, alkaloids, catechin and lycorine. Using of phytotherapies as antiviral agents has many advantages over the corresponding antiviral drugs including the safety, tolerability, availability, and eco-friendly agents. Many plant species have been used in vaccine production against viruses. The choice of plant used depends mainly upon the way of vaccine administration either edible or in injectable form. The major factors that drive the plant-based platform towards potential competitors for the conventional expression system are cost-effectiveness, scalability, flexibility, versatility, and robustness of the system. Many biopharmaceuticals including recombinant vaccine antigens, monoclonal antibodies, and other commercially viable proteins are produced in plants, some of which are in the pre-clinical and clinical pipeline.

Keywords: viral disease, phytotherapy

Presented by: Abeer A.H. Boseila

Viral Research Department. Egyptian Drug Authority

Email: abeerboseila@gmail.com



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ABSTRACT 10

Drug repurposing in dermatology and cosmeceutics: phytochemistry, molecular biology and omics approach

Farid A. Badria

ABSTRACT

The withdrawal of several blockbuster drugs due to severe adverse effects and the failure of several developed drugs in clinical trials raised questions about the efficacy of current approaches of drug discovery. Moreover, the limitation of resources and the long and costive process of drug discovery made a lot of pharmaceutical companies to employ drug repurposing strategies to get new insights about activities that were not considered during their initial discovery. The development of therapeutics for treatment of many dermatological disorders is not considered as priority although it affects the lifestyle of thousands of people around the world. Serendipity and observations have contributed significantly in this field but immerse efforts have been exerted to find systematic methods to identify new indications for drugs especially with the unprecedented progress in molecular biology and omics. So, in this chapter we will emphasize on different approaches used for drug repositioning and how it was applied to find new therapeutics for different skin disorders; e.g hair loss, psoriasis, acne, hirsutism, and melisma.

Keywords: Drug repositioning, omics, molecular biology, psoriasis, acne, metformin

Presented by: Farid A. Badria

FAB-Lab, Liver Research La, Department of Pharmacognosy, Faculty of Pharmacy, Mansoura University, Mansoura 35516 Egypt

Email: faridbadria@gmail.com



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ABSTRACT 11

Dual PI3K/Akt inhibitors bearing coumarin-thiazolidine pharmacophores as potential apoptosis inducers in MCF-7 cells

Rasha Abdelhady, Mohamed Abdelhady

ABSTRACT

Breast cancer is the most common malignancy worldwide therefore, the development of new anticancer agents is essential for improved tumor control. A range of coumarin derivatives were prepared. The in vitro anticancer activity was assessed against MCF-7 cells adopting the MTT assay. Nine compounds showed significant cytotoxicity. The most promising compound, VIIb, induced remarkable cytotoxicity (IC₅₀ of 1.03 ± 0.05 μM). Further investigations were conducted to explore its pro-apoptotic activity demonstrating S-phase cell cycle arrest. Apoptosis rates following VIIb treatment revealed a 5-fold and 100-fold increase in early and late apoptotic cells, correspondingly. Moreover, our results showed caspase-9 dependent apoptosis induction as manifested by an 8-fold increase in caspase-9 level following VIIb treatment. Mechanistically, VIIb was found to target the PI3K-/Akt-1 axis, as evidenced by enzyme inhibition assay results reporting significant inhibition of examined enzymes. These findings were confirmed By Western blot results indicating the ability of VIIb to repress levels of Cyclin D1, p-PI3K, and p-Akt. Our results suggest that VIIb has pharmacological potential as a promising anti-cancer compound by the inhibition of the PI3K/Akt axis.

Keywords: coumarin, anticancer, breast cancer

Presented by: Rasha Abdelhady

Email: ram14@fayoum.edu.eg



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ABSTRACT 12

Effect of climate changes on the abundance of natural plant raw materials as an input for the manufacture of cosmetics and foods supplements

Mohammed Abdelwahab, Fatma Ali Ahmed

ABSTRACT

The effect of climate changes on the abundance of natural plant raw materials as an input to the manufacture of cosmetics and nutritional supplements. Climatic changes led to a severe shortage of raw materials as a result of fluctuations in temperature. This was recorded in Egypt very clearly in the season 2020/2022, as some plants rushed to early flowering, seeds atrophy, and a severe shortage of crops (anise and fennel plants), especially in the south of Cairo, Or the lack of urban growth (violet plants) in the north of Cairo, or the low percentage of essential oils (*Pelargonium graveolens*, mint, jasmine flowers and violet leaves) in addition to the spread of the severity of insect infestations as a result of successive generations at times that were not suitable for the growth cycle. Therefore, more measures and agricultural research must be taken, such as changing the usual planting dates - quantities, periods, irrigation rates, planting areas, and non-traditional means and materials to control and prevent pests. And research to develop strains tolerant of temperature fluctuations.

Keywords: Climate changes in Egypt, plants, Egypt, essential oils, natural extracts

Presented by: *Mohammed* Abdelwahab

Desert Research Center, Egypt

Email: abdelwahab2007@gmail.com



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ABSTRACT 13

Era of COVID-19 pandemic: Global distribution and evolution of SARS-CoV-2 clades

Walid F. Elkhatib

ABSTRACT

Global extension of COVID-19 increases attention to exploring genomic variations of novel SARS-CoV-2 virus. Metadata of 408,493 SARS-CoV-2 genomes deposited in GISAID database were analyzed in terms of genotypes (clades) and their geographic, age, and gender distributions. Regarding known SARS-CoV-2 genotypes, clade GR is the most globally ubiquitous followed by GV then GH. Sequential analysis demonstrated extension in SARS-CoV-2 clades carrying D614G mutations with the preponderance of the most recent clade, GV, in the last three months of this analysis. D614G genotypes prevail in countries with more COVID-19 cases. Of various genotypes, clades GR and GH were more commonly recovered from severe COVID-19 cases. On contrary, G and GV clades revealed a significantly superior prevalence between asymptomatic patients or those with mild disease. Metadata scrutiny demonstrated higher prevalence ($p < 0.05$) of severe/deceased cases among males than females and predominance of GR clade in female patients. Higher frequency of the GV clade was observed in children as compared to other age groups. Moreover, severe disease/death was more dominant in elderly ($p < 0.05$) than in adults/children. This study provides detailed evidence on the genetic evolution of SARS-CoV-2 leading to altered virulence, infectivity, and mortality.

Keywords:

Presented by: *Walid F. Elkhatib*

Department of Microbiology & Immunology, Faculty of Pharmacy, Galala University, New Galala city, Suez, Egypt

Microbiology and Immunology Department, Faculty of Pharmacy, Ain Shams University, African Union Organization St., Abbassia, Cairo 11566, Egypt

Email: walid-elkhatib@gu.edu.eg



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ABSTRACT 14

Extraction and evaluation of natural antioxidants extracted from grape waste by using eco-friendly solvents and novel assisted extraction methods

Eman Fawzi Al-Amrousi, Mohamed Hassan El-Malah, Mohamed Helmy Areif, Minar Mahmoud M. Hassanein

ABSTRACT

Background: Phenolic compounds are known to have potential health benefits. They can reduce the risks of neurodegenerative and cardiovascular disease, as well as diabetes, cancer, and osteoporosis. In addition, polyphenols are considered as the most attractive natural antioxidants. Large amounts of wastes were produced during food processing all over the world such as grape waste. These wastes have heavy environmental impact, in the same time it considers as good source of phytochemicals that can be displayed wide spread uses as food additives, pharmaceutical, cosmetics as well as antioxidants. **Materials and Methods.** Grape waste was air dried for 2 days, homogenized and ultimately ground. Moisture content was amounted. Natural bioactive compounds were extracted by different hydrophilic and lipophilic solvents (distilled water, ethanol, isopropanol, ethyl lactate, ethyl acetate and n-hexane) and Novel assisted extraction methods (ultrasonic-assisted extraction (UAE) and microwave-assisted extraction (MAE)) in comparison with conventional stirring extraction method at 20 and 60°C for stirring time of 10, 20, 30, 40, 50 and 60 min. Total phenolic content (TPC) and total flavonoid content (TFC) of grape waste extracts were determined by colorimetric methods. Antioxidant activity of different extracts was measured by DPPH• Radical Scavenging Assay and measured by β-carotene-linoleic acid bleaching method (coupled autoxidation). HPLC analysis was carried for the selected samples with best results to determine the most important components in grape waste. **Results and Discussion:** The yield and natural antioxidant contents: The higher yields were obtained after 60 min of extraction process. In addition, it was also found that extraction of natural antioxidants at 60 °C gave higher yield than that at 20 °C. Water and ethanol were found to be the most efficient solvents in extracting the higher yields from grape waste. Ethanol extracts were determined to have the highest TPC and TFC at different times, temperatures and methods. It was observed that when increasing temperature and extraction time, both phenolic and flavonoid contents increased. **Conclusion:** The eco-friendly and safe solvents (water and ethyl lactate) were proved to be more selective and powerful solvents in extraction of antioxidant components. The best results also, were obtained by higher extraction temperature and after longer extraction time. Novel assisted extraction methods (UAE and MAE) were found to give the higher antioxidant yield and antioxidant potency in most cases, which make it a new promising method that can save time and power in the field of natural antioxidants extraction.

Keywords: Natural antioxidants, phenolic compounds, eco-friendly solvents, novel extraction methods, antioxidant activity, natural sources

Presented by: Eman Fawzi Al-Amrousi

Oils and Fats Department, Food and Nutrition Division, National Research Center, Cairo, Egypt

Email: menoamrousi@yahoo.com



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ABSTRACT 15

Formulation and evaluation of coconut milk based cold cream: A treatment of facial hyper-pigmentation

Raghda Rabe Hamed

ABSTRACT

Coconut milk is a white aromatic liquid that is obtained by soaking the shredded coconut meat in hot distilled water for 24 hours and then squeezing and filtering them. This extract is rich in natural fatty acids and contains antiseptics so can be used for softening the inflamed skin and eliminating its hyperpigmentation. The objective of the present study is to develop a cold cream of coconut milk to provide the prolonged residence of the coconut extract over the skin and so improve its efficacy. The aimed cream was prepared using the freshly prepared coconut milk in addition to jojoba oil via water in oil method that enhances the nourishment of the dry skin. Five formulae were prepared using different ratios of cetyl, alcohol, stearic acid, lanoline, mineral oil, jojoba oil, methylparaben, glycerin, vanilla essence, KOH and coconut milk. Then they were evaluated for appearance, pH, spreading ability, and rheology. The prepared creams were white and homogenous with good consistency, spreading ability, pH, and non-greasy. There was no evidence of phase separation or microbial growth during the research study period. The current study provides a suitable formula that increases the contact time of the prepared extract with the skin and so enhances its deep nourishing, whitening, and de-pigmentation effect on the skin.

Keywords: Coconut Milk, jojoba oil, hyperpigmentation, cold cream

Presented by: Raghda Rabe Hamed

Pharmaceutics and Industrial Pharmacy, College of Pharmaceutical Sciences and Drug Manufacturing, MUST University, Cairo, Egypt

Email: raghda.hamid@must.edu.eg

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ABSTRACT 16

Guggul, the mysterious gum

Kholoud Hamdy

ABSTRACT

Despite the great progress in medical industry, there is an increasing interest in evidence-based herbal products. In this context, guggul, the aromatic oleo-gum resin obtained from the guggul tree (*Commiphora wightii* (Arn.) Bhandari), has a long history of traditional use in Asia and recognized worldwide for treating arthritis, obesity, and allied disorders. Also, guggul sterones, its major active constituents, and several of their synthetic derivatives were experimentally active against number of inflammation mediators and associated cancer. Unfortunately, the expanding market of guggul and its products drives overharvesting, threaten its sustainability, and may lead to extinction of the species.

Keywords: *Commiphora*, traditional use, evidence-based medicine

Presented by: **Meselhy** Ragab Meselhy

Cairo University

Email: meselhy.meselhy@pharma.cu.edu.eg



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ABSTRACT 17

Health benefits of turmeric

Nenad Mićanović*, Aleksandar Ž. Kostić, Jelena Popović-Djordjević*

ABSTRACT

Curcuma longa (*C. longa*), also known as turmeric, is a plant that has a long history of use in traditional medicine, particularly for the treatment of inflammatory conditions. *C. longa* and its main constituent, curcumin (CUR), demonstrated a variety of pharmacological effects, including antioxidant and anti-microbial properties. This review article provides up-to-date information on *C. longa* and CUR's anti-inflammatory, antioxidant, and immune modulatory effects. *C. longa* and CUR have pharmacological effects such as anti-inflammatory, antioxidant, and immune modulatory properties. Informations were combed through using various databases and relevant keywords until September 2020. Several studies have shown that *C. longa* and CUR have anti-inflammatory effects, including decreased white blood cell, neutrophil, and eosinophil numbers, as well as protective effects on serum levels of inflammatory mediators such as phospholipase A2 and total protein in various inflammatory disorders. Several studies have also found that *C. longa* and CUR have antioxidant properties. In oxidative stress conditions, plant extracts and CUR decreased malondialdehyde and nitric oxide levels while increasing (thiol, superoxide dismutase, and catalase levels)

Keywords: Curcumin, turmeric, *Curcuma*

Presented by: Kholoud Hamdy

Email: kholodhamdydodi987@gmail.com

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ABSTRACT 18

Hepatitis C virus -796 protease inhibitors assisted by *in silico* modeling and metabolic profiling of the ethanol extract from Red Sea green algae *Halimeda opuntia*

Iman A. M. Abdel-Rahman, Eman Zekry Attia, Omar M. Aly, Hani Saber, Mohammed I. Rushdi, Usama Ramadan Abdelmohsen

ABSTRACT

Ethanol extracts of *Caulerpa racemosa*, *Halimeda opuntia*, *Padina pavonica*, *Polycladomyrica* and *Turbinariaornata* were tested for anti-hepatitis C virus activity. *H. opuntia* ethanol extract has anti-HCV activity, $IC_{50} = 7.14 \mu\text{g/mL}$. LC-HR-ESI-MS metabolic profiling of *H. opuntia* ethanol extract characterized fifteen metabolites, which were screened for their inhibitory HCV-796 binding site in the HCV polymerase based on molecular docking simulation on the HCV binding site in the HCV polymerase. Interestingly 4,9-Diacetoxtudoteal showed good interaction energies and formed significant interactions HCV-796 binding site.

Keywords: *Caulerpa racemosa*, *Halimeda opuntia*, *Padina pavonica*, *Polycladomyrica*, *Turbinariaornata*, 4,9-Diacetoxtudoteal

Presented by: Usama Ramadan Abdelmohsen

Department of Pharmacognosy, Faculty of Pharmacy, Deraya University, Universities Zone, 61111 New Minia City, Egypt

Email: usama.ramadan@mu.edu.eg



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ABSTRACT 19

Investigation of hyaluronidase enzyme inhibition of natural fatty oils and evaluation of the results in terms of derma products

Gökşen Dilşat Durbilmez, Ufuk Koca-Caliskan

ABSTRACT

Background: Hyaluronic acid, an important factor for skin health and prevention of aging, is responsible for the moisture balance of the skin. Interest in natural oils in many cosmetics/dermacosmetic preparations has been increasing in recent years. In this study, we aimed to evaluate the hyaluronidase enzyme inhibition of bear and dolphin oils, which have been used in folk medicine.

Materials and Methods: In the study, hyaluronidase enzyme inhibition is based on turbidimetric method, the reaction of hyaluronic acid with the albumin solution to form turbidity. Each sample on the ELISA microplate was studied at 5 different concentrations, in 3 parallels. 20 μ L of the test solutions were taken and added to the wells. Then, hyaluronic acid solution at a concentration of 0.4 mg/mL was added and incubated in the oven for 5 minutes at room temperature. Then, 0.05 mg/mL hyaluronidase enzyme was added to them. Lastly, 180 μ L of albumin solution was added to the wells. It was incubated for 10 min. After the incubation process, the absorbance values obtained at 540 nm wavelength were read in the ELISA microplate reader (Madan, 2018). (Madan, K., and Nanda, S. (2018). In-vitro evaluation of antioxidant, anti-elastase, anti-collagenase, anti-hyaluronidase activities of safranal and determination of its sun protection factor in skin photoaging. *Bioorganic Chemistry*, 77, 159-167.)

Results: As a result of our preliminary studies, hyaluronidase enzyme inhibition effect is seen in both bear oil and dolphin oil compared to our reference tannic acid.

Discussion and Conclusions: Our preliminary study shows that animal-derived bear and dolphin oils can be used as a moisturizer in new generation dermacosmetic formulations. However, the toxicity of these oils should also be examined.

Keywords: antihyaluronidase, natural, cosmetic

Presented by: Ufuk Koca-Caliskan

Gazi University

Email: ukoca@gazi.edu.tr



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ABSTRACT 20

Investigation of *Teucrium parviflorum* and *Teucrium polium* extracts in terms of their chemistry and *in vitro* biological activities

Ezgi Ersoy, Goncagul Suvvari, Esra Eroglu-Ozkan, Mehmet Boga

ABSTRACT

Background: *Teucrium* species have been among the most commonly used traditional medicinal plants in the Mediterranean region since ancient times. They have been mainly used to treat gastrointestinal problems, dermatological disorders, and to maintain the healthy functioning of endocrine glands. The main focus of this study, *Teucrium polium* and *Teucrium parviflorum* are also renowned for being important medicinal plants in Turkey. Bearing all in mind, this study aimed to investigate the chemical constituents and various *in vitro* biological activities of these species.

Materials and Methods: Root and aerial parts of *T. polium* and aerial parts of *T. parviflorum* were extracted by ethanol, their chemical compounds were identified by LC-MS/MS. Volatile oils obtained from the plants by Clavenger method, and they were analyzed by GC-MS. Antioxidant activities were determined by DPPH, ABTS, metal binding and CUPRAC methods. Also, anticholinesterase activities were determined via Ellman method, cytotoxicity was evaluated by Sulforhodamine B (SRB) Cell Viability Assay. A micro broth dilution technique described by the Clinical and Laboratory Standards Institute was used to determine the antimicrobial activity of the studied *Teucrium* extracts.

Results: *T. polium* roots were found that they include the highest amounts of total phenolic and flavonoid contents. None of the extracts have demonstrated the metal binding and acetylcholinesterase inhibition activity. Activities of root and aerial parts extracts of *T. polium* have shown better antioxidant potential than *T. parviflorum* by all methods. Also, it was determined that root extracts of *T. polium* shows better activity than BHT used as standard for DPPH, and than of BHA compounds which were used as standard for ABTS method. All extracts exerted strong anti-tyrosinase activity and moderate anti-urease activity. Major compounds of volatile oil contents obtained by GC-MS analysis were revealed as germacrene D (32.7%) for *T. parviflorum*, and (Z)- β -farnesin (28.9%) for *T. polium*. Also, the most abundant compounds of phenolic contents obtained by LC-MS/MS analysis were identified as naringenin (16327 $\mu\text{g/g}$ extract) for *T. polium* aerial parts, (-)-epigallocatechin gallate (3694 $\mu\text{g/g}$ extract) for *T. polium* roots, and hesperidin (5687 $\mu\text{g/g}$ extract) for *T. parviflorum* aerial parts.

Conclusions: Being rich in pharmacologically important secondary metabolites and having shown to demonstrate strong biological activities, both *T. polium* and *T. parviflorum* extracts may be considered to have medicinal potentials and they appear to be promising agents for future drug development advances.

Keywords: *Teucrium*, phytochemistry, biological activities LC-MS/MS, medicinal potential

Presented by: Ezgi Ersoy

Biruni University, Faculty of Pharmacy, Dept. of Pharmacognosy, 34010, Zeytinburnu, Istanbul, Turkey

Email: ezgie@biruni.edu.tr



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ABSTRACT 21

In Vitro antioxidant properties, phytochemical investigation and caffeine content evaluation of Kombucha

Kurar B.N., Barak T.H., Ozdemir K., Bardakci H.

ABSTRACT

The fact that many products used in phytotherapy, that is, in the treatment carried out with plants, are also used as food, leads to a vague line between the two. The term “functional food” can be defined as food products that are a part of normal nutrition and have positive effects on human health. Providing a suitable combination of organic acids, vitamins, minerals, polyphenols, fiber, and other essential nutrients, “Kombucha” is a functional beverage that has been very popular in recent years. There is “Kombucha” on the market from many small and large producers. Kombucha is an acidic fermented beverage of Asian origin with a slightly sour and sweet taste. There are numerous studies related to kombucha. However, studies evaluating the phytochemical composition and antioxidant properties of unflavored green tea-based kombucha beverages from different producers are very scarce. Aim: The primary purpose of this study is to evaluate the antioxidant potentials and chemical composition of unflavored kombucha beverages prepared from green tea, obtained from online shopping platforms and markets in the Istanbul region by using various in vitro methods, as well as to determine their caffeine content using HPTLC. Materials and Method: Methanolic solutions were prepared from the lyophilisates of the unflavored green tea-based kombucha beverages after their filtration. Antioxidant capacity of the kombucha sample lyophilisates were evaluated using free radical scavenging (DPPH) and metal reducing based assays (FRAP, CUPRAC, and TOAC). Total phenolic, phenolic acid, and flavonoid contents were spectrophotometrically analyzed to determine the phenolic composition. HPTLC was used to determine the quantity of caffeine in the samples. Results and Discussion: Results indicated that kombucha beverages have antioxidant activity and rich in phenolic content. Amongst samples brand A has the highest antioxidant activity and the highest phenolic content with the medium amount of caffeine. On the other hand, antioxidant activities and chemical compositions were in a similar trend in all the examined samples. Conclusion: Results showed that kombucha beverages can be used due to the significant antioxidant activities, rich phenolic content as well as low caffeine contents.

Keywords: Kombucha, functional food, phytochemical composition, antioxidant activity, HPTLC, caffeine

Presented by: Bardakci H.

Acibadem Mehmet Ali Aydinlar University, Faculty of Pharmacy, Department of Pharmacognosy, Istanbul, Turkey

Email: hilalbardakci@hotmail.com



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ABSTRACT 22

***In vitro* antioxidant properties, phytochemical investigation and chorogenic acid content of Hawthorn vinegar**

Haydargil O., Barak T.H., Bardakci H.

ABSTRACT

Background: During the last decades, health services costs have been increased, in parallel with the awareness of health, the desire to increase life expectancy and quality of life, the demand for functional foods that improve health has increased. Functional foods can be defined as dietary elements that not only provide nutrients and energy, but also modulate our health positively by increasing a certain physiological response or reducing the risk of disease. Protecting the human body against free radicals is critical because oxidative damage causes significant diseases ranging from aging to degenerative disorders. The main reason for hawthorn vinegar's use as a functional food is its prominent antioxidant activity. The presence of phenolic compounds with significant antioxidant capabilities in hawthorn fruit has drawn attention. The primary purpose of this study is to evaluate the antioxidant potentials and chemical composition of unflavored hawthorn vinegar obtained from online shopping platforms and markets in the Istanbul region by using various *in vitro* methods.

Materials and Methods: Mixture of distilled water and methanolic solutions were prepared from the lyophilisates of the unflavored hawthorn vinegar. To evaluate phenolic contents of samples total phenolic content, total flavonoid content and total phenolic acid content assays were performed. Antioxidant bioactivities were determined by using CUPRAC (Cupric Reducing Antioxidant Capacity), FRAP (Ferric Reducing Antioxidant Power), DPPH radical scavenging activity and TOAC (Total Antioxidant Capacity) methods.

Results and Discussion: Results showed that there is a significant difference amongst the vinegar samples in terms of antioxidant activity and phenolic compositions. Sample A showed almost as twice as phenolic content as well as antioxidant capacity when compared with the other samples.

Conclusions: Results demonstrated that vinegar samples contain phenolic substances and antioxidant capacity at some point. However, results differ significantly amongst the brands

Keywords: Antioxidant, *Crataegus* sp., functional food, Hawthorn vinegar, phytochemical composition

Presented by: Bardakci H.

Acibadem Mehmet Ali Aydinlar University, Faculty of Pharmacy, Department of Pharmacognosy, Istanbul, Turkey

Email: hilalbardakci@hotmail.com



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ABSTRACT 23

***In vitro* potential of medicinal plants from upper Egypt
in the treatment of chronic myeloid leukemia**

Shimaa M. Abdelgawad, Mona H. Hetta, Ghada A. Fawzy, Hesham I. El-Askary

ABSTRACT

Leukemia is Egypt's fourth most common cancer, with higher incidence rates in Upper Egypt. The goal of this study is to discover the antileukemic potentials in some medicinal plants that grow, are cultivated, and are used ethnomedicinally in Upper Egypt, where chronic myeloid leukemia (CML) is prevalent. One hundred grams of air-dried powders from fifty-six different medicinal plants were extracted with 75% ethanol, and their hydro-ethanolic extracts were tested against the leukemia K562 cell line at a concentration of 10 mg/mL using the trypan blue exclusion assay, and the percentage of inhibitions were calculated. The results showed that *Sesbania sesban* L. Merr leaves, *Curcuma aromatic* Salisb. roots, *Spinacia oleracea* L. leaves, *Quercus infectoria* gall, and *Thymus vulgaris* L. leaves were the most active plant extracts against leukemia K562 cell line (percentage of inhibition = 100, 90.2, 88.9, 87, and 85.2 percent inhibition, respectively, compared to Taxol, 90.7 percent). In conclusion, flora of Upper Egypt is a valuable source of plants rich in antileukemic phytochemicals.

Keywords: Antileukemic, CML, medicinal plants, screening, upper Egypt.

Presented by: Shimaa M. Abdelgawad

Pharmacognosy Department, Faculty of Pharmacy, Fayoum University, 63514, Egypt

Email: smm13@fayoum.edu.eg



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ABSTRACT 24

Licensing of traditional herbal medicinal products in Turkey

I. Irem Tatli Cankaya

ABSTRACT

Traditional herbal medicinal product refers to bibliographically proven medicinal plants in its composition have been used for at least fifteen years in Turkey or in the European Union member countries and for thirty years in other countries before the application date, in terms of composition and use, designed and intended to be used without medical supervision or prescription for diagnosis or follow-up of treatment, with special indications suitable for traditional medicinal products, means only preparations for oral, external or inhalation, which have specific applications by a specifically determined dose and posology. The main purpose in the development of traditional herbal medicinal products and in the relevant regulations is to issue the licenses of herbal medicinal products and herbal preparations prepared from medicinal plants with traditional uses, which have protective and therapeutic effects on human health, and to determine the procedures and principles to be followed regarding their effectiveness, safety, and quality. In parallel with the European Union's directive on medicinal products for human use numbered 2001/83/EC and regulation numbered 2004/24/EC, GBTÜ regulation has been established and license studies are carried out for this legislation. In this study, information will be given about the relevant regulation, legislation, and OTD guideline for traditional herbal medicinal products in Turkey.

Keywords: Phytotherapy, legislation, licensing, traditional herbal medicine products, folk medicine

Presented by: I. Irem Tatli Cankaya

Hacettepe University, Faculty of Pharmacy, Department of Pharmaceutical Botany, Ankara, Turkey

Email: itatli@hacettepe.edu.tr



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ABSTRACT 25

Neuroprotective effects of *Pulicariaundulata* essential oil in rotenone model of Parkinson's disease in rats: Insights into its anti-inflammatory and antioxidant effects

Marwa Y. Issa, Marwa I. Ezzat, Rabab H. Sayed, Eman M. Elbaz, Farghaly A. Omar, Engy Mohsen

ABSTRACT

Parkinson's disease (PD) is a neurodegenerative disorder described by severe motor symptoms involving postural imbalance, uncontrolled shake, slowness of motion and rigidity. Searching for a natural remedy for PD to overcome the common adverse effects of conventional treatments, the neuroprotective effects of three dose levels (50, 100, and 200 mg/kg) of *Pulicariaundulata* essential oil (PUEO) in rotenone-induced model in male Wistar rats were investigated. PUEO was analyzed by GC and GC/MS resulting in the identification of twenty-one compounds. Carvotanacetone was the major component (80.14%). The middle and high doses of PUEO attenuated rotenone-induced behavioral deficits besides, hindering the decrease in striatal dopamine and ATP levels, with partial retardation in rotenone-induced body weight loss. Biochemical assessments illustrated that PUEO mitigated rotenone-induced increment in striatal interleukin-1b (IL-1b), tumor necrosis factor-a (TNF-a), and inducible nitric oxide synthase (iNOS). The reduction in malondialdehyde and increase in glutathione striatal contents depicted its antioxidant potential. Molecular docking study of carvotanacetone might justify the observed normalization of the elevated iNOS level induced after exposure to rotenone. This is the first study indicating the ability of PUEO to protect rats against rotenone-induced PD via anti-inflammatory and antioxidant activities with the ability to reduce a-synuclein gene expression.

Keywords: *Pulicariaundulata* essential oil, carvotanacetone, Parkinson's disease, rotenone, dopamine, molecular docking

Presented by: Eman M. Elbaz

Department of Biochemistry, Faculty of Pharmacy, Cairo University, Cairo 11562, Egypt

Email: eman.el-baz@pharma.cu.edu.eg



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ABSTRACT 26

Phytochemical investigation of different extracts of *Casuarina equisetifolia* and their biological activities

Walid Elsayed Abdallah

ABSTRACT

Cancer is a complex disease affecting public health worldwide. *C. equisetifolia* has the widest natural distribution of all *Casuarina* species. The unsaponifiable fraction of pet. ether extract consists mainly from a mixture of a series of hydrocarbons ranging from C8 to C44 representing 87% in which C10 (10.32 %) was the main hydrocarbon, in addition to α -Sitosterol (1.53 %). The fatty acids fraction revealed the presence of 13 fatty acids which represented 89.44 % of the total acids, in which palmitic acid, methyl ester (C16:0) was the main fatty acid (54.75 %). Six different extracts (Chloroform, Ethyl acetate, Butanol, Methanol, Water and Petroleum ether) of *C. equisetifolia* needles were evaluated for total phenolic contents (TPC), total flavonoid contents (TFC), antioxidant, antimicrobial and cytotoxic activity. The methanolic extract (10 CE) showed the highest total phenolic content (58.44 ± 0.37 mg/g gallic acid eq.), highest total flavonoid content (32.05 ± 0.30 mg/g quercetin eq.), and the methanolic extract exhibited the best antioxidant. Screening of six extracts for their antimicrobial activity had been conducted using six various microorganisms, 2 Gram- positive, 2 Gram-negative bacteria and fungal species. The ethyl acetate extract (8 CE) showed a larger inhibition zone against Gram-positive bacteria *Staphylococcus aureus* and *Bacillus suchloroformtilis*, and against Gram-negative bacteria *E. coli* and *Pseudomonas aeruginosa*. The different extracts of *C. equisetifolia* under investigation were tested for cytotoxic activity against liver (HEPG-2) and colon (HCT-116) cancer cell lines. The methanolic extract (10 CE) have a strong cytotoxic activity against both (HEPG2) and (HCT-116) cancer cell lines represented by the lowest IC_{50} value (3.68 μ g/ml) and (5.59 μ g/ml) respectively.

Keywords: Casuarinaceae, *C. equisetifolia*, antioxidant, antimicrobial, cytotoxic activity

Presented by: *Walid* Elsayed Abdallah

Chemistry of Medicinal Plants Department, Pharmaceutical Industries Division, National Research Centre, El Bohouthst. Dokki, Giza, Egypt. P.O. 12622

Email: walsay2003@yahoo.com



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ABSTRACT 27

Phytocosmetic cellulite cream developed from plant cell with biotechnology

Levent Alparslan

ABSTRACT

When plant tissues are mechanically damaged, they form undifferentiated cell aggregates called callus to repair the damage. Callus cells can transform into all cells and organs of the plant and even to form a new plant. Callus plant stem cell technology is based on the principle of controlled reproduction of undifferentiated plant cells in culture and obtaining plant components specific to stem cells. Oxidative stress, weakening of connective tissue, decrease in microcirculation, lymph circulation and increase in the amount of adipocyte cause cellulite problems on the skin. With this technology, a cream formulation containing extracts of four different plant stem cells, which is expected to show activity against cellulite formation when applied to the skin, has been prepared. The formulation was made available to consumers by going through all stages until it became a commercial product. Plant stem cells were obtained with a unique cell manipulation method (ProliCELL), which enables the production of active molecules contained in plants efficiently and synergistically. A combined extract mixture was prepared for the purpose of strengthening the connective tissue and high antioxidant activity against oxidative stress. This mixture contains, 200 µg/ml avocado 90% ethanolic cell extract, 200 µg/ml almond 80% ethanolic cell extract that can increase elastin, 200 µg/ml soy 10% ethanolic cell extract and 200 µg/ml Centella asiatica 70% ethanolic cell extract. An easily absorbed and water-based cream has been developed that contains this extract combination as a phytocosmetic active. Physicochemical and macroscopic properties, stability and microbiological tests of the cream were carried out. Patch tests were performed dermatologically on 12 healthy volunteers, male and female, aged between 18-60, for 48 hours. No adverse events were encountered in the short-term stability and microbiological tests of the formulation. In accordance with the legislation, a product safety file has been prepared to be submitted to the national authority. In dermatological testing, the Dermatologist did not observe any serious skin reaction (such as edema, irritation) at the test site of any of the volunteers. With plant biotechnology, phytocosmetic active substances are obtained without being affected by seasonal, climatic, and geographical factors, unlike plants grown by traditional methods. Plant biotechnology reduces water consumption, does not harm the ecosystem and is sustainable. Dermocosmetic products are products that have claims and clinical evidence, unlike cosmetic products. For this reason, female volunteers will be studied in cooperation with the university-industry for the claims of plant cell extract cream and cellulite effectiveness by obtaining permission from the cosmetic clinical research ethics committee. Studies on the dermocosmetic claims of a phytocosmetic product prepared with innovative technology and consumer satisfaction are very important in terms of both scientific and cosmetics market.

Keywords: plant cells, biotechnology, phytocosmetic, cellulite, cream, dermocosmetic

Presented by: Levent Alparslan

Istinye University, Turkey

Email: levent.alparslan@istinye.edu.tr



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ABSTRACT 28

Plant-derived functional foods, nutraceuticals, and cosmeceuticals: Trends, prospects and challenges

Hari Prasad Devkota

ABSTRACT

Medicinal plants play an important role in human healthcare as an integral part of traditional medicine systems and one of the main sources for the discovery and development for modern drugs. Plant extracts and their phytochemicals have also received increased attention in recent years as functional foods, food supplements, nutraceuticals, and cosmeceuticals. As the number of people with lifestyle-related diseases including diabetes, hypertension, hyperlipidemia, and associated complications is increasing worldwide, various plant-derived functional foods, food supplements, and nutraceuticals are marked as potential agents in the prevention and management of these complications. However, many such products do not have strong scientific evidence for their claimed activities. There is a growing need for detailed research related to the identification of new sources, characterization of active compounds, elucidation of mechanisms of action using in vitro, in vivo, and clinical studies, and product formulation. In this presentation, I will discuss about current trends, potentials and future prospective of plant-derived functional foods, nutraceuticals, and cosmeceuticals using some of our recent research outcomes.

Keywords: Functional foods, nutraceuticals, bioactive, natural products

Presented by: *Hari* Prasad Devkota

Graduate School of Pharmaceutical Sciences, Kumamoto University, Kumamoto, Japan

Email: devkotah@kumamoto-u.ac.jp



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ABSTRACT 29

Pleiotropic effects of dietary pomegranate peel on ruminants' health and production

Ariel Shabtay

ABSTRACT

During the last two decades, pomegranate peels (POP) have become an abundant agricultural byproduct, due to the increase in production of pomegranate juice and "ready to eat" arils. It is for their combined wound-healing, immunomodulatory, antibacterial, anti-atherosclerotic and anti-oxidative properties that POP were expected to carry "pleiotropic effects" on ruminants health and production. In a series of *in vivo* studies, involving dietary supplementation of fresh, dried or water-extracted POP, we have demonstrated effects on milk yield, composition, antioxidant capacity and somatic cell count, suggesting, among others, involvement of POP with energy metabolism in the mammary gland. In addition to the above, the current presentation will also focus on long-term influence of dietary POP on production efficiency, attenuation of weaning related oxidative stress, improvement of gut health, plasma antioxidant capacity and vitamin E bioavailability and manipulation of odorants emission.

Keywords: pomegranate peel, ruminants, health, production, antioxidant capacity, vitamin E

Presented by: Ariel Shabtay

Beef Cattle Unit, NeweYa'ar Research Center, Agricultural Research Organization

Email: shabtay@volcani.agri.gov.il

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ABSTRACT 30

Potential application of herbal medicine in treatment of Obesity

Khaled Mostafa Mohamed Elghondakly

ABSTRACT

Obesity is a global epidemic associated with high morbidity and mortality. The ultimate cause of obesity is an imbalance between caloric intake and energy expenditure resulting from complex interactions between physiological, genetic, environmental, psychological, hormonal, metabolic, eating behavior and lack of physical activity. Therapeutic strategies include synthetic drugs and surgery, which may entail high costs and serious complications. The use of herbal medicine or natural products has increased, based on reliability, expected safety, and low cost. Recently, Herbal medicine agents offer an alternative approach for treatment of obesity through different mechanisms specially those containing dietary fibers. In addition, herbs are a good supplement for man with vitamins and minerals. However, the product derives from a natural source does not necessarily mean it is absolutely safe because data regarding safety and efficacy is still lacking. On the other hand, a successful control of weight requires permanent lifestyle changes that include adoption of a healthful low-fat diet together with regular physical activity. Pharmacists have an important role in educating the public about the prevention and management of obesity. Weight management provides an excellent opportunity for pharmacists to work with other health professionals and patients to decrease the morbidity and mortality associated with obesity.

Keywords: Potential application,herbal medicine,treatment of obesity

Presented by: *Khaled* Mostafa Mohamed Elghondakly

Faculty of Pharmacy, Fayoum University, Egypt

Email: gondakly@yahoo.com



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ABSTRACT 31

Promising antimicrobial applications of Egyptian Quinoa

Rehab Bahy, Nouran Assar

ABSTRACT

Quinoa is a highly nutritious food that has been farmed worldwide for thousands of years, with excellent protein quality and a high content of a variety of vitamins and minerals. The saponins found in the seed hull and the lack of gluten are two more advantages of quinoa. Quinoa has recently gained popularity in the United States, Europe, and Asia. Quinoa has been named by the FAO as one of the crops that will provide food security in the twenty-first century. Antibiotics have evolved recently an increasing in microorganisms' resistance. To combat this issue, scientists are looking for novel antibiotics that come from natural sources. Antibiotics can be replaced with natural products that are generally safe and effective. The aim of this research is to determine the possible use of Egyptian Quinoa as a natural source of antibiotics. Results revealed that Phenolic extract of Egyptian Quinoa has high antimicrobial activity against Gram positive, Gram negative and yeast. These promising findings provides evidence that Quinoa extract can be contributed in further different pharmaceutical dosage forms having several antimicrobial applications.

Keywords: Quinoa, antimicrobial, plant Extract

Presented by: *Rehab* Bahy

Fayoum university, Egypt

Email: rhb11@fayoum.edu.eg



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ABSTRACT 32

Regression of fibrosis by apigenin in thioacetamide-induced liver fibrosis rat model through suppression of HIF-1/FAK pathway

Hany M. Fayed, Rehab F. Abdel-Rahman, Alyaa F. Hessin, Hanan A. Ogaly, Gihan F. Asaad, Abeer A.A. Salama, Sahar AbdelRahman, Mahmoud S. Arbid, Marwan Abd Elbaset Mohamed

ABSTRACT

Liver fibrosis is a serious global health problem that occurs as a result of a variety of chronic liver disorders. Apigenin, a flavonoid found in many plants, has several pharmacological properties. The aim of this study was to evaluate the antifibrotic efficacy of apigenin (APG) against experimentally induced hepatic fibrosis in rats via using thioacetamide (TAA), and to explore the possible underlying mechanisms. TAA (100 mg/kg, i.p.) was given three times each week for two weeks to induce liver fibrosis. After TAA injections, APG was given orally (5 and 10 mg/kg) daily for two weeks. Biochemical, molecular, histological and immunohistochemical analyses were performed on blood and liver tissue samples. The functioning of the liver, oxidative stress, inflammation, and liver fibrosis indicators were all evaluated. The findings showed that TAA markedly increased the activities of aspartate aminotransferase (AST) and alanine aminotransferase (ALT), as well as the levels of malondialdehyde (MDA), focal adhesion kinase (FAK), hypoxia inducible factor-1 (HIF-1), nuclear factor- κ B (NF- κ B), transforming growth factor-beta (TGF- β), tumor necrosis factor-alpha (TNF- α) and interleukin-1 β (IL-1 β) with a reduction in albumin, total protein, A/G ratio, GSH content and interleukin-10 (IL-10). Moreover, TAA elevated the content of collagen I, α -smooth muscle actin (α -SMA), and hydroxyproline in the liver. The treatment with APG in a dose-dependent manner has obviously prevented these alterations and amended the harmful effects induced by TAA. The histopathological and immunohistochemical observations supported these biochemical evidences. The higher dose of APG produced the most significant antifibrotic effect. As a result of these data, APG appears to be a promising antifibrotic drug and could be used as a new herbal medication or dietary supplement in the future for the treatment of liver fibrosis. This effect might be related to the inhibition of HIF-1/FAK signaling pathway.

Keywords: Apigenin, FAK, HIF-1, liver fibrosis, rat, thioacetamide

Presented by: Hany M. Fayed

Department of Pharmacology, Medical Research and Clinical studies Institute, National Research Centre, Giza, Egypt

Email: drhany_fayed2000@yahoo.com



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ABSTRACT 33

Renal protective effects of 7-hydroxycoumarin cisplatin-induced renal injury: An *in vivo* study and molecular modeling

Omnia A. M. Abd El-Ghafar

ABSTRACT

Nephrotoxicity is the most common adverse effect of gentamicin (GNT). This study aimed to investigate the possible nephroprotective effect of umbelliferone (UMB), against GNT-induced nephrotoxicity. Rats were allocated into the control group, UMB group (50 mg/kg/day, P.O. for 15 days), GNT group (100 mg/kg/day, i.p., for 8 days), and GNT + UMB group. By the end of the experimental period, serum creatinine, urea, and uric acid as well as urine KIM-1 and urine albumin/creatinine ratio were evaluated to estimate kidney function. Moreover, tissue samples were collected for assessment of ERK1/2, pERK1/2, TLR-4, p38 MAPK, NF- κ B-p65, NLRP-3, I κ B α , TNF- α , IL-1 β , JAK1, STAT-3, pSTAT, and cleaved caspase-3. In support, the histopathological examination of renal tissues was performed. UMB improves kidney function through regulation of renal serum biomarkers, with alleviations of histological abrasions induced by GNT. Besides, UMB downregulates renal protein expressions of ERK1/ERK2, TLR-4, and p38MAPK, with subsequent suppression of NF- κ B-p65/NLRP-3 inflammasome and JAK1/STAT-3 pathways as well as cleaved caspase-3. In parallel, UMB induced I κ B α upregulation. Collectively, UMB markedly amended all GNT-induced renal changes. These nephroprotective outcomes could be attributed to its ability to impede TLR-4/NF- κ B p65/NLRP-3 inflammasome and JAK1/STAT-3 pathways activation, as well as to its anti-inflammatory property.

Keywords: Umbelliferone, cisplatin, renal Injury

Presented by: Omnia A. M. Abd El-Ghafar

Department of Pharmacology and Toxicology, Faculty of Pharmacy, Nahda University, Beni-Suef, Egypt

Email: omnia.mohamed@nub.edu.eg



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ABSTRACT 34

Rosehips as a non-traditional source of phytochemicals and the evaluation of Greek wild rosehips in terms of ascorbic acid, total phenolic content and antioxidant activity

T. Papagrigoriou, E. Patelou, S. Kostas, D. Lazari, A. Kanellis

ABSTRACT

Even though the pseudofruits of roses have been used in traditional medicine, as well as in some culinary preparations, they remain a relatively unconventional dietary choice. In recent years, however, rosehips have earned a place in the spotlight as potential functional foods, due to their unique composition and high content of nutrients that exert a wide array of beneficial health effects. Within the general context of exploitation of Greek medicinal plants, ripe rosehips from *Rosa canina* populations growing wild in Northern Greece (Pindos Mt., Rhodopi Mt. and Chalkidiki) were collected and assessed for their content in ascorbic acid (AsA) and total polyphenols, by the ascorbate oxidase and Folin-Ciocalteu method, respectively. The antioxidant activity of the hips was also measured by the DPPH method. Finally, a drought and salinity stress experiment was conducted on cultivated *Rosa canina* plants, whose leaves were subsequently assessed for their phenolic content and antioxidant activity. Results showed that the ripe rosehips had a high AsA content, with the samples from Chalkidiki being the richest, whereas the ones from Rhodopi Mt. showed the highest total phenolic content, and the ones from Pindos Mt. had the strongest antioxidant activity. As far as the drought stress experiment is concerned, it was observed that a decrease in the watering frequency resulted in a decreased TPC, a pattern that was followed in the case of the radical scavenging activity measurement. Salinity had a seriously negative impact on the polyphenol content of the leaves however, their antioxidant activity was not as severely impacted.

Keywords: rosehips, ascorbic acid, polyphenols, radical scavenging

Presented by: D. Lazari

Aristotle University of Thessaloniki, Greece

Email: dlazari@pharm.auth.gr



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ABSTRACT 35

Safety assessment of natural ingredients in cosmetic products

Simone Fanan

ABSTRACT

Natural ingredients can be of mineral, animal or plant origin. Plant-derived extracts are often complex mixtures of substances. The popular belief that natural ingredients are not toxic to human health is misguided and far from true. Their commercialization in the European Union (EU) requires compliance with two regulations: the regulation on cosmetic products (Regulation EC 1223/2009) and the regulation on chemicals REACH (Registration Evaluation Authorization and Restriction of Chemicals, Regulation EU 1907/2006). Appropriate chemical characterization of a plant derived ingredient is crucial both from a botanical and chemical point of view. Chemical characterization of a complex mixture is the most important component of an accurate and reliable safety assessment of Herbal extracts and is crucial to the application of New Approach Methodology (NAM) and Next-Generation Risk Assessment (NGRA) for Toxicology of 21st Century.

Keywords: Natural Ingredients, safety assessment, cosmetic, toxicology

Presented by: *Simone* Fanan

ASSESSA-Brazil

Email: simone.fanan@assessa.com.br



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ABSTRACT 36

***Simmondsia chinensis* (Jojoba) wax attenuates *Herpes Simplex 1* in a Simmonds in an independent manner**

Zipora Tietel, Arnon Dag, Guy Cohen

ABSTRACT

Background: Jojoba, *Simmondsia chinensis* (Link) C.K. Schneider, is an ever-green dioecious shrub mainly grown for its non-edible natural wax, used for dermatological and cosmetic applications. Recent reports have shown health-promoting properties of jojoba wax and extracts, including antimicrobial activity. The objective of the current research was to evaluate the impact of jojoba wax on skin residential bacterial, fungal, and virus infection.

Materials and Methods: Both industrial and laboratory cold press jojoba wax preparations were evaluated. GC-MS was used to mature fatty acid and fatty alcohol composition. Anti-bacterial (*Staphylococcus aureus* and *Staphylococcus epidermidis*) and anti-fungal (*Malassezia furfur*) activities were evaluated by MIC assays. The anti-viral activity was assessed HSV-1 infected Vero cells plaque formation was recorded in several pharmacological relevant jojoba concentrations. PCR with specific primers to HSV-1 and immunohistochemical staining of its protein were also used to validate the results.

Results: This initial biological evaluation was performed on four independent commercial wax preparations to evaluate lot-to-lot alterations. The growth of *Staphylococcus aureus*, *Staphylococcus epidermidis*, and *Malassezia furfur* was unaffected by jojoba in all the tested concentrations. Nevertheless, the wax significantly attenuated HSV-1 plaque formation in Vero cells. Dose-dependent analyses of defined jojoba varieties (Benzioni, Shiloah, Hatzerim, and Sheva) demonstrated that all preparation had comparable anti-viral potency and efficacy, indicative that the active compound(s) are abundant in the wax. Reduction in HSV-1 infection was also confirmed by PCR with specific primers to the virus and, by immunohistochemical staining of viral protein. In addition, a targeted approach revealed that the jojoba key active molecule simmondsin, repeatedly associated with the medicinal impact of Jojoba wax, is not responsible for the antiviral action. Chemical characterization of the fatty acid and fatty alcohol composition was performed, showing high similarity between the wax of the investigated varieties and the biological action of the wax. Preliminary data will also be presented from ex vivo studies demonstrating profound dermo-cosmetic activities.

Discussion and Conclusions: Collectively, the current study supports the use of jojoba wax against HSV-1 skin infections as well as a potent cosmetic phytochemical.

Keywords: skin, HSV-1, jojoba, *Simmondsia chinensis*

Presented by: Guy Cohen

The Dead-Sea and Arava Science Center, The Skin Research Institute, Masada 86910, Israel
Eilat Campus, Ben-Gurion University of the Negev, Eilat 8855630, Israel

Email: guy@adssc.org



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ABSTRACT 37

Suppression of advanced glycation end products by phycocyanin from *Spirulina platensis*

Additiya Paramanya, Ahmad Ali

ABSTRACT

Background: Diabetic complications are manifested due to products generated during Glycation and oxidative stress. These products alter the structure of molecules, cause their functional loss and lead to abnormal behaviour of the cells. There is an increased interest in natural products for the prevention of glycation. Phycocyanin is a major constituent of cyanobacterium *Spirulina platensis* and is known for several therapeutic properties.

Materials and Methods: BSA and glucose were used as standard in vitro glycation system and samples were incubated for 4 weeks. The amount of early and advanced glycation end products was measured in the absence and presence of Phycocyanin by using standard spectroscopic and fluorimetric methods. Glycation induced aggregation of BSA was assessed by ThT and SDS-PAGE methods. Agarose gel electrophoresis was used to assess the glycoxidative damage of DNA.

Results: There was a significant increase in the amount of early and advanced glycation products after four weeks in the glycation system. The presence of Phycocyanin caused a drastic decrease in the products at both early and advanced stages. The studies related to aggregation also indicate that Phycocyanin prevented the glycation induced aggregation. There was a reversal of glycoxidative damage of DNA by this natural product.

Discussion and Conclusions: All these results indicate that phycocyanin interferes with formation of Schiff bases, amadori products as well as advanced glycation end products. The decrease in carbonyl content, an indicator of advanced stage, could be due to both prevention of generation of glycation products as well as antioxidant properties of phycocyanin. It can be concluded that phycocyanin can be developed as potential drug for the prevention of glycation as well as its related processes like aggregation and structural alterations of proteins.

Keywords: Advanced glycation end products (AGEs), aggregation, glycoxidation, phycocyanin, *Spirulina*

Presented by: Ahmad Ali

Department of Life Sciences, University of Mumbai, Vidyanagari, Mumbai, INDIA

Email: ahmadali@mu.ac.in

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ABSTRACT 38

Thymol and carvacrol prevent doxorubicin-induced cardiotoxicity by abrogation of oxidative stress, inflammation, and apoptosis in rats

Mohammed SamiR, Ahmed Mohammed Ibrahim

ABSTRACT

The aim of this study was to assess the possible protective effects of thymol and carvacrol (CAR) against doxorubicin (DOX)-induced cardiotoxicity. A single dose of DOX (10 mg/kg i.v.) injected to male rats revealed significant increases in serum lactate dehydrogenase, creatine kinase, creatine kinase isoenzyme-MB, aspartate transaminase, tumor necrosis factor-alpha, and cardiac troponin levels. It also increased heart contents of malondialdehyde and caspase-3 accompanied by a significant reduction in heart content of reduced glutathione as well as catalase and superoxide dismutase activity as compared with the control group. In contrast, administration of thymol (20 mg/kg p.o.) and/or CAR (25 mg/kg p.o.) for 14 days before DOX administration and for 2 days after DOX injection ameliorated the heart function and oxidative stress parameters. Summarily, thymol was more cardioprotective than CAR. Moreover, a combination of thymol and CAR had a synergistic cardioprotective effect that might be attributed to antioxidant, anti-inflammatory, and antiapoptotic activities

Keywords: Thymol, carvacrol, anti-oxidant, doxorubicin, cardiotoxicity, anti-apoptotic

Presented by:

Fayoum University, Egypt

Email: sinklar18@gmail.com



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ABSTRACT 39

Transdermal targeting of breast cancer using phytochemicals-loaded polymeric nanoparticles

Rania M. Hathout

ABSTRACT

The transdermal delivery of drugs using polymeric nanoparticles always raised a large debate. And despite that targeting breast cancer *in-vivo* was previously successful using transdermal soft nano-carriers such as the microemulsions delivering a natural product viz. methyl dihydrojasmonate, yet, the use of polymers remained very tempting due to their better stability and multifunctional properties. Hereby, the successful delivery of two other natural anticancer molecules, curcumin and sesamol through the transdermal route and using two different polymeric-based nano carriers, the chitosan nanoparticles and the oleic-acid conjugated gelatin counterparts is reported. Moreover, the cytotoxicity of both drugs on MCF-7 breast cancer cell lines was not only maintained but also augmented due to the particles better uptake and internalization. This new approach propose the use of these novel formulations in the treatment of the subcutaneous and the skin proximal solid tumors such as the breast cancer solid masses where a transdermal patch can be applied directly on the location of the cancerous cells concentrating the drug molecules in this site and therefore hitting where it is really needed to hurt.

Keywords: Nanotechnology, breast cancer, polymeric nanoparticles

Presented by: Rania M. Hathout

Department of Pharmaceutics and Industrial Pharmacy, Faculty of Pharmacy, Ain Shams University, Cairo, Egypt

Email: rania.hathout@pharma.asu.edu.eg



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ABSTRACT 40

Vanillin augments liver regeneration effectively in thioacetamide induced liver fibrosis rat model

Amal Ghanim, Nancy Younis

ABSTRACT

Background: This study has been designed to investigate the role of vanillin either as prophylaxis or treatment in liver regeneration augmentation and liver fibrosis regression in thioacetamide (TAA) induced liver damage.

Materials and Methods: Animals were injected with TAA to induce liver injury (200mg/kg twice weekly) for 8 weeks. In vanillin prophylaxis group, rats were administered vanillin (100 mg/Kg, IP, daily) from day 1 of TAA injection for 8 weeks. In vanillin treatment group, rats were confronted with the same dose of TAA injection for 8 weeks then treated with vanillin (100 mg/Kg, IP, daily) for 4 weeks. ALT, AST activities, serum albumin, hepatic GSH, MDA, HGF, VEGF, IL-6 and TNF- α levels were measured and also, MMP-2, TIMP-1 and cyclin D gene expression were determined. Liver sections were stained with H&E and Sirius red and immune-stained for Ki-67 and α -SMA for histological and immune-histological changes analysis.

Results: Vanillin improved liver function and histology. Also, showed a remarkable increase in hepatic HGF and VEGF level, and up-regulation of cyclin D1 expression accompanied by a significant up-regulation of MMP-2 and down-regulation of TIMP-1. All these effects were accompanied by TNF- α , IL-6 and oxidative stress significant attenuation.

Conclusions: In conclusion, vanillin enhanced liver regeneration in TAA induced liver damage model, targeting growth factors (HGF, VEGF) and cellular proliferation marker cyclin D1. As well as stimulating fibrosis regression by inhibition of ECM accumulation and enhancing its degradation.

Keywords: Liver regeneration, vanillin, thioacetamide

Presented by: Amal Ghanim

Fayoum University, Egypt

Email: amh11@fayoum.edu.eg