Phytochemical Investigation and Biological screening of Euphorbia pulcherrima and Micromeria biflora

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February 11–12, 2019

(Monday, Tuesday)

Venue:

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Oral Presentation

1. A combinatorial approach to discovery of enzyme inhibitory molecules from nature via ethnomedical, in vitro, in vivo and in silico data

Ilkay Erdogan Orhan

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Abstract

Nature has always been a fruitful source for bioactive molecules which can be further developed into clinically available drugs. Many current drugs acting through the mechanism of enzyme inhibition are effectively used in therapy. Among them, natural ones have played a vital role such as galanthamine, an alkaloid-derivative drug from snowdrop plant used for the treatment of Alzheimer's disease, taxol from yew tree against breast cancer, first generation statins used against hypercholesterolemia obtained from microfungi, aspirin from willow bark, ziconotide from a sea slug as well as captopril, a synthetic drug originated from a snake venom. Consequently, an extensive research is being conducted on screening natural products for their enzyme inhibitory potentials. For this kind of research, ethnobotanical/ethnomedicinal information is also quite important, which is allied to pharmacological activity studies on medicinal plants in order to prove their folkloric use on scientific platform.During our continuous studies since the year of 2000 in order to find new natural enzyme inhibitors, we have screened quite a good number of natural products for their inhibitory capabilities against a number of enzymes, *e.g.* cholinesterases, tyrosinase, lipoxygenase, elastase, collagenase, xanthine oxidase, etc. Taking folkloric use of medicinal plants into account, we have so far obtained many promising inhibitors proved by *in vivo* (in some cases), *in vitro*, and *in silico* experiments. In this lecture, our latest outcomes obtained with natural compounds from different chemical classes such as pteryxin, resveratrol derivatives, phenolic acids, hyperforin, hyuganin C, etc will be highlighted (Fig. 1).

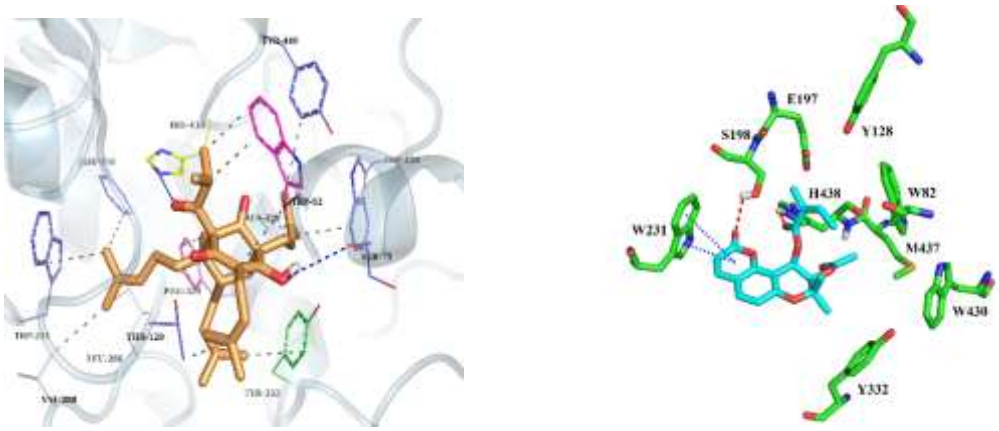

Figure 1. Interactions of hyperforin (orange skeleton, representation in sticks) with residues within binding site of BChE (on the left) and docking solution of natural product pteryxin (in blue) inside the active site of BChE (on the right)

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2. Drug design: identification of pharmacophore sites of drugs on the basis of modern bioinformatic pom analyses

Taibi BEN HADDA

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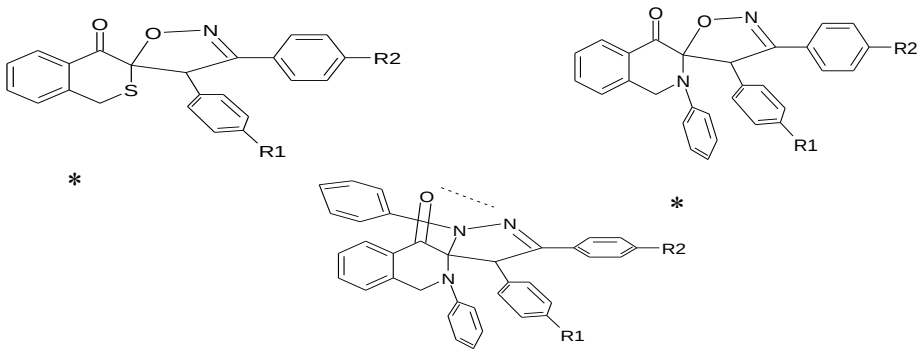
Abstract

A computational Petra/Osiris/Molinspiration (POM) Theory based model has been developed for the identification of physic–chemical parameters governing the bioactivity of quinoxaline and spiro derivatives of thiochromane containing combined antibacterialal/antiviral pharmacophore sites. Various compounds analyzed here were previously experimentally and now virtually screened for their antibacterial/antiviral activity. The highest antiviralal activity was obtained for compound having an antiviral ($O^{\square-}$ --- $N^{\square\square-}$) pharmacophore site, which exhibited excellent % inhibition, comparable to standard drugs. Compounds having an ($O^{\square-}$ --- $O^{\square\square+}$) pharmacophore site, represents increased antibacterial activity as compared to its analogues. The increase of antiviral bioactivity could be attributed to the existence of *pi*-charge transfer from oxazol ring to its aryl group, which plays a crucial template role in the organization of antiviral O,N-

phramacophore site. Moreover, it is cheap, has fewer side effects. So the purpose of this oral communication is to help both chemist and biologist in drug design.



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3. Synthesis and bioassay of micheliolide derivatives

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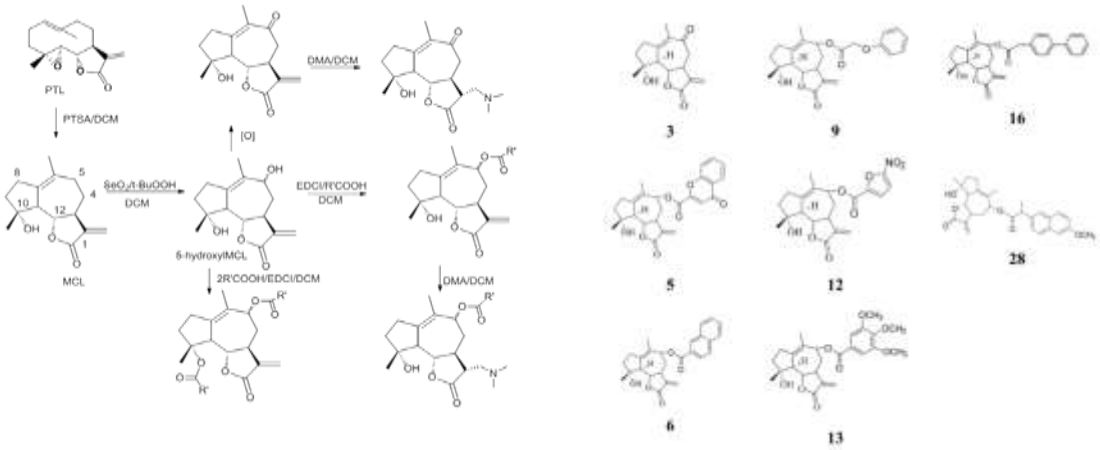
Abstract

The medicine from natural products has recently become a hotspot in the development of anticancer drugs. In the past 20 years, 61% of the small molecule new chemical entities of drugs launched worldwide can be traced back to natural products. Micheliolide (MCL) is a sesquiterpene lactone compound, which widely distributes in the root bark of Magnoliaceae plant, such as *Mickelia Champaca L.* It has been reported that micheliolide and its derivatives possessed anticancer activity against leukemia, breast cancer and many other cancers. Based on previous research findings, we synthesized a series of micheliolide derivatives. Total 35 MCL derivatives were prepared by the method showed in Scheme 1, their cytotoxicities against seven human tumor cell lines were evaluated by MTT assay. The result *in vitro* showed that compound **3, 5, 6, 9, 12, 13, 16** showed superior cytotoxicity to MCL. All derivatives have significant cytotoxicity on glioma cells (U-87 MG). The derivatives of **3, 6, 12** and **13** were selected to study the antitumor activity *in vivo* according the *in vitro* result. The results indicated that compounds **3** had a

significant growth inhibition on liver cancer H_{22} and glioma G422 in mice, however it had no effect on the blood and immune system of tumor bearing mice. The inhibition rate is as same as temozolomide which is the effective drug for brain tumors at present. The preliminary anti-tumor mechanism showed that compound **3** could inhibit the transcriptional activity of NF-κB and STAT3. The IC_{50} of compound **3** to NF-κB was 21.76 μmol/L, and the inhibition rate of compound **3** to STAT3 was 37.7% at 25 μmol/L dose. Compound **3** may affect the expression of STAT3 regulatory protein and induce apoptosis of cancer cells by inhibiting the signal pathway of NF-κB /IL-6/STAT3 in tumor tissues.



Scheme 1: synthesis of micheliolide derivatives

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4. Synthesis and anticancer activity of amidrazone derivatives and related congeners

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Abstract

Cancer continues to be a global burden, despite the advent of technological and pharmaceutical improvements over the past two decades. Methods of cancer treatment include surgery, radiotherapy, anti-cancer drugs (chemotherapy) in addition to other specialized techniques. Published reports indicated that approximately 90–95% of all cancers is attributed to lifestyle, such as alcohol consumption, obesity, outdoor pollution, food additives, among other things, and the

remaining 5–10% to defective genes. Accordingly, scientist keep searching for new anticancer agents whether synthetic or natural. In this context, several series of amidrazones incorporating N-piperazines and related congeners were synthesized and characterized with the aid of several spectroscopic techniques and by elemental analysis. These compounds were screened for anticancer activity against several cell lines. Results obtained from different investigations revealed the some of the prepared compounds displayed potent anticancer activity. These compounds could be useful leads or candidates as anticancer drugs.

Keywords: Anticancer activity, synthetic, amidrazone derivatives

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5. The medicinal properties of some indonesian traditional plants

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Abstract

Indonesian traditional plants or *Jamu* have been widely used for the treatment of some diseases. Those plants provide a huge biomass that promises a potent resource for medicinal properties. This research focused on bioassay guided fractionation for finding the bioactive chemical constituents of *Sonneratia ovata*, *Chromolaena odorata* and *Stachytarpheta jamaicensis*. They are a popular folk medicine widely used by people in some region in East Indonesia. From this ethnobotanical study, the extracts of these plants have been screened their bioactivity by antioxidant, antimicrobial, and anti-diabetes *in vitro* and *in vivo* assays. The results showed that *S. ovata, C. odorata* as well as *S. jamaicensis* have fine inhibitory activity against 2,2-diphenyl-1-picryl-hydrazyl (DPPH) and 2,2'-azinobis-(3-ethylbenzothiazoline-6-sulfonic acid) (ABTS) radical, bacterial pathogen including gram-positive and negative bacteria, α-glucosidase as well as aldose reductase enzyme. In this research, antibacterial activity has been performed. Next, anti-diabetes investigation has been done against α-glucosidase as well as aldose reductase enzyme. α-Glucosidase is an enzyme, a catalyse the cleavage of polysaccharides to simple sugar namely

glucose, located in small intestinal tissue. The accumulation of glucose in the blood was potent to be caused hyperglycaemia. Aldose reductase is the first enzyme in the polyol pathway. The enzyme catalyses the reduction of glucose to sorbitol. Diabetic complications are considered to be caused by the accumulation of sorbitol. Furthermore, some isolated compounds have been isolated to have some inhibition of those medicinal properties assays. This research indicated that the plants could be a potential resource for medicinal purposes.

Keywords: anti-diabetes, antimicrobial, antioxidant, Indonesian plants

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6. Study of the binding epitopes of urease inhibitors by molecular docking, std-nmr spectroscopy and biochemical analyses; strategies for drug design and discovery

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Abstract

Discovery of inhibitors of clinically relevant enzymes is an important area in drug discovery and development. A large number of synthetic and natural inhibitors have been developed which are now used as drugs against a variety of diseases. Specific inhibitors interact with enzymes and block their activity towards their corresponding natural substrates, thus treating a number of pathological conditions. The binding of inhibitor can be reversible or irreversible. Irreversible inhibitors chemically alter the active site residues of enzymes by binding covalently. While, reversible inhibitors bind through hydrophobic interactions, hydrogen bonding, and ionic bonds. There are four classes of reversible inhibitors, competitive, un-competitive, non-competitive, and mixed-type inhibitors. This process involve the use of various mechanism-based biochemical assay of varying through put. To design, develop and validate robust enzyme inhibition assays, it is critical to have a thorough understanding of the enzyme biochemistry and the kinetics of enzymatic action. Understanding the mechanism of action of the target enzyme is critical in early discovery and development of drug candidates through extensive Structure-Activity Relationship (SAR) studies.

Urease enzyme is one of clinically important enzyme and their inhibition is recognized as an important approach towards the treatment of ulcer, urolithiasis and related diseases. The kinetics studies were performed, to fine out the mechanism of urease inhibitor. Saturation transfer difference (STD) NMR experiments were used to identify the structural features responsible for the inhibition of urease enzyme at the atomic levels.

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7. Marine bioactive compounds; innovation pathways for drug discovery

Hafiz Ansar Rasul Suleria[1, 2, 3]

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Abstract

Marine organisms are rich sources of bioactive compounds. These bioactive compounds have various pharmacological properties, especifically free radical scavenging, anti-tumor, anti-thrombotic, anti-coagulant, antimicrobial, anti-cancer, neuroprotective and immunomodulatory. In a current scenario, abrupt change in diet patterns and environment, new diseases are arising in worldwide. For the reason, demand for effective, safe and low-cost drugs are also elevating with the continuously disease influx. Marine drugs may provide an alternative source to fight against these crises. In Western countries, thrombosis, inflammation and cancer is among the leading reasons of mortality. In spite of outstanding developments in drug discovery from last three decades, there is still an insistent necessity for innovative drugs, especially in the unexplored area of marine-based drugs. Recent technological innovations in extraction, isolation, structure explication, synthesis and amalgamation of new bioactive compounds and their biological activities have made possible to explore unique and innovative bioactive compounds from marine environment.

In this plenary talk, I am happy to present my collaborative research project on "marine processing waste – innovative trends in drug discovery" conducted at the University of Queensland (UQ), Australia - UQ School of Medicine (Translational Research Institute, TRI) and the Commonwealth Scientific and Industrial Research Organisation (CSIRO, Agriculture & Food) funded by the Australian Government. Marine processing waste especially the Blacklip Abalone (*Haliotis rubra*) processing waste contains sulphated polysaccharides with anti-thrombotic, anti-coagulant, anti-oxidant, anti-inflammatory and anti-cancer activities. Our study confirmed the presence of anti-thrombotic, anti-coagulant and anti-inflammatory molecules in the blacklip abalone viscera and suggested as a potential source of nutraceutical or bioactive ingredients for future drugs. Our findings indicate the potential value of this abalone marine waste can target and prevent unwanted clot formation leading to deep vein thrombosis or pulmonary embolism in people at risk. Overall, this research provides a vision to consider marine biodiversity and their bioactive compounds in the file of drug discovery.

Keywords: marine bioactive compounds; abalone; marine processing waste, anti-thrombotic, anti-coagulant activities.

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8. Drug discovery through bioactivity of phytochemicals: evidence based study

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Abstract

Herbal/traditional medicines are the developing option for treatments because of its easy accessibility and cost effectiveness. A large number of populations depend on traditional and alternative medicines in developing countries. Traditional Medicine has not yet been incorporated into the National Health Care System. WHO emphasize on standardization of medicinal herbs and establish guidelines for their production and quality control.

The modern available allopathic treatments are very costly, associated with numerous undesired affects which resulting in loss of patient compliance. Therefore, there is serious need to develop

alternative treatment option particularly from traditional herbal formulations as these accounts for cost effective with minimal harmful effects. Worldwide, herbal medicines received a boost when WHO encouraged developing countries to use traditional plant medicines to fulfill need unmet by modern systems.

In the past centuries so many herbal treatments were provided to get rid of different disease conditions like anxiety, hypertension, hyperlipidemia, infections, diabetes etc. The investigation on passion fruits gives out positive results by exerting the anti anxiety action at low doses. The literature established prove many dietary supplements possess mind relaxing and anxiolytic actions hence these secondary cures to anxiety are cheap source of earning valuable agents that aims to reduce tension and stress. Similarly, in recent past the global dilemma of antimicrobial resistance is predominantly pressing in developing countries, where the infectious disease burden is high and cost constraints put off the appliance of expensive agents. Although there are splendid advancements in modern medicine, yet traditional medicine has always been accomplished for treating infections.

In this study, a collection of phytochemical constituents bioactivity has been discussed which are evident for several pharmacological activities like anti anxiety, antimicrobial, antioxidant, antihypertensive, antimicrobial, anti-inflammatory, anticancer, antiviral, hepatoprotective, cardiotonic and immunomodulating properties of certain plants and fruits.

Based on this evident study, it can be concluded that drug discovery through herbal resources may serve as an excellent alternative treatment option in different diseases and only need is to emphasize on standardization and to establish guidelines for their production and quality control.

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9. Synthesis, antimicrobial, antiurease and molecular docking studies of 1-(3-trifluoromethyl)benzoyl-3-aryl thioureas

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Abstract

Thiourea derivatives are of remarkable interest due to their wide range of pharmacological significance, medicinal importance as well as their crucial role in drug delivery along with their

applications in agriculture industry. Keeping in mind the significance of thiourea derivatives, synthesis of new 3-trifluoromethyl benzoic acid thiourea derivatives was carried out. For this purpose, freshly prepared 3-(trifluoromethyl)benzoyl chloride from respective acid was condensed with various anilines to generate the required thioureas **(1-10)**. Structures of all the synthesized compounds were confirmed by FT-IR, NMR, EI-MS and ESI-HRMS spectroscopic analysis. In order to check their biological potential, all the synthesized compounds were subjected to antimicrobial and antiurease activities. In case of antibacterial activities maximum inhibition was observed by compound **9** against four bacterial strains *i.e; Pesudomonas aerouginosa*, *E. Coli*, *S. Aureus* (ATTC# 6538) and MRSA-10 while rest of compounds showed moderate to no activity. In case of antifungal activity all comounds were active againts *C. Albican* while no activity was observed against *C. Prapsilosis* strain of fungi. The compound **1** proved to be the most potent urease inhibitor showing the highest enzyme % inhibition (93.1%) with IC_{50} value of 8.17± 0.24 µM and found more active as compare to standard. All the synthesized compounds were docked into the binding cavity of Urease (PDB ID: 4ubp). The most active compound **1** was also ranked as top on the docking score as it was found to show valuable interactions with the target protein along with good docking scores.

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10. Green chemistry: solvent free synthesis of pyridine derivatives and their biological activities.

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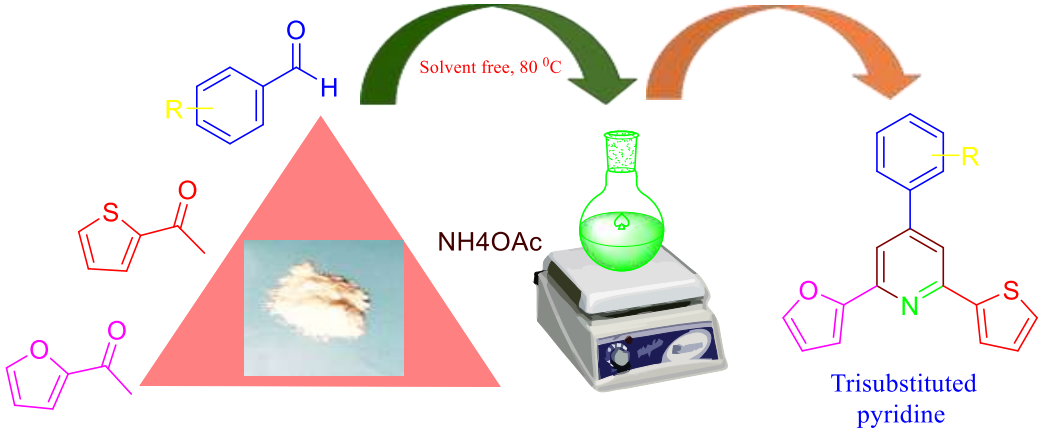
Abstract

A versatile heterocyclic ring pyridine has got substantial attention in medicinal chemistry due to its unique structural features. Pyridine showed diversity in anti-bacterial, anti-viral, anti-inflammatory, anti-diabetic, anti-diuretic and anti-cancer activities. Its broad biological spectrum persuaded the investigator to disclose a series of new, effective and highly active derivatives through an efficient method. A green synthetic strategy that offered less time requirement,simplicity, eco-friendliness and excellent product yields was employed for the

synthesis of different derivatives. The synthesized derivatives were subjected to structure elucidation by Fourier Transform Infrared (FT-IR), and ^{1}H-NMR spectral techniques. The prepared pyridine derivatives were evaluated for various biological activities such as,anti-bacterial, anti-oxidant and anti-urease activity. All the compounds gave excellent results against urease enzyme with IC_{50} values between 12.8 ± 1.04 – 23.7 ± 0.23 µM.



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11. Prelim ray phytochemical screening test and antimicrobial evaluation of *Thymus linearis*

Ghias UDDIN

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Abstract

Thymus plants are the most attractive plants all over the world due to aromaticity, curative properties and phenolic contents of the essential oils. The pharmacological and biological qualities of*Thymus* species are considered as medicinal plants. In traditional medicine, flowering parts and leaves of *Thymus* species are commonly used as tonic, herbal tea, antitussive, carminative, expectorant, antiseptic, food preservation and for treating colds. *Thymus* species have strong antifungal, antibacterial, antiparasitic, herpes antiviral, spasmolytic and antioxidant activities. All the extracts of *T. linearis* showed significant antibacterial and antifungal activities when tested against nine bacterial and four fungal strains.Nanoparticles were also synthesized from the crude

extracts which were confirmed by UV-visible spectroscopy, Infrared spectrophotometry and atomic force microscopy (AFM). It was concluded from this study that extracts of *T. linearis* have an array of important phytochemicals and significant activities against some of the multidrug resistant bacterial and medically important fungal strains.

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12. Nanoparticles from dexamethasone prodrugs for passive targeting in the treatment of inflammatory diseases (rheumatoid arthritis)

Mujeeb-ur-Rehman[1,2], Nicolas Tsapis[1], Sinda Lepetre[1], Franceline Reynaud[1], and Elias Fattal[1]

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Abstract

Despite, glucocorticoids (GCs) have been used as immunosuppressive and anti-inflammatory drugs for a long time, they still possess several serious adverse effects especially in case of long term treatment. The undesirable pharmacokinetics of these drugs, with short half-life, rapid elimination, and increased volume of their distribution, needs frequent administration to yield efficient anti-inflammatory activity. These drawbacks cause some severe adverse effects to human healthcare such as osteoporosis, diabetes, hydro-electrolytic perturbations, Cushing's syndrome and so on. Nanocarriers, as delivery vehicles for GCs, could be considered to improve GCs pharmacokinetics and increased their concentration at inflamed sites. Though several successful nanocarriers have been formulated yet they still possess many issues such as limited drug loading and premature drug release, which ultimately prevent them from reaching clinical translation. Recent approaches to address these issues, consist of formulating prodrugs of GCs such as palmitate derivatives as colloidal nanocarriers. Here we have synthesized three dexamethasone prodrugs **1-3** each possessing a different lipid-drug chemical linkage, i.e., ester, carbamate, and carbonate. Prodrugs **1-3** were then formulated into nanoparticles (NPs) using a biocompatible and biodegradable lipid, DSPE-PEG_{2000}-Methoxy, as colloid stabilizer and crystallization inhibitor. Formulated NPs were then subjected to their physico-chemical characterization, drug release in

mice plasma, cytotoxicity (MTT assay), and in vitro anti-inflammatory activity (cytokines release inhibition). The lipid/prodrugs ratio and their concentration were adjusted to formulate prodrugs **1-3** nanoparticles (NPs) having size between 140 and 180 nm. As high as 98% encapsulation efficiency was achieved in the formulated NPs, meaning a very high drug loading (50-56% w/w). In addition, NPs stored at 4 ºC were proved to be stable in terms of size, pdi and zeta potential up to 45 days. Anti-inflammatory activity of prodrugs **1** and **3** NPs were preserved when incubated with lipopolysaccharide (LPS) activated macrophages, corresponding to the drug release from their respective NPs.

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13. Phytochemical investigation, biological effectiveness and docking study of active compounds isolated from *Diospyros lotus*

Abdur Rauf

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Abstract

Recently reported dimeric naphthoquinones (**1-3**), were isolated from chloroform fraction of *Diospyros lotus* roots. The chemical structures of isolated compounds were identified by using advance NMR analysis. The pure constituents (**1-3**) were evaluated for their enzymes inhibitory activities such as urease, carbonic anhydrase and α-chymotrypsin inhibition. Selective inhibition of compounds **1**, **2** and **3** against urease showed IC_{50} values of 37.21± 2.00, 78.57± 2.17, 29.12 ± 2.45 μM, respectively. The IC_{50} values of compounds are comparable with standard thiourea (IC_{50} = 21 ± 0.11 µM). Structure-activity-relationship of the active compounds against urease was built through molecular docking studies using Auto Dock Vina and i-GEM DOCK software's.

Keywords: *Diospyros lotus*; phytochemicals, urease; carbonic anhydrase (CA); α-chymotrypsin, molecular docking.

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14. Plant and plant-based materials for biological studies and environmental remediation

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The plant and its derivatives is one of the fundamental materials which serve as potent biological agents. In the last few decades several pure chemical ingredients were isolated from the plant which act as a therapeutic agents. Right now the plant and plant based materials are largely used for the stabilization of zero-valent nanoparticles. These zero-valent nanoparticles act a potent biological agent as well as acting as a catalyst for the removal of toxic pollutants from the environment. In this study we will considered the dual character of the plant and plant based materials. We will discussed that plant are not the only rich sources for the potential biological targets but we will discussed that plant based nanoparticles can also be a potential sources for the removal toxic carcinogenic pollutants.

Keywords: Plant Materials, Therapeutic agents, carcinogenic substance, Zer-valent Nanoparticles

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15. Phytochemistry and biological potecy of *Rumex nervosus* Vahl

Rasool Khan, Mohammed Mansour Quradha

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Abstract

The present study aim to determine phenolic compounds and evaluate the antioxidant potential of *R. nervosus* using different methods. The crude methanolic extracts of leaves and stem of *R. nervosus* were analysis by HPLC to determine phenolic compounds. Antioxidant potentials has been evaluated using ABTS, FRAP, and DPPH assays. HPLC analysis showed a presence of gallic acids and flavonoids in the extracts. Crude extracts of both leaves and stems of *R. nervosus* exhibited promising antioxidant agent. Crude methanolic extract of stems showed highest level of antioxidant activity using ABTS (2.32 ± 0.0505 mmol Trolox/g), while, the crude extract of leaves showed highest level of antioxidant activity using FRAP assays (1.70 ± 0.09 mmol Fe^{2+}/g). crude of methanolic extract of leaves recorded highest level of antioxidant activity (94.6 %) at concentration 100 µg/ml using DPPH assays. Further highest level of antioxidant activity was recorded (98.05 %) at concentration 100 µg/ml by synergism crude extract of leaves and stems at ratio (60:40) respectively. Among of sub-fractions, ethyl acetate fraction of both leaves and stem

showed highest level of antioxidant activity. *R. nervosus* is rich source of phenolic compounds and other secondary metabolites which poses promising antioxidant effect.

Keywords: *Rumex nervosus*; antioxidant activity; HPLC Analysis.

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16. Luteolin as anticancer compounds from natural source

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Abstract

Many food-derived phytochemicals and their derivatives represent a cornucopia of new anti-cancer compounds. Luteolin (3,4,5,7-tetrahydroxy flavone) is a flavonoid found in different plants such as vegetables, medicinal herbs, and fruits. It acts as an anticancer agent against various types of human malignancies such as lung, breast, glioblastoma, prostate, colon, and pancreatic cancers. Luteolin can additionally reverse epithelial-mesenchymal transition (EMT) through a mechanism that involves cytoskeleton shrinkage, induction of the epithelial biomarker E-cadherin expression, and by down-regulation of the mesenchymal biomarkers *N*-cadherin, snail, and vimentin. Furthermore, luteolin increases levels of intracellular reactive oxygen species (ROS) by activation of lethal endoplasmic reticulum stress response and mitochondrial dysfunction in glioblastoma cells, and by activation of ER stress-associated proteins expressions, including phosphorylation of eIF2α, PERK, CHOP, ATF4, and cleaved-caspase 12.

Keywords: Flavonoids, luteolin, breast cancer, stomach, prostate, colon, skin cancer

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17. Functional implication of B-Cell Translocation Gene-2 in myeloid leukemia cells differentiation and its regulation under stress conditions

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Abstract

Human B-cell translocation gene 2 (BTG2) an orthologue of mouse 12-O-tetradecanoyl phorbol-13-acetate inducible sequence 21 (TIS21), and rat PC3, is a tumour suppressor that belongs to the antiproliferative gene family, and is implicated in a variety of biological processes. c-Myc is a transcription factor and its deregulation is common in leukaemia and lymphomas; the tumours are highly proliferative and often blocked at an earlier phase than the terminal stage of differentiation. The interrelation and the functional interplay of these two different proteins are not defined yet. We have shown here that the tumour suppressor BTG2/TIS21/Pc3 negatively regulated c-Myc expression during all-trans-retinoic acid (ATRA)-induced differentiation that accelerated differentiation and reduced proliferation of acute myeloid leukaemia (AML) HL-60 cells. Employing various inhibitors, we observed that BTG2/TIS21/Pc3 downregulated c-Myc mRNA and additionally decreased c-Myc protein stability by increasing its phosphorylation at S62 and T58 residues via activation of Erk1/2 and inhibition of PI3K/Akt along with the subsequent activation of GSK-3β in response to ATRA treatment. HL-60 cells treated with GSK-3β or proteasome inhibitors revealed marked accumulation of c-Myc both in the presence and absence of ATRA plus BTG2/TIS21/Pc3, confirming ATRA plus TIS21 mediated c-Myc phosphorylation and its consequent degradation in proteosome. Immunoprecipitation assay revealed that BTG2/TIS21/Pc3 hindered the interaction of p-Erk1/2 with Akt, thus directly regulating MAPK and Akt activities without interaction with c-Myc. Using various small molecule inhibitors, we further observed that ATRA treatment under stress conditions switches leukemia cells differentiation from granulocytes to macrophages involving upregulation of BTG2/TIS21/Pc3. Stress conditions-mediated up-regulation of BTG2/TIS21/Pc3 was confirmed to occur through ROS-Erk1/2-NFκB-BTG2 cascade. These findings exhibit anticarcinogenic potential of BTG2/TIS21/Pc3 *via* downregulation of c-Myc expression during ATRA induced differentiation of HL-60 cells involving activation and deactivation of two major c-Myc regulators, Erk1/2 and Akt, respectively and additionally highlights the regulatory mechanism of BTG2/TIS21/Pc3 under stress conditions.

Keywords: BTG2/TIS21/Pc3, c-Myc, Differentiation, Leukemia, NF-κB, ROS

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18. Antioxidant and antimicrobial activities of peel part of tarap (*artocarpus odoratissimus*) species from tarakan, Indonesia

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Abstract

The purpose of this study is to investigate antioxidant and antimicrobial activities of various extracts of peel part of Tarap (*Artocarpus odoratissimus*) species from Tarakan, Indonesia. The antioxidant property was assessed by DPPH while the antimicrobial activity was assessed according to zones of inhibition against *Escherichia coli*, *Staphylococcus aureus*, *Bacillus subtilis* and *Pseudomonas aeruginosa*. Crude extracts had antioxidant activity in the order of methanol > water > methyl chloride > ethyl acetate > n-hexane extracts with the IC_{50} value were 0.018, 0.025, 0.047, 0.168 mg/mL, respectively. Among all of extracts, methanol extract showed the highest antioxidant activity, while *n*-hexane extract had no activity. However, *n*-hexane extract of peel part of *A. odoratissimus* revealed antimicrobial activity when assayed against *E. coli*.

Keywords: Antioxidant; antimicrobial; Tarap; *Artocarpus odoratissimus*; *Escherichia coli*

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19. Anti-dengue, antimicrobial, toxicity and molecular docking study of the new synthesized 3-*O*-phospo-*α*-*D*-glucopyranuronic acid

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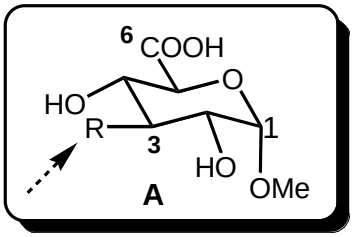
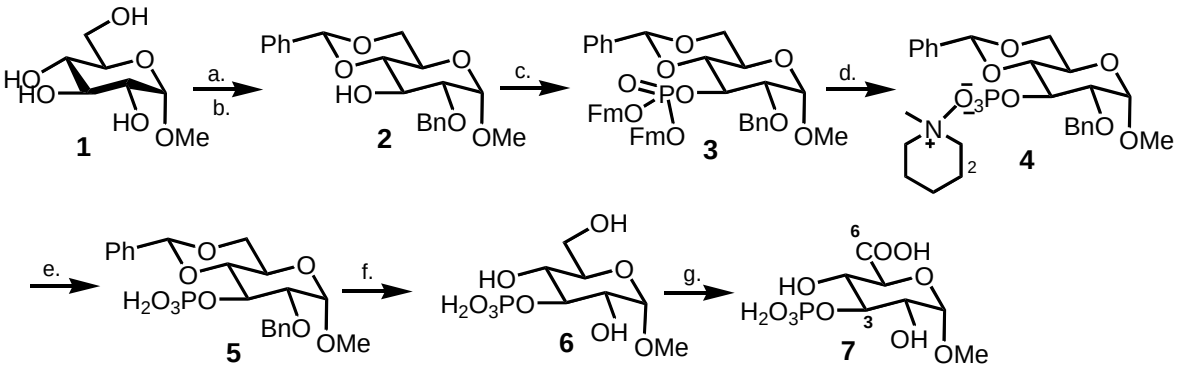
Abstract

Dengue virus infection (DENV) is currently expanding worldwide since it is present in more than 128 countries in the world [1]. DENV is the most prevalent mosquito-borne viral disease causing clinical syndromes in humans. As there is no available vaccine or treatment, DENV infection has become a major international public health concern and the search for anti-dengue treatment is of extreme importance and it is an active field of research. The entry of the dengue virus into the host cell is a complex process, mediated mainly by the DENV cell surface (E) glycoprotein under acidic conditions. The first step of dengue virus entry is binding of the viral (E) glycoprotein to a cellular receptor and/or attachment factors, followed by incorporation of the virus-receptor complex inside cells.[1, 2, 3]. *Hidari et al*. has reported the synthesis of a series of 12 methyl 3-*O*-phospo-α-D-glucopyranuronic acid of the general structure **(A)** by introduction of a sulfate group at specific positions and evaluated their activities against dengue virus (DENV) infection as well as binding to BHK-21 cell surface [1]



Based on these finding the main objective of this project to synthesize a new compound namely methyl 3-*O*-phospo-α-D-glucopyranuronic acid (**7**) and screen for their therapeutic application. The structure of compound **7** was identified by spectroscopic technique.



Scheme 1.

The synthesize compounds were also screen for *in-vitro* anti-microbial activity. The results achieved showed that compound **7** exhibited excellent antifungal activity against tested fungal strains. Molecular docking analysis of synthesize compound **7** was also performed to find mechanism for anti-dengue and anti-fungal activities. In silico study was performed to predict the binding modes of newly-compound (**7**). The docking results revealed that the compound has strong attraction towards the target protein, as characterized by good bonding networks. On the basis of the developed results, it can be predicted that compound (**7**) might show good inhibitory activity against dengue envelope protein. Synthesize compounds (**2-7**) were also tested for cytotoxicity but interestingly no considerable toxicity was observed.

Keywords: *3-O*-phosphated glucuronide derivative; Synthesis, Antimicrobial; Docking analysis

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20. Design, synthesis and in vitro antioxidant activity of 3,5-disubstituted-2-pyrazolines

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Abstract

Heterocyclic compounds containing pyrazoline were reported to possess worthwhile bio-activity. Taking substituted chalcones and azachalcones as the starting material two novel series of pyrazolines were synthesized by conventional heating and microwave irradiation. Claisen Schmidt condensation between intended aryl methyl ketones (1a-b) and different substituted aromatic aldehydes (2a-c) resulted in the formation of corresponding chalcones (3a-c; 4a-c) which were cyclized using hydrazine hydrate to yield final pyrazolines (5a-c; 6a-c) in good yields (59-81%). Reaction time and %ag yield data ratified the superiority of microwave assisted technique over

classical heating. The structures of all the synthesized compounds were confirmed on the basis of physical data, spectroscopic studies and micro analysis. The infrared spectral group frequencies of chalcones and pyrazolines have been found in good correlation that approved the synthetic routes. Further, the compounds of both series (5a-c; 6a-c) have been screened against 1,1-diphenyl-2-picrylhydrazyl free radical (DPPH•) to assess their antioxidant potentials and results were compared with positive control. All the compounds showed good free radical scavenging activity which is comparable to that of standard galic acid. Amongst all the tested compounds 5a (75%) and 5b (79%) were found to be more active. The highest DPPH• potential of 5a-b owed to the presence of multi-chloro groups on the phenyl rings.

Keywords: Heterocyclic, pyrazolines, chalcones, microwave irradiation, Claisen Schmidt condensation, hydrazine hydrate, DPPH•, anti-oxidant.

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21. Bioactive chemical constituents of *Garcinia hombroniana* (Seashore Mangosteen)

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Abstract

The study describes isolation of bioactive chemical constituents from *Garcinia hombroniana*, traditionally used to treat itching and infections after childbirth. Its dichloromethane and ethyl acetate bark extracts afforded several new (**1**, **5**, **12**, **21**, **22**) together with known compounds characterized and identified by nuclear magnetic resonance and mass spectral techniques. The constituents include 2,3',4,5'-tetrahydroxy-6-methoxy benzophenone (**1**), 2,3',4,4'-tetrahydroxy-6-methoxybenzophenone (**2**), 2,3',4,6-tetrahydroxybenzophenone (**3**), 1,3,6,7-tetrahydroxyxanthone (**4**), (2*R*, 3*S*) volkensiflavone-7-*O*-hamnopyranoside (**5**), volkensiflavone (**6**), 4"-*O*-methyl-volkensiflavone (**7**), volkensiflavone-7-*O*-glucopyranoside (8), morelloflavone (**9**), 3"-*O*-methyl-morelloflavone (**10**), morelloflavone-7-*O*-glucopyranoside (**11**), 2*β*-hydroxy-3*α*-*O*-caffeoyltaraxar-14-en-28-oic acid (**12**), abeo-3*β*-acetoxy-9*α*,13*β*-lanost-24*E*-en-26-oic

acid (**13**), garcihombronane B (**14**), garcihombronane C (**15**), garcihombronane D (**16**), garcihombronane F (**17**), garcihombronane G (**18**), garcihombronane I (**19**), garcihombronane J (**20**), garcihombronane N (**21**), (22*Z*,24*E*)-3*β*-hydroxycycloart-14,22,24-trien-26-o-ic acid (**22**), 3*β*-acetoxy-9*α*-hydroxy-17,14-friedolanostan-14,24-dien-26-oic acid (**23**), (22*Z*, 24*E*)-3*β*, 9*α*-dihydroxy-17,14-friedolanostan-14,22,24-trien-26-oic acid (**24**), 3*β*, 23*α*-dihydroxy-17,14-friedolanostan-8,14,24-trien-26-oic acid (**25**). Among the constituents evaluated for *in vitro* cytotoxicity against MCF-7, DBTRG, U2OS and PC-3 cell lines, compounds **1** displayed good cytotoxic effects against DBTRG cancer cell lines. Compounds **1**-**12** were also found to possess significant antioxidant activities. In anticholinesterase activity, compounds **12** and **21** were the most active dual inhibitor of both acetylcholinesterase (AChE) and butyrylcholinesterase (BChE).

Keywords: *Garcinia hombroniana*, biflavonoids, garcihombronane, cytotoxic, anticholinesterase

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22. Copper accumulation in soils of orchards and its toxicological effects on humans

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Abstract

The uses of copper based fungicides on peaches orchards is increasing day by day which is responsible for copper accumulation in soil and then it's up taken by the seasonal crops, cultivated in orchards. This research was conducted to study the copper content in soil and wheat crop grown under orchard and non-orchard fields with an objective to know about the toxicological effects of copper based fungicides and copper content in soil and different parts of wheat plant. 10 soil samples were collected from both fields (orchard and non-orchard) covering an area of about 60150.4 m^2. The collected soil samples were analyzed for total copper contents using Aqua-regia extraction method. Wheat plants were collected from both fields at maturity and were analyzed for copper contents. Results showed that copper content in orchard soils was significantly high ($p<0.05$) in the range of 46.52 to 53.31mg kg-1. In non-orchard soils the range was 11.18 to 20.71mg kg-1. Among different parts of wheat crop, significantly higher ($p<0.05$) copper content

was observed in seed (23.11 to 37.1mg kg-1) with the maximum metal transfer factor (0.8) for orchard crop indicating a higher risk factor for consumption. Compared to non-orchard copper concentrations (5.02 to 8.03mg kg-1) and metal transfer factor (0.12) results concluded that higher copper content in orchard fields arise from the use of copper based fungicides. Higher accumulation of copper causes lung cancer in humans. It is therefore, recommended to introduce the alternate source of copper based fungicides.

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23. Isolation and pharmacological evaluation of compounds from *Sophora mollis*

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Abstract

The aim of this investigation to isolate metabolic compounds from aerial parts of *Sophora mollis* and evaluated their pharmacological potential. The isolated compounds identified using NMR (1D and 2D) and mass spectroscopy. Five known compounds were isolated and characterized as: Scopoletin (**1**), Pinitol (**2**), 2-Propenoic acid, 3-(3,4-dihydro- xyphenyl)-, octacosyl ester (**3**), Betulin (**4**), *β*-sitosterol glucoside (**5**) were isolated, compounds (**2**), (**3**) and (**4**) were the first time isolated from this species. Pharmacological evaluation of isolated compounds revealed that the compound (**1)** exhibited significant anti-inflammatory effect with IC_{50} = 1.56 ± 0.34µg/mL followed by compound (**3)** with IC_{50} = 124.1± 16.4 µg/ml. Furthermore, compound (**3)** shows significant radical scavenging capacity toward DPPH. The highest personage inhibition of DPPH was recorded 95.646 ± 0.003 % at concentration 400µg/ml followed by 94.766±0.014% and 94.516±0.011 % at concentration (200 and 100) µg/ml respectively. Evaluation of anticancer activity of isolated compounds reveals weak effect against HeLa and 3T3 fibroblast cell lines.

Keyword: *Sophora mollis*, Scopoletin, anti-inflammatory, DPPH

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24. Synthesis and ruthenium coordination complexes of the chelating phosphine phosphonium-1-indenylide1,1-bis(diphenylphosphino)methane-1-indenylide,1 $c_9h_6ph_2pch_2pph_2$

Riaz Hussain[1,2], Kevin G. Fowler[1], Francoise Sauriol[1], Michael C. Baird[1*], Peter H. M. Budzelaar[1*]

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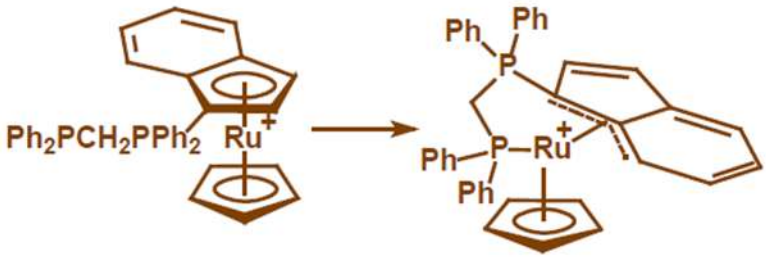
[2]*Department of Chemistry, University of Education Lahore, D. G. Khan campus, D. G. Khan.*

Abstract

Bis(diphenylphosphino) methane-1-indenylide, 1-C9H6PPh2CH2PPh2 (1-C9H6dppm, **I**) has been synthesized and characterized by NMR spectroscopy and X-ray crystallography. **I** reacts with [CpRu(MeCN)3]PF6 to form the conventional sandwich complex [CpRu(η5-**I**)]PF6 (**II**), which contains a dangling -PPh2 group. Complex **II** isomerizes to an 18-electron species **IIIc** in which the dangling -PPh2 group coordinates to the ruthenium, forcing slippage of the five-membered ring to an unanticipated 1,9,8-η3 exo mode of coordination.



25. Click one pot synthesis, spectral analyses, crystal structures, DFT studies and brine shrimp cytotoxicity assay of two newly synthesized 1,4,5-trisubstituted 1,2,3-triazoles

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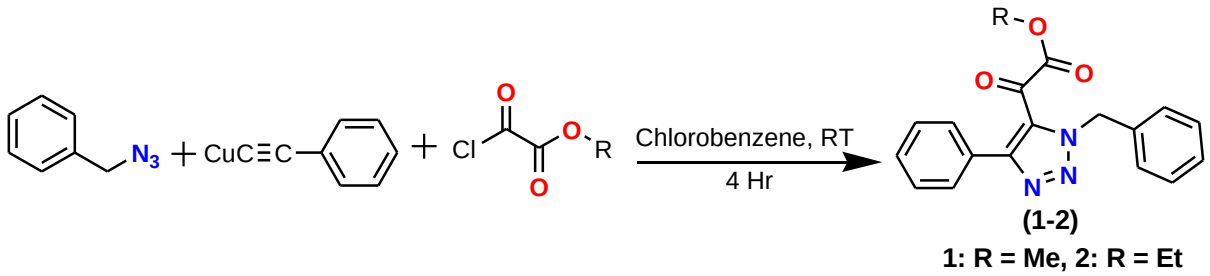
Abstract

Methyl-2-(1-benzyl-4-phenyl-1*H*-1,2,3-triazol-5-yl)-2-oxoacetate (**1**) and ethyl-2-(1-benzyl-4-phenyl1*H*-1,2,3-triazol-5-yl)-2-oxoacetate (**2**) were synthesized by one pot three component strategy, and characterized by FT-IR, NMR (1 H and 13C) spectroscopy and TOF-MS spectrometry. Finally, the structures were unequivocally confirmed by single crystal X-ray

diffraction analyses. Both compounds, **1** and **2** exist in monoclinic crystal packing having space group P21/n and P21/c, respectively. Crystal structures investigations revealed that the molecular structures of the title compounds are stabilized by weak intermolecular hydrogen bonding interactions to form dimers. Density functional theory (DFT) calculations were performed not only to compare with the experimental spectroscopic results but also to probe structural properties. The molecular electrostatic potential (MEP) mapped over the entire stabilized geometries of the molecules delivered information about the electrophilic and nucleophilic sites. Furthermore, frontier molecular orbital analysis gave the idea about stability and reactivity of compounds. Both compounds were also screened for brine shrimp cytotoxicity assay and showed promising results.

Keywords: Click chemistry, Triazole, X-ray diffraction, DFT, Brine shrimp assay



(1-2)

1: R = Me, 2: R = Et

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26. Synthesis, single crystal analysis and antibacterial activity of two new calcium and barium complexes using sodium 2-mercaptobenzothiazole and 1,10-phenanthroline ligands

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Abstract

2-Mercaptobenzothiazole has been used as a reagent for the detection and gravimetric determination of a number of metal ions i.e. Osmium forms yellow color systems in aqueous ethanol with 2-mercaptobenzothiazole [1]. X-ray absorption near-edge structures (XANES) and density functional theory (DFT) calculations of mercaptobenzothiazole (MBT), its anion and its adsorbate on cadmium sulfide show distinct qualitative differences and characteristic peak shift [2]. Interaction of 2-mercaptobenzothiazole, potassium, pyrite and galena has been investigated using surface enhanced Raman Scattering (SERS) Spectroscopy. For metals and minerals, adsorption occurs via charge transfer to form a metal-sulfur bond [3].

Although a number of Ca^{+2} complexes are known in the literature where Ca^{+2} acts as central metal with 1,10-phenanthroline. In order to bring new ligands novelty in coordination complex of Ca (II) and to search new antibacterial agents, Sodium 2-mercaptobenzothiazole has been used as an additional new ligand with 1,10-phenanthroline. The resultant complex 1 is the newly reported complex showing excellent antibacterial activity against Pseudomonas aeruginosa with an inhibition zone of 25mm that is comparable to the Levofloxacin drug. The pinkish crystals of the complex 1 have been characterized through IR and X-ray crystallographic analysis.

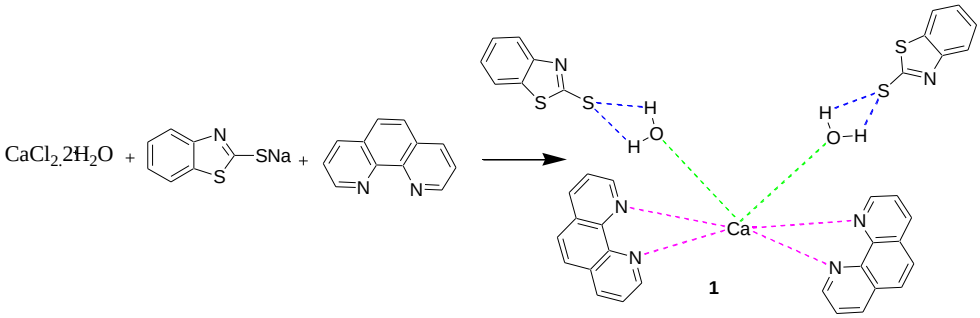

Fig.1 Synthesis of Ca Mercaptobenzothiazole and 1,10-phenanthroline complex

Similar results of mercaptobenzothiazole with barium complex is obtained showing potent antibacterial activity.

A brief talk regarding the synthesis of the above two new complexes will be discussed.

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27. Chromatographic profile and cytotoxic effect of *Piper aduncum* L. essential oil on human tumor cell lines

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[2]*Faculty of Medicine, Universidad Nacional Mayor de San Marcos, Lima, Perú*

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Abstract

Cancer in one of the most common diseases in developing and developed countries. The natural therapy based on medicinal plants is known as a powerful alternative when the conventional medicine shows serious side effects and damage to vital organs.

To evaluate the chromatographic profile by using gas chromatography and the cytotoxic effect of *Piper aduncum* essential oil on human tumor cell lines.

Gas chromatography was assessed in order to determine the terpenes and other compounds present in the essential oil of *Piper aduncum* leaves from Peru. The cytotoxic activity was determined on human tumor cell lines followed as: MCF-7 (breast cancer), H-460 (lung cancer), HT-29 (colon cancer), M-14 (amelanotic melanoma), K-562 (myeloid leukemia) and DU-145 (prostate cancer). Gas chromatography confirmed the presence of cis-γ-Cadinene (17.16%), Germacrene D (17.16%), γ-Elemene (14.48%), Nerolidol (13.41%), α-Carophyllene (7.65%), β-Caryophyllene (6.8%), δ-Cadinene (5.95%), β-Elemene (3.1%) and Linalool (2.44%) in the essential oil of *P. aduncum*. Furthermore, it showed a low cytotoxicity on human tumor cell lines ($IC_{50} > 20$ μg/mL) for DU-145, HT-29, MCF-7 and M-14. Meanwhile, the cytoxicity was high ($IC_{50} < 20$ μg/mL) for H-460 and K-562 tumor cell lines.

Based on our findings, the main phytochemical marker for the essential oil of *P. aduncum* leaves was Germacrene D. According to the cytotoxic indexes, we could conclude that was positive only for lung cancer and leukemia *in vitro*.

Keywords: *Phytochemicals, essential oil, cancer, Piper aduncum, cytotoxicity.*

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28. Synthesis, biological activities of black cumin *(bunium persicum)* based gold and silver nanoparticles and their catalytic applications

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Abstract

Recently scientists utilized plant extract for the synthesis of metallic nanoparticles (Au, Ag, Zn, Fe, Pt, Cu) instead of using complicated physical and chemical methods. Such a biogenic method

for synthesis of metallic nanoparticles is preferred due to ecofriendly, less expensive, does not need hard condition (high temp, pressure and toxic chemicals) and synthesize the nanoparticles which have therapeutic and catalytic applications. Due to the above mentioned benefits, the synthesis of plant based nanoparticles by green method is preferred. Silver and gold nanoparticles have gained much importance due to their catalytic properties by degradation of toxic dyes and biological activities i.e. enzyme inhibition antifungal and antibacterial activities [1].

Our present work is the synthesis, characterization, biological activities and catalytic applications of gold and silver nanoparticles by using the alcoholic seed extract of Black cumin *(Bunium persicum)*. This plant belong to family Apiaceae. Generally this plant grows in Pakistan, Iran, South Africa, Mexico, India, Afghanistan, and South America. Black cumin seeds are used by indigenous as stimulants, carminatives, and are useful in diarrhea and dyspepsia.[2] The extracts of B. persicum have hypoglycemic activity and can prevent diabetes and obesity [3]. The plant possesses some secondary metabolites included flavonoids, saponins di- and triterpenes, saponins, , and a complex mixture of other phenolic compounds, alkaloids, tannins, steroids, and volatile oily compounds [4]. The synthesized gold and silver nanoparticles of *cumin (bunium persicum)*. Alcoholic extract. These nanoparticles were tested for their biological activities (enzyme inhibition, antibacterial, antifungal) and catalytic activities for the degradation of persistant organic pollutants or dyes i.e methyl blue, methyl red rhodamine-B , 2 and 4-nitrophenol.

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29. Appraising Moringa oleifera Lam. via phytochemicals and in vitro biological assays

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Abstract

About three fourth of the world population still depend upon natural product remedies specially obtained from the plants. There is high proportion of plant diversity on the earth which needs screening for the evaluation of important secondary metabolites. Approximately 10,000 to 53,000

herbs/plant species used traditionally worldwide are reported. *Moringa oleifera* tree has been referred as the 'miracle tree' for not only its nutritional value but also pharmacological prospects. The present study utilizes leaf, stem, bark and root of *Moringa oleifera* for extraction optimization and to determine most proficient solvent extract for chosen pharmacological attributes.

Different plant parts (leaf, stem, bark and root) were subjected to successive extraction by using solvents of escalating polarities i.e. n-hexane, ethyl acetate, methanol and distilled water. *In vitro* phytochemicals and biological potential determination was carried out on different extracts obtained during successive solvent extraction. Total phenolics and flavonoids content were determined calorimetrically. Multimode antioxidant (total antioxidant capacity, total reducing power and free radical scavenging) assays were performed by calorimetric method. Antibacterial, antifungal and protein kinase inhibition spectrums of different plant parts extracts were determined by disc diffusion assays. Glucose modulation ability was assessed by-amylase inhibition assay. Brine shrimp lethality assay was used to determine the cytotoxic potential of the extracts.

Among the various solvent extracts, maximum percent extract recovery was obtained from aqueous leaf extract. Total phenolics contents were mostly depicted in stem methanolic extracts, while maximum total flavonoids contents were quantified by aqueous leaf extract. Total antioxidants capacity and reducing power potential were identified upto significant amounts in aqueous leaf extracts and stem methanolic extracts respectivley.Aqueous leaf extract showed highest DPPH free radical scavenging activity. Significant antibacterial activity was exhibited by aqueous leaf extract against *Pseudomonas aeruginosa*, *E. coli* and *Klebsiella pneumonia.* Maximum zone of inhibition against *Mucor* was shown by stem methanolic extract. Medium polarity ethyl acetate stem extract depicted most potent protein kinase inhibition activity against *streptomyces* 85E strain. A noteworthy α-amylase inhibition was revealed by leaf n-hexane extract. Cytotoxic activity against brine shrimp categorized non polar n-hexane leaf extract as the most potent when compared to stem, bark and root extracts.

From the current study, it was concluded, that extraction efficiency and biological activities strongly rely upon the nature of extraction solvent polarity, due to diverse compounds of varied chemical characteristics. By using bioassay guided isolation technique, novel chemical entities can be isolated from *Moringa oleifera*.

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30. Saccharification of sweet potato peel: An alternative and sustainable source for the production of α-1, 4-glucosidase from *Bacillus licheniformis* KIBGE-I

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Abstract

The biodegradable agro-industrial wastes are mostly considered as potential sustainable source for the production of various value-added products from microbial species. Due to easy availability and economical profitability, agro-industrial wastes are preferred for large-scale production of enzymes and also to improve microbial cell growth. The hydrolytic enzymes can selectively hydrolyze the internal linkages of complex carbohydrates to release glucose moieties which can be further utilized in different industrial bioprocess. In the current study, sweet potato peel (*Ipomoea batatas*) was observed as the most favorable substrate for the maximum synthesis of α-1, 4-glucosidase among various agro-industrial wastes. *Bacillus licheniformis* KIBGE-IB4 produced maximum quantity of α-1, 4-glucosidase when growth medium was supplemented with 1% substrate. It was evident from the results that bacterial isolate secreted high titer of α-1,4-glucosidase in the presence of peptone, yeast extract and meat extract with optimum concentration of 0.4%, 0.1% and 0.4% respectively. *Bacillus licheniformis* KIBGE-IB4 revealed maximum enzyme productivity at 40°C and pH-7.0 after 48 hours of fermentation period. An improved and cost effective growth medium design resulted 570.63±28.53 U mg^{-1} of α-1,4-glucosidase from *B. licheniformis* KIBGE-IB4. This enzyme can be used to fulfill the accelerating demand of food and pharmaceutical industries. Further purification and immobilization of this enzyme can also enhance its utility for various bioprocesses.

Keywords: Saccharification, Sweet potato peel, Agro-industrial waste, α-1,4-glucosidase, Production, Optimization

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31. *In vivo* analgesic, gastrointestinal tract (GIT) motility, and anti-termite activities of extract of *Sarcococca saligna* fruits

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Abstract

The current study deals with the evaluation of the alcoholic extract of *Sarcococca saligna* fruits for acute toxicity, analgesic, GIT motility modulation, and anti-termite properties. The extract was evaluated for analgesic activity using acetic acid-induced writhing model while charcoal meal model was adopted for GIT motility estimation in mice. The fruit extract exhibited significant analgesic and GIT motility potential at 700, 1000 mg/kg i.p. in comparison to standard drug (Diclofenac sodium). The extract also showed good anti- termite activity. The extract was also evaluated for toxicological effects which showed that the fruit extract is safe for the consumption of mice at 1000 mg/kg i.p.

Key words: *Sarcococca saligna, extract,* analgesic, gastrointestinal tract (GIT, anti-termite

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Association of XPD Lys751Gln gene polymorphism with susceptibility and clinical outcome of colorectal cancer in Pakistani population: a case-control pharmacogenetic study

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Abstract

XPD Lys751Gln polymorphism may modulate inter-individual variation in repair capacity of DNA, which may enhance a person's susceptibility to develop colorectal cancer (CRC) .To date, XPD Lys751Gln polymorphism has emerged as a molecular marker for both CRC risk and for prognosis prediction in CRC patients. The analysis of XPD Lys751Gln polymorphism may provide important information for identifying high-risk individuals and for selecting the most appropriate treatment for poor prognostic CRC patients. We sought to investigate the association between XPD Lys751Gln polymorphism and the risk of CRC in Pakistani population. In this case-control study a total of 300 study subjects, including 150 CRC cases and 150 controls, were genotyped for XPD Lys751Gln using PCR-RFLP methods. In addition to overall risk assessment, genotyping results were also investigated with respect to the lifestyle risk factors as well as in relation to clinicopathological characteristics. We also analyzed the association of XPD Lys751Gln variants with the occurrence of severe toxicity in Pakistani CRC patients treated with oxaliplatin-based chemotherapy. The overall correlation between the XPD Lys751Gln genetic variation and the CRC risk was observed to be significant with both the homozygous variant genotype Gln/Gln as well as heterozygous genotype Lys/Gln being associated with the increased risk of CRC (OR = 3.599; 95%CI=1.76-7.34; P =0.004 and OR=1.688; 95%CI=1.007-2.827; P =0.046) respectively. Additional stratified analyses revealed that XPD Lys751Gln variants remarkably increased risk of CRC in males and younger individuals (≤ 50 years). Naswar users with variant genotypes of XPD Lys751Gln polymorphism had an 8.09-fold higher risk (OR=8.09; 95% CI=2.44-26.8; P=0.0006) to develop CRC. Similarly, high intake of red meat in association with the XPD Lys751Gln polymorphism was found to significantly influence the risk of CRC in Pakistani population (OR=2.66; 95% CI=1.32-5.38; P=0.0060). The CRC patients carrying homozygous variant genotype of XPD Lys751Gln polymorphisms were found to have larger tumor size (> 5 cm) (P=0.005), advanced tumor stages (P< 0.0001), T3-T4 tumor invasion (P=0.005), lymph node metastasis (P=0.003), regional recurrence (P=< 0.0001) and distant metastasis (P=0.001). Thus, XPD Lys751Gln variants seem to be related with more aggressive form of CRC. CRC patients with homozygous variant genotype of XPD Lys751Gln had 11.34-fold (OR=11.34; 95%CI=4.11-31.351; P =0.0001) and 13.11-fold (OR = 13.11; 95%CI: 4.82-35.69; P =0.0001) increased risk of severe grade 3-4 hematological and non-hematologic toxicity,

respectively. Our findings suggest that the relationship between the XPD Lys751Gln variants and lifestyle factors modulates the risk for CRC in Pakistani population and may be prognostic factors in CRC patients.

Keywords: Colorectal cancer, PCR-RFLP, XPD Lys751Gln polymorphism, lifestyle factors, clinicopathological characteristics, Pakistani population.

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33. Mechanistic approach of *Sphaeranthus indicus* in the treatment of Benign Prostate Hypertrophy

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Abstract

Sphaeranthus indicus Linn. (Asteraceae) commonly used as traditional medicine for various ailments including GIT and urinary problems in various herbal formulas. The present study was aimed to explore the pharmacological potentials of *S. indicus*, according to its importance in Benign prostate hypertrophy, and its possible mechanism of action. The crude extract of the plant was screened for their pharmacological agonistic/antagonistic effects on various receptors present on different tissues to find out its role in benign prostate hypertrophy using Powerlab (AD-Instrument-26T, Australia). The plant extract successfully proved to have significant alpha-1 blocking potentials. i.e. relaxed the circular muscles of intestine near to cardiac sphincter, with IC_{50} value 5.31 (4.78-5.84) confirmed from various mechanistic approaches on various tissues. It is therefore conculded from the current study that the plant extract may be used for the treatment of benign prostate hypertropy preferably to that of alpha-1 blockers which might have less side effects and potent activity due to natural origin.

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34. Antibacterial efficacy of crude extracts of endophtic aspergilli under different culture conditions

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Abstract

The metabolites of various endophytic fungi have been proved a successful tool to control many pathogenic bacteria without any harmful effect. The present study was planned to evaluate the efficacy of three endophytic *Aspergilli* that were isolated from local medicinal plants. The endophytic *Aspergillus terrus, Aspergillus flavus* and *Aspergillus niger* were evaluated for their antimicrobial metabolites production under different growth media amended with carbon and nitrogen sources. Ethyl acetate was used to obtain crude extracts of these fungal entophytes. The clinical strains of *Escherichia coli*, *Staphylococcus aureus, Salmonella typhi* and *Enterococcus faecalis* were used to check the inhibitory effect of crude extracts of fungal species. It was found that *Aspergillus flavus* showed maximum percentage of inhibition against all selected bacteria. *The Aspergillus niger* showed maximum inhibition with maltose and peptone against all bacterial strains. The efficacy of the crude extracts of endophytic fungal strains was greatly affected by different carbon and nitrogen sources. The present study revealed that the endophytic fungi have a number of bioactive compounds that can be isolated and purify for the production of new antibiotics.

Keywords: *Endophytic fungi, Aspergilli, Escherichia coli, Staphylococcus aureus, Salmonella typhi*

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35. *In vitro* enhancing efficacy of chemo-drugs through photochemical internalization for cancer treatment

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Abstract

Combination therapies aim to reduce treatment-associated morbidity while retaining high efficacy. In oncology to improve the patient's quality of life, treatment duration also desirable. Therapies resulting in rapid, tumor bulk removal while sparing adjacent normal tissue are preferable or even required. Photodynamic therapy (PDT) is commonly applied in a single treatment, so its efficacy can be limited particularly for rapidly bleached photosensitizer or in the presence of low photon

densities. Here the efficacy of combination therapy comprised of doxorubicin (DOX) or methotrexate (MTX) with Photosens mediated PDT was determined in three cell lines (Hela, MCF-7, and RG2) for multiple incubation sequences for the chemo and PDT drugs, *in vitro*. Analysis of the results demonstrated that highest synergistic effects of the combination therapy are obtained when DOX or MTX-mediated chemotherapy preceded PDT light activation by 24 hrs. The reverse does not generate significant additional cell kill. The shorter time separation between either therapy did not produce significant synergistic effects. In combination with Photosens mediated PDT; MTX is marginally more cytotoxic than DOX. While MTX and DOX exposure prior to Photosens incubation influenced the photosensitizer's localization to the mitochondria this appears insufficient to be considered as cause for the observed synergistic effects of the combination therapy.

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36. Design, synthesis and bioevaluation of tricyclic fused ring system as dual binding site acetylcholinesterase inhibitors

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Abstract

Alzheimer disease is characterized by the acetylcholine (ACh)-mediated abrupt blockade of cortical cholinergic neuron population and the deposition of extracellular amyloid-β (Aβ) and tau proteins into plaques and neurofibrillary tangles. The inactivation of ACh is a unique process carried out by two cholinesterases; acetylcholinesterase (AChE) and butyrylcholinesterase (BChE), resulting in release of choline and acetate. Thus, the inhibition of both cholinesterases (acetylcholinesterase AChE and butyrylcholinesterase BChE) is found to be the only effective therapeutic approach for AD up till now. Due to recently discovered non-classical acetylcholinesterase (AChE) function, dual binding-site AChE inhibitors have acquired a paramount attention of drug designing researchers. The unique structural arrangements of AChE peripheral anionic site (PAS) and catalytic site (CAS) joined by a narrow gorge, prompted us to

design the inhibitors that can interact with dual binding sites of AChE. We have designed different *mono-*, *bi-* and *tri*-cyclic ring systems with diverse tethers length and sizes. The synthesized compounds showed excellent in vitro acetylcholinesterase inhibition activity in nanomolar range. We identified a six-carbon tether heterodimer of desloratadine and indanedione based tricyclic dihydropyrimidine (**4c**) as potent and selective inhibitor of eeAChE with IC_{50} value of 0.09± 0.003 μM and 1.04± 0.08 μM (for *eq*BChE) with selectivity index of 11.1. Binding pose analysis of potent inhibitors suggest that tricyclic ring is well accommodated into the AChE active site through hydrophobic interactions with Trp84 and Trp279.

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37. Design, synthesis and bioevaluation of tricyclic fused ring system as dual binding site acetylcholinesterase inhibitors

Umer Rashid[1*], Abdul Sadiq[2]

[1]*Department of Chemistry, COMSATS University Islamabad, Abbottabad Campus 22060, Pakistan*

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Abstract

Alzheimer disease is characterized by the acetylcholine (ACh)-mediated abrupt blockade of cortical cholinergic neuron population and the deposition of extracellular amyloid-β (Aβ) and tau proteins into plaques and neurofibrillary tangles. The inactivation of ACh is a unique process carried out by two cholinesterases; acetylcholinesterase (AChE) and butyrylcholinesterase (BChE), resulting in release of choline and acetate. Thus, the inhibition of both cholinesterases (acetylcholinesterase AChE and butyrylcholinesterase BChE) is found to be the only effective therapeutic approach for AD up till now. Due to recently discovered non-classical acetylcholinesterase (AChE) function, dual binding-site AChE inhibitors have acquired a paramount attention of drug designing researchers. The unique structural arrangements of AChE peripheral anionic site (PAS) and catalytic site (CAS) joined by a narrow gorge, prompted us to design the inhibitors that can interact with dual binding sites of AChE. We have designed different *mono-*, *bi-* and *tri*-cyclic ring systems with diverse tethers length and sizes. The synthesized compounds showed excellent in vitro acetylcholinesterase inhibition activity in nanomolar range.

We identified a six-carbon tether heterodimer of desloratadine and indanedione based tricyclic dihydropyrimidine (**4c**) as potent and selective inhibitor of eeAChE with IC_{50} value of 0.09± 0.003 µM and 1.04± 0.08 µM (for *eq*BChE) with selectivity index of 11.1. Binding pose analysis of potent inhibitors suggest that tricyclic ring is well accommodated into the AChE active site through hydrophobic interactions with Trp84 and Trp279.

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38. Chemical features and biological activities of Sauromatum venosum.

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[1]*Department of Chemistry, Mohi-ud-Din Islamic University Nerian Sharif, Azad Jammu and Kashmir*

[2]*Department of Chemistry, Faculty of Sciences, University of Kotli Azad Jammu and Kashmir.*

Abstract

Medicinal plants have played vital role in the life of human; they are the main sources to treat number of diseases. Sauromatum venosum an ornamental plant (Araceae family) was fractioned into n-hexane, ethyl acetate and methanol fraction by soxhlet apparatus. All fractions were screened for the indication of secondary metabolites. Components including terpenoids, coumarins, saponins, alkaloids, emodins, and phenolics compounds were determined. The DPPH free radical scavenging activity, ABTS cation radical decolorization activity, metal chelating activity, cupric reducing antioxidant capacity, β-carotene antioxidant activity, Acetylcholinesterase (AchE), butyrylcholinesterase (BchE) inhibition activity and enzyme inhibition tyrosinase activity were performed for the n-hexane, ethyl acetate and methanol fraction of *Sauromatum venosum* with different concentration 100 mg/L, 200 mg/L, 400 mg/L, and 800 mg/L. IC_{50} value of methanol fraction and ethyl acetate fraction of metal chelating was determined to be best inhibitory concentration 18.49 ±1.24 µg/mL and 26.68 ± 0.95 µg/mL from all fractions followed by methanol fraction of ABTS and β-carotene 48.67± 1.31 µg/mL and 53.54 ± 0.97 µg/mL respectively.

The phenolics contents of the methanolic fraction of Sauromatum venosum were also determined by using LC-MS/MS analysis. The amount of malic acid, p- coumaric acid, hesperidine and tr-caeffic acid were indicated to be 6079.47µg/g, 11.54 µg/g, 5.93 µg/g and 3.4µg/g respectively.

Keywords: *Sauromatum venosum,* Phytochemical screening, Biological activities, Phenolic contents, LC-MS/MS analysis,

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39. Co-targeting of Tiam1/Rac1 and Notch ameliorates chemoresistance against doxorubicin in a biomimetic 3D a natural polymer-based hydrogel lymphoma model

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Abstract

Malignant lymphoma (ML), a heterogeneous disease with highly variable clinical course and prognosis, which accounts for about 10 percent of human neoplasm. Malignancy includes growth, metastasis, cell-to-matrix and cell-to-cell interaction, intracellular signaling, and resistance to chemotherapy and radiation therapy. The objective of this study was to elucidate the potential involvement of three-dimensional spatial environment in lymphoma cells to malignancy and resistance to chemotherapy. We found that three-dimensional environment enhances the activation various cellular activities associated with drug resistance malignancy in this study. Signals from the tumor microenvironment promote survival, and proliferation of lymphoma cells. We found upregulation of notch signaling molecule and cancer stem cells. Tiam-1 / and Rac-1 expression was induced in the malignant lymphoma cells in line with increased MMPs and VEGFs level in 3D microenvironment. EL4 Lymphoma cells cultured in the 3D hydrogel matrix exhibited a difference in cell proliferation activity compared to those in the 2D monolayer culture both with and without treatment of anticancer agents like doxorubicin and resveratrol at their higher doses. Furthermore, treatment of EL4 T and A20 B lymphoma cells with NSC-23766, a specific inhibitor of Tiam-1/Rac-1 reduced their proliferation antagonizing the chemoresistance of lymphoma cells cultured in hydrogel toward doxorubicin.

Collectively, that spatial organization strongly influences the response to malignancy of EL4 cells, and that Tiam-1/Rac-1 inhibition could be of clinical use by selectively interfering with resistant lymphoma cells proliferation and chemoresistance.

Keywords: Hydrogel, spheroid, ovarian cancer, 3D cell culture

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40. Anti-diabetic studies of *Taraxacum officinale*

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Abstract

Medicinal plants have played vital role in the life of humans, especially for their betterment and to sustain life. Natural products isolated from plants, to be considered as main sources for treating number of diseases. Taraxacum officinale belong to the family Asteraceae and its subfamily is Cichorieae, its tribe is Lactuceae. The entire parts of Taraxacum officinale locally known as "Hund" were collected from village Pirkot Tehsil Hajira District Poonch, in April 2017.

Antidiabetic activity of T. officinale root, leaves, and flower fractions (n-hexane, ethanol, and water) was evaluated in diabetic mice. Fifty mice were distributed in 10 separate cages each having 5 mice and designated according to following arrangement. G-I considered as negative control, G-II considered as positive control or diabetic control. G-III considered as antidiabetic control and G –IV to G-X were considered as treatment groups.

It was observed that all parts of the Taraxacum officinale showed activity against diabetes. These fractions decreased blood glucose level after administration of the extracts (n-hexane, ethanol, and water) of roots, leaves and flowers. But n-hexane fraction of flowers, water fraction of leaves and water fraction of roots showed remarkable antidiabetic activity.

Keywords: Anti-diabetic, Taraxacum officinale, Mice and Blood glucose level

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41. Biological activities of Portulaca *oleracea* L used in traditional medicine in Rawalakot AJK

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[2]*Department of Botany, University of Malakand, Chakdara, Pakistan*

Abstract

The current study was focused to evaluate the phytochemical, antimicrobial and cytotoxic activities of ethanolic extract of *Portulaca oleracea* L. The extraction of ethanol in *Portulaca oleracea* plant has flavonoids, alkaloids, saponins and tannins. These activities were confirmed by *in vitro* cytotoxic studies in which *Portulaca oleracea* showed the maximum control over HeLa cell lines with the IC_{50} value of 40 µg/ml. Ethanolic extracts were used against infectious pathogenic bacteria i.e *Bacillus atropeous, Bacillus subtlilis, Staphylococcus aereus* (Gram positive bacteria) and *Salmonella typhi, Pseudomonas aeruginosa, Escherichia coli* and *Klebsela pneumonia* (Gram negative bacteria). In vitro antimicrobial activity disc diffusion method was used. The activity was expressed as mg/µl. Ethanolic extracts of *Portulaca oleracea* was found active against all microbes. With phytochemical activities, the toxicity, pharmacological activities and establishing safety was required for the further studies. This research supports the uses of the selected medicinal plant against bacterial infection.

Keywords: Phytochemical; In vitro Antimicrobial activity and cytotoxicity; *Portulaca oleracea*

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42. Antidiarrheal potential in the aerial and root parts extracts of *Verbena officinalis*

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[2]*Department of Chemistry, University of Swabi, Pakistan*

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Abstract

Diarrhoea is the body condition which results in watery stool or a frequent bowl movement resulting in dehydration of the body. The main cause is an intestinal infection due to a virus, bacteria or a parasite. According to WHO every year there are about 2.5 billion cases of diarrhoea occurs worldwide. Each year 1.9 million of children especially from developing countries die due to diarrhoea. *Verbena officinalis* has a vast history of various pharmacological effects including; anti-inflammatory [1], antibacterial, neuroprotective, analgesic, antioxidant, antifungal, ameliorative, anti-tumor [2], antiradical [3], wound healing, anti-trypanosoma cruzi, antinociceptive, anti-rhinosinusitis, anti-skin infection, anti-depressant and sleep promoting [4]. This study was conducted to test the effectiveness of extracts of root and aerial parts of *Verbena officinalis* against diarrhoea.

Magnesium sulphate induced diarrheal agent was injected in healthy pigeons following the method of Bhattacharya and Roy, 2010 [5]. ANOVA test followed by Dunnett's test was used to evaluate antidiarrheal activity results. The results revealed that root extract is the best one ($p<0.05$) for antidiarrheal activity. The aerial extract also showed significant result at the dose of 50 mg/kg. According to our literature survey, antidiarrheal activity for *Verbena officinalis* has not been reported so far and this is the first study conducted upon it with significant results.

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43. Evaluation of antiproliferative, antioxidant and anti-inflammatory effects of *Cassia nemophila* flowers (a source of effective anticancer agents)

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Abstract

Cancer is described as uncontrolled differentiation and proliferation of cells, effecting variety of normal body processes. It is multidimensional disease with multiple causes. Medicinal plants are valued for their significant potential of treating number of disorders. *Cassia nemophila* was selected for present study because of long history of genus *Cassia* in field of traditional and modern drug discovery, stipulated with active compounds. The study was planned to explore pharmacological properties of ethanolic and n-hexane extract of *C. nemophila* flowers. The

contribution of both extracts against oxidants was verified using DPPH radical scavenging assay. Anti-inflammatory activities were explored by HRBC membrane stabilization assay. While cytotoxic effects were investigated against viability of Hct115 cell line. The results implied the pharmacological importance of both extracts of *C. nemophila* flowers and its effectiveness against antioxidant, anti-inflammatory and anti-proliferative activities. So, it can be explored further as an anticancer drug.

Keywords: *Cassia nemophila*, anticancer, antioxidant, anti-inflammatory, in-vitro assays

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44. Green way synthesis of Iron nanoparticles from *Mentha arvensis* associated with antimicrobial activity against human pathogens

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Abstract

Nanotechnology is emerging as a rapidly growing field with its application in biotechnology. Biosynthesis of metallic iron nanoparticles has now become an alternative to physical and chemical approaches. In the present research, iron nanoparticles were synthesized using *Mentha arvensis* extract. Iron nanoparticles were characterized by UV–visible spectroscopy, X-ray diffraction (XRD), Fourier transform infrared (FT-IR), scanning electronic microscopy (SEM). The iron nanoparticles formation was confirmed by UV–visible spectroscopy through color conversion while the crystalline nature of nanoparticles was confirmed from the XRD pattern. Our results proved that these iron nanoparticles were effective against human pathogenic bacterial species such as *Staphylococcus aureus*, *Bacillus subtilis*, *Pseudomonas aeruginosa*, *E. coli*, and *Salmonella typi*. These nanoparticle could be utilized in future for the treatment of such pathogens.

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45. Synthesis and antibacterial evaluation of pyrimidine-based azo compounds

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Abstract: Compounds containing –N=N- are called azo compounds, which are generally synthesized by azo coupling reaction. In the present study, diazotized sulfanilamides/aromatic amines were coupled with pyrimidine derivative, 2-amino-4,6-dihydroxypyrimidine. The yield of synthesized compounds was about 20 % to 40 %. The products formed were identified by FTIR and ^{1}H NMR spectroscopic techniques. The antibacterial activity of the synthesized compounds were evaluated by disk diffusion method against two Gram positive (*Bacillus cereus*, *Staphylococcus aureus*) and two Gram negative (*Escherishia coli Pseudomonas aeuruginosa*) bacterial strains. The zone of inhibition for each compound was measured and compared with Gentamicin, a commercial antibiotic drug. No significant biological activity was shown by any of the tested compounds which may be due to their poor solubility in the common organic solvents.

Keywords: azo compound, pyrimidine, sulfanilamide, antibacterial activity

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46. Anti-inflammatory and antioxidant activities of a new caffeate ester from the stem bark of *Cassia artemisioides* (Gaudich. Ex. DC) Randell

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[1]*Department of Chemistry, Abdul Wali Khan University, Mardan, Pakistan;*

[2]*Phytopharmaceutical & Neutraceutical Research Lab, Institute of Chemical Sciences, University of Peshawar, Pakistan*

Abstract

The phytochemical investigation of the stem bark of *Cassia artemisioides* leads to the isolation of one new caffeates along with two known caffiates, *β*-Sitosterol-3-*O*-*β*-D-glucopyranoside and tricontyl palmitate. One of the caffeate is reported as natural product for the first time and the other reported caffeate is reported only in mixture form and we report it in pure form and publishing all the spectral data. The structures of the new compounds were elucidated on the basis of UV, IR, ^{1}H NMR, ^{13}C NMR, HMQC, COSY and HMBC techniques. The isolated compounds were also evaluated for anti-inflammatory and antioxidant activities using Carrageenan-induced oedema and

DPPH radical scavenging assay respectively. All the caffeats showed good anti-inflammatory and antioxidant activities.

Keywords; *Cassia artemisioides* L., caffeaets, anti-inflammatory, antioxidants.

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47. Chemical features and biological activities of Sauromatum venosum.

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2Department of Chemistry, Faculty of Sciences, University of Kotli Azad Jammu and Kashmir

Abstract

Medicinal plants have played vital role in the life of human; they are the main sources to treat number of diseases. Sauromatum venosum an ornamental plant (Araceae family) was fractioned into n-hexane, ethyl acetate and methanol fraction by soxhlet apparatus. All fractions were screened for the indication of secondary metabolites. Components including terpenoids, coumarins, saponins, alkaloids, emodins, and phenolics compounds were determined. The DPPH free radical scavenging activity, ABTS cation radical decolorization activity, metal chelating activity, cupric reducing antioxidant capacity, β-carotene antioxidant activity, Acetylcholinesterase (AchE), butyrylcholinesterase (BchE) inhibition activity and enzyme inhibition tyrosinase activity were performed for the n-hexane, ethyl acetate and methanol fraction of *Sauromatum venosum* with different concentration 100 mg/L, 200 mg/L, 400 mg/L, and 800 mg/L. IC_{50} value of methanol fraction and ethyl acetate fraction of metal chelating was determined to be best inhibitory concentration 18.49 ±1.24 µg/mL and 26.68 ± 0.95 µg/mL from all fractions followed by methanol fraction of ABTS and β-carotene 48.67± 1.31 µg/mL and 53.54 ± 0.97 µg/mL respectively.

The phenolics contents of the methanolic fraction of Sauromatum venosum were also determined by using LC-MS/MS analysis. The amount of malic acid, p- coumaric acid, hesperidine and tr-caeffic acid were indicated to be 6079.47µg/g, 11.54 µg/g, 5.93 µg/g and 3.4µg/g respectively.

Keywords: *Sauromatum venosum*, Phytochemical screening, Biological activities, Phenolic contents, LC-MS/MS analysis

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48. Chitosan built nanohydrogel as smart micellar drug carriers

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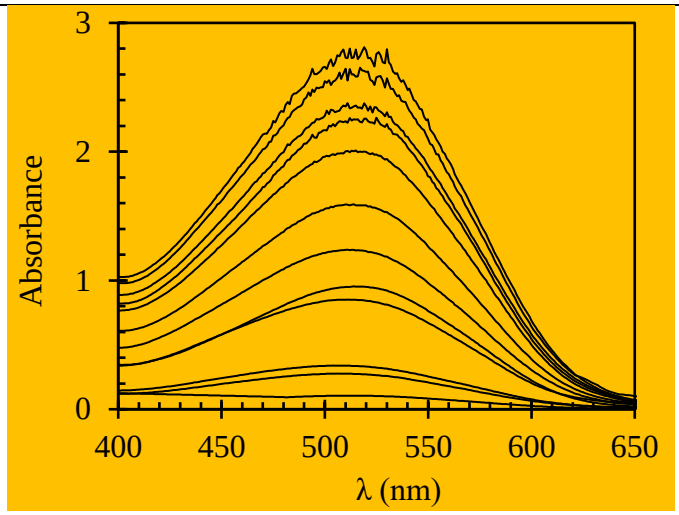
Description	
Nanohydrogel based micellar drug carriers aim to interact physically with the drug and deliver it to the targeted intracellular tumor is revealed. The micellization, thermokinetic, phase-transition, physicochemical and electrokinetic phenomena refleced the art of micelles-based tumor-targeted drug delivery at physiological conditions.	

Abstract

Addressing the therapeutic strategies, to deliver hydrophobic drugs to the targeted intra-cellular tumor, chitosan-built hydrogel as micellar drug carrier were blended via free radical copolymerization and were tested against Fluorescein as a hydrophobic model drug. The critical micelle concentration of hydrogel nanoparticles (CMC≈ 2.80 mg.L^{-1}), Zeta potential (z.p≈ 30 mV) and lower critical solution temperature (LCST≈ 38.60 ^{o}C) were explored in aqueous solution by

using dynamic light scattering (DLS) and differential scanning calorimetry (DSC) respectively. The self-assembled blank and Flourescein loaded micelle were spherical in shape with an average Hydrodynamic diameter $D_{h,av}$≈ 50-100 nm, as probed by DLS and SEM, respectively. The in vitro drug loading (78.31%) and drug release (71.04%) profiles in the system exhibited both pH- and temperature dependant swelling, where the release rate was significantly enhanced by increasing the pH from 4.0 - 6.85, due to swelling caused by protonation of the amine groups in chitosan per segment. The system presented a higher degree of swelling in the pH range of 6.05 - 6.85, Urea (15.08mg.L^{-1}) and ionic strength (Nacl ≈ 0.05 M) at 37 ºC (physiological temperature). The results demonstrated the potential of smart-micellar drug carriers to deliver and addresses the bioavailability of a hydrophobic drug to the targeted intracellular tumor with auto on/off responses.

Keywords: Hydrogel; Micelle; LCST; Physicochemical; Thermokinetics; Micellar drug carrier;

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49. Discovery of a novel flavonol having long chain fatty acid from *Dodonaea viscosa* which inhibits Human neutrophil elastase (HNE)

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Abstract

A series of flavonoids were isolated from *Dodonaea viscosa* and tested for inhibition of human neutrophil elastase (HNE), an enzyme involved in several inflammatory disorders. Isolated compounds were identified as a novel flavonol (**1**) along with eight known flavonoids (**2**–**9**). The novel flavonol, visconata (**1**) has a very rare skeleton having odd numbered long chain (C19) fatty acid, which was completely identified by extensive mass fragmentation and 2D NMR analysis as (*Z*)-4-(5-(5,7-dihydroxy-3,6-dimethoxy-4-oxo-4H-chromen-2-yl)-2-hydroxyphenyl)-2-methylbutyl-18,19-dihydroxy-nonadec-10-enoate. All compounds (**1**–**9**) effectively inhibited HNE in dose dependent manner with IC_{50}s ranging between 2.4 and 150 µM. The novel compound, visconata (**1**) emerged to be the most potent one with 2.4 µM of IC_{50}. Furthermore, detailed kinetic study was performed in which compound (**1**) was observed to be reversible, noncompetitive

inhibitor of HNE having *K*i = 1.8 µM, whereas rest of flavonoids (**2**–**9**) displayed mixed type inhibition.

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50. Synthesis characterization and biological evaluation of some metal complexes of sulfonamides derived from cephadroxyl, cephalexin, cephradine

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Abstract

The present work focuses on preparation of metal complexes of sulfonamides synthesized by reacting some cephalosporins containing amine (–NH_2) moiety in their chemical structures with *N*-acetylsulfanilyl chloride. For the synthesis of sulfonamides a facile one-pot environmentally benign literature method was employed. Product formation was monitored using thin layer chromatography. The resulting sulfonamides and metal complexes were subjected to structural characterization by different instrumental techniques including FT-IR Spectroscopy and TGA-DSC. Antimicrobial activities in terms of Minimum Inhibitory Concentration (MIC) of the newly formed molecules were evaluated against *Escherichia coli* and *Staphylococcus arueus*.

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51. Metabolites profiling of *Prunus dulcis* nuts and exploring their potential against diabetes

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Abstract

Phytopharmaceutical industries require quality control of raw material as well as finished products to fulfill the legal guidelines, to achieve the satisfaction of consumers and to get the position in the global market. Quality control of phytopharmaceuticals relies on the determination of chemical constituents qualitatively and quantitatively as well as pharmacological evaluation of the raw materials employed for the production of finished products. It is a challenging task as the herbs as a whole or their parts, contain hundreds of biologically active chemicals which work together in term of their synergistic relationship to produce the pharmacological effect. This study relates to the metabolites profiling in *Prunus dulcis* (commonly called Almond) nuts (defatted) alcoholic

extract which was achieved through chromatographic separation using reversed phase HPLC from AB Sciex followed by their identification through mass spectrometry employing 4000 Q-TRAP mass spectrometer. Compounds were authenticated by comparing their fragmentation pattern with the already published data. These experiments resulted in the identification of different compounds majorly of polyphenolic compounds i.e. various flavonoids aglycon and their glycosides, catechin and its polymers etc.

Further, alcoholic extracts and their fractions in n-hexane, chloroform, ethylacetate, n-butanol and water, were evaluated for their activities against the diabetes using the PTP1B inhibition assay procedure in order to gain best product for the treatment of this metabolic disorder. Among these samples, alcoholic extract showed strong antidiabetic (PTP1B inhibition) activity while the rest of the samples showed activity in the decreasing order as: hexane extract > ethyl acetate extract > chloroform extract > n-butanol extract. The study lends the importance of alcoholic extract of almond nuts (defatted) over their fractions to be used in antidiabetic formulations. Study from the published literature shows that no such detailed study of the whole nuts has been presented as the main focus has been on the brown skin of the almond nuts.

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52. *Echinacea purpurea* (cone flower): an immunomodulatory agent in Newcastle disease infected broiler chicks

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Abstract

Vaccination nowadays is the utmost reliable approach to reduce the fatality rate due to Newcastle disease virus (NDV). In spite of vaccination and biosecurity, Newcastle disease (ND) is still prevalent globally in poultry. Various drugs shield the poultry birds for short period of time, while immune modulators work for longer duration against infection. The present study was planned to examine the immunomodulatory effects of *Echinacea purpurea (E.P)* dried extracts against NDV infection. For the present trial, a flock of 120 day old broiler chicks were randomly distributed into 4 equal groups A, B, C and D with 30 birds per replicate. Experimental shed was properly cleaned and disinfected with 4% formalin solution a day before the arrival of chicks. Fresh water was

available for chicks *ad libitum*. All chicks were vaccinated against infectious bursal disease (IBD), NDV and hydropericardium syndrome (HPS) according to routine schedule. Group A served as control negative received no treatment and *E.purpurea* treatment was offered @2.5g/kg to group C and D in feed till 40th day of age. At day 19th of trial, the chicks of control positive group B were challenged with velogenic NDV strain. Anticoagulant added blood was collected at day 26th, 33rd and 39th day post infection (DPI) for haemagglutination (HA) and haemaagglutination inhibition (HI) assay against NDV and sheep red blood cells (SRBCs). The Duncan multiple range test results concluded that body weight was significantly higher in group C from 3rd week onward as compared to control negative group. Geometric mean titers $\log_2$ against NDV was higher in control positive group B & treatment group D as compared to control groups at 26th, 33rd and 39th DPI. Cellular immunity and phagocytic index; lymphoproliferative response (LPR) against avian tuberculin was higher significantly at 24th and 48th hour post inoculation in group D while carbon clearance assay (CCA) was higher in treatment group C at 0,3rd & 15th minute. In conclusion, the present study revealed that use of *Echinacea purpurea* @2.5g/kg in feed enhanced the overall performance and immune response of broiler birds against NDV.

Keywords: *Echinacea purpurea*, Newcastle disease, Immunity, Broiler chicks

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53. Mechanochemical synthesis characterization of cu (ii) amino acids complexes

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Abstract

In this work the synthesis of copper (II) amino acids complexes by use of mechanochemical method has been reported. The complexes were synthesized by grinding vigorously the appropriate quantities of metal salt and amino acids in the solid state in pestle and mortar. Absolutely no solvent was used in these syntheses.

The complexes were characterized by elemental analysis, FT-IR spectra, electronic absorption spectra, thermal analysis and powder x-ray diffraction. The synthesized complexes were found to be ML2 type with square-planar geometry.

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54. Isolation of noval bioactive polysacharides from aqueous plant extract of *dodonaea viscosa* and their utilization for the synthesis of silver nano particals

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Abstract

Natural Polysaccharide are important class of carbohydrates. These macromolecules have wide range of applications in different areas such as food and food industry , madicines, papers and wood products etc. During last few decayed attention has been focussed on the extraction, isolation and utillization of bioactive compounds of plant origins. Efforts are being made to increase the efficacy of these noval bioactive compunds against different diseases and deaseses cuses microorganisms. During present study we selected the *Dodonaea Viscosa* plant and its aqueous extract was used to isolate the noval bioactive polysacharides. Earlier it was reported that this plant showed biological activities against stomic pain, ulcer and piles. This plant also found to have anti-malarial, anti-inflammatory, anti fugal, anti-diabetic, anesthetic and hepatoprotective activities in human. The aim of present stduy was to extract, isolate bioactive polysacharides form aqueous plant extract of *Dodonaea Viscosa* and their utillization in the synthesis of silver nano particals to enhance their antimicrobial activities. The aquous extract and synthesized Silver nano particals were characterized and their antimicrobial and anticancer activities were studied.

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55. Repurposing and mechanistic insight of drugs with serum albumin

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Abstract

Drug repurposing is a promising field in drug discovery that identifies new therapeutic opportunities for existing drugs. In order to circumvent some of the most expensive drug discovery processes, companies pursue this strategy to increase their new productivity by reducing the discovery and development timeline. Various data-driven and experimental approaches have been

suggested for the identification of re-purposable drug candidates; however, there are also major technological and regulatory challenges that need to be addressed. Especially, the study of molecular interactions of drug-protein are extremely important from the biological aspect in all living organisms, and therefore such type of investigation hold a tremendous significance in rational drug design and discovery. In the present study, the molecular interactions between paromomycin (PAR) and human serum albumin (HSA) have been studied by different biophysical techniques and validated by in-silico approaches. The results obtained from Ultraviolet–visible spectroscopy (UV) and Fourier transform infrared spectroscopy (FT-IR) demonstrated a remarkable change upon the complexation of PAR with HSA. Circular Dichroism (CD), Dynamic Light Scattering (DLS) and Resonance Rayleigh scattering (RRS) results revealed a significant secondary structure alteration and reduction of hydrodynamic radii upon the conjugation of PAR with HSA. The fluorescence spectroscopy results also apparently revealed the static quenching mechanism. The number of binding sites, binding constants, and Gibbs free energy values were calculated to illustrate the nature of intermolecular interactions. Similarly, the in-silico docking and molecular dynamics simulation clearly explain the theoretical basis of the binding mechanism of PAR with HSA. The experimental and docking approaches suggested that PAR binds to the hydrophobic cavity site I of HSA. Moreover, inclusive outcomes and findings of current scientific input will deliver a valuable platform for the drug designers and inventors to further explore the drugs binding mechanism, pharmacodynamics and pharmacokinetics structures of the designated drugs in order to attain a healthier therapeutic efficacy.

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56. Minocycline alleviates neuroinflammation, neurodegeneration and cognitive impairments to enhance survival and improve behavioral abnormalities in prion infected hamsters

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Abstract

Prion infections of the central nervous system (CNS) are characterized by initial reactive gliosis followed by overt neuronal death. Gliosis is likely to be initially caused by the deposition of misfolded, proteinase K-resistant, isoforms (termed PrP^{Sc}) of the normal cellular prion protein (PrP^{c}) in the brain. Proinflammatory cytokines and chemokines released by PrP^{Sc}-activated glia and stressed neurons as well may contribute directly or indirectly to the disease development by enhancing gliosis and inducing neurotoxicity. Recent studies have illustrated that early neuroinflammation activate the calcineurin nuclear factor of activated T-cells (NFAT) signaling cascade, resulting in nuclear translocation of nuclear factor kappa-b (NF-kB) to promote apoptosis. Hence, useful therapeutic approaches to slow down the course of prion disease development should control early inflammatory responses to suppress NFAT signaling. Here we used a hamster model of prion diseases to test, for the first time, the neuroprotective and NFAT-suppressive effect of a second-generation semisynthetic tetracycline derivative, minocycline, in comparison to a calcineurin inhibitor, FK506, with known NFAT suppressive activity. Our results indicate that prolonged treatment with minocycline, starting from the pre-symptomatic stage of prion disease was more effective than FK506 given either during pre-symptomatic or symptomatic stage of prion disease. Specifically, minocycline treatment reduced the accumulation of PrP^{Sc}, lowered the expression of the astrocytes activation marker GFAP and of the microglial activation marker IBA-1, subsequently reducing the level of pro-inflammatory cytokines interleukin 1 beta (IL-1β) and tumor necrosis factor alpha (TNF-α). We further found that minocycline and FK506 treatment inhibited mitogen-activated protein kinase (MAPK) p38 phosphorylation and NF-kB nuclear translocation in a caspase dependent manner, and enhanced phosphorylated cAMP response element-binding protein (pCREB) and phosphorylated Bcl2-associated death promoter (pBAD) levels to reduce cognitive impairment and apoptosis. Taken together our results indicate that,

minocycline is a better choice for prolonged use in prion diseases and encourage its further clinical development as a possible treatment for this disease.

Keywords: Central Nervous System (CNS); Gliosis; Prion Protein Scrapie (PrP^{Sc}); Nuclear Factor of Activated T-cells (NFAT); Phosphorylated Mitogen-Activated Protein Kinase (MAPK) p38; Nuclear Factor Kappa-b (NF-kB); Phosphorylated cAMP Response Element-Binding protein (pCREB); Phosphorylated Bcl2-Associated Death Promoter (pBAD)

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57. Antimicrobial resistance among aerobic biofilm producing bacteria isolated from chronic wounds in the tertiary care hospitals of Peshawar, Pakistan

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Abstract

Chronic wound infections impose major medical and economic costs on health-care systems, cause significant morbidity, mortality and prolonged hospitalization. The presence of biofilm producing bacteria in these wounds is considered as an important virulence factor that leads to chronic implications including ulceration. The undertaken study aimed to isolate and identify the biofilm aerobic bacterial pathogens from patients with chronic wound infections, and determine their antibiotics resistance profiles.

During this study, swab specimens were collected from patients with chronic wounds at teaching hospitals of Peshawar, Pakistan between May 2013 and June 2014. The isolated aerobic bacterial

pathogens were identified on the basis of standard cultural characteristics and biochemical tests. Antibiotics resistance profiles of biofilm producing bacteria against selected antibiotics were then determined.

Among the chronic wound infections, diabetic foot ulcers were most common 37 (37%), followed by surgical ulcers 27 (27%). Chronic wounds were common in male patients older than 40 years. Among the total 163 isolated bacterial pathogens the most prevalent bacterial species were *Pseudomonas aeruginosa* 44 (27%), *Klebsiella pneumoniae* 26 (16%), *Staphylococcus species* 22 (14%) and *Streptococcus spp.* 21 (13%). The isolation rate of bacterial pathogens was high among patients with diabetic foot ulcers 83 (50.9%). Among bacterial isolates, 108 (66.2%) were observed as biofilm producers while 55 (33.8%) did not form biofilm in our model. The investigated biofilm producing bacterial isolates showed comparatively high resistance against tested antibiotics compared to non-biofilm producing bacterial isolates. The most effective antibiotics were amikacine and cefepime against all isolates.

Increased multidrug resistance in biofilm producing bacteria associated with chronic wounds was observed in this study. Judicious use of antibiotics is needed to control the wound associated biofilm associated pathogens.

Keywords; chronic wound infections, bacterial profile, antibiotic resistance, biofilm, Pakistan

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58. In silico identification and evaluation of leads for the simultaneous inhibition of protease and helicase activities of hcv ns3/4a protease using complex based pharmacophore mapping and virtual screening

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Abstract

Hepatitis C virus (HCV) infection is an alarming and growing threat to public health. The present treatment gives limited efficacy and is poorly tolerated, recommending the urgent medical demand for novel therapeutics. NS3/4A protease is a significant emerging target for the treatment of HCV

infection. This work reports the complex-based pharmacophore modeling to find out the important pharmacophoric features essential for the inhibition of both protease and helicase activity of NS3/4A protein of HCV. A seven featured pharmacophore model of HCV NS3/4A protease was developed from the crystal structure of NS3/4A protease in complex with a macrocyclic inhibitor interacting with both protease and helicase sites residues via MOE pharmacophore constructing tool. It consists of four hydrogen bond acceptors (Acc), one hydrophobic (Hyd), one for lone pair or active hydrogen (Atom L) and a heavy atom feature (Atom Q). The generated pharmacophore model was validated by a test database of seventy known inhibitors containing 55 active and 15 inactive/least active compounds. The validated pharmacophore model was used to virtually screen the ChemBridge database. As a result of screening 1009 hits were retrieved and were subjected to filtering by Lipinski's rule of five on the basis of which 786 hits were selected for further assessment using molecular docking studies. Finally, 15 hits of different scaffolds having interactions with important active site residues were predicted as lead candidates. These candidates having unique scaffolds have a strong likelihood to act as further starting points in the development of novel and potent NS3/4A protease inhibitors.

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59. Biogenic synthesis, characterization of gold and silver nanoparticles and pharmaceutical evaluation of *Arisaema jacquemontii*, *Hedera nepalensis* and *Valeriana jatamansi*

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Abstract

The aim of the present study was to investigate the green synthesis and characterization of nanoparticles (NPs) and pharmacological evaluation of the test plants. Silver nanoparticles (AgNPs) and gold nanoparticles (AuNPs) were synthesized from methanolic extract solution (50mg/100ml deionized water) of selected parts of the test plants. UV-Vis spectrophotometer further confirmed the synthesis of AuNPs and AgNPs by giving SPR peak in 500-600nm and 400-500nm range respectively. Salt and temperature stability studies of AuNPs and AgNPs revealed the stability of NPs at milimolar salt concentration and at 20-40°C temperature. XRD analysis revealed that AuNPs of tubers, leaves, stem, shoot and root of the test plant species were crystalline

in nature and the average nanocrystallite size was recorded as 9.85nm, 9.8nm, 12.00nm, 10.92nm and 6.23nm respectively. Crystals were cubic in nature. Mainly carboxylic acid/phenol, tertiary alcohol, alkene, alkane and alcohol of plant extracts contributed in reduction of Au-metal to form AuNPs (FTIR). SEM analysis revealed average size of 36nm, 29nm, 32nm, 24nm and 25nm for tubers, leaves, stem, shoot and root nanosphere AuNPs. Mainly AgNPs were crystalline in nature (XRD). SEM results reported synthesized AgNPs size in 30nm-49nm range and spherical in shape for all the samples. FTIR analysis revealed the involvement of mainly carboxylic acids, ether, alkenes, aromatic ring (aryl) groups in reduction of Ag-metal. Overall, among all the tested microbes, the most sensitive microbe was P. aeruginosa (62-88% growth inhibition) followed by C. albicans (59-82% growth inhibition). The most resistant bacterium was K. pneumonia (35-47% growth inhibition). V. jatamansi showed better antimicrobial activities than the other two tested plant species. AgNPs reported better antimicrobial activity than AuNPs. Generally, methanolic crude extract and n-butanol fractions showed higher antioxidant activity among all the tested extracts. Phytochemical screening indicated the presence of several bioactive compounds including sterols, tannins, flavonoids, alkaloids, saponins and oils in different extracts of different parts of all the three plant species. On the basis of these results, all the three plants can be used for stable and active NPs synthesis along with antifungal, antibacterial and antioxidant agent.

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60. Phytochemicals investigation, biological screening and molecular docking analysis of *Euphorbia pulcherrima*

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Abstract

This study deals with the phytochemical investigation, isolation, structure elucidation and biological activities of Euphorbia pulcherrima. The preliminary phytochemical analysis and bioassay-directed isolation of secondary metabolites of Euphorbia Pulcherrima extract exhibited the presence of terpenoids, flavonoids, steroids and alkaloids which correlate the medicinal value

of the *E. pulcherrima*. The chloroform fraction yielded 2 compounds spinacetin and patuletin by employing column chromatography. Their structures were elucidated by advanced spectroscopic analysis. The extract, fractions and constituents were screened for in-vitro, enzyme ureases, antioxidant and antibacterial activities. It also exhibited such activities against urease enzymes, anti-nociceptive, sedative, anti-inflammatory, antipyretic and acute toxicity. The compounds showed significant muscle relaxant and antipyretic activity against standard.

Keywords: *Euphorbia pulcherrima*, extract, enzyme ureases, antioxidant and antibacterial activities

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61. Echinacea purpurea (cone flower): an immunomodulatory agent in Newcastle disease infected broiler chicks

Waqas Ahmad*, Farzana rizvi, Azmatullah, Sadaf faiz

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Abstract

Vaccination nowadays is the utmost reliable approach to reduce the fatality rate due to Newcastle disease virus (NDV). In spite of vaccination and biosecurity, Newcastle disease (ND) is still prevalent globally in poultry. Various drugs shield the poultry birds for short period of time, while immune modulators work for longer duration against infection. The present study was planned to examine the immunomodulatory effects of Echinacea purpurea (E.P) dried extracts against NDV infection. For the present trial, a flock of 120 day old broiler chicks were randomly distributed into 4 equal groups A, B, C and D with 30 birds per replicate. Experimental shed was properly cleaned and disinfected with 4% formalin solution a day before the arrival of chicks. Fresh water was available for chicks ad libitum. All chicks were vaccinated against infectious bursal disease (IBD), NDV and hydropericardium syndrome (HPS) according to routine schedule. Group A served as control negative received no treatment and E.purpurea treatment was offered @2.5g/kg to group C and D in feed till 40th day of age. At day 19th of trial, the chicks of control positive group B were challenged with velogenic NDV strain. Anticoagulant added blood was collected at day 26th,

33rd and 39th day post infection (DPI) for haemagglutination (HA) and haemaagglutination inhibition (HI) assay against NDV and sheep red blood cells (SRBCs). The Duncan multiple range test results concluded that body weight was significantly higher in group C from 3rd week onward as compared to control negative group. Geometric mean titers log2 against NDV was higher in control positive group B & treatment group D as compared to control groups at 26th, 33rd and 39th DPI. Cellular immunity and phagocytic index; lymphoproliferative response (LPR) against avian tuberculin was higher significantly at 24th and 48th hour post inoculation in group D while carbon clearance assay (CCA) was higher in treatment group C at 0,3rd & 15th minute. In conclusion, the present study revealed that use of Echinacea purpurea @2.5g/kg in feed enhanced the overall performance and immune response of broiler birds against NDV.

Key words: Echinacea purpurea, Newcastle disease, Immunity, Broiler chicks

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62. A simple, rapid and sensitive RP-HPLC-UV method for the simultaneous determination of sorafenib & paclitaxel in human plasma and pharmaceutical dosage forms: Application to pharmacokinetic study.

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Abstract

A simple, economical, fast, and sensitive RP-HPLC-UV method has been developed for the simultaneous quantification of Sorafenib and paclitaxel in biological samples and formulations using piroxicam as an internal standard. The experimental conditions were optimized and method was validated according to the standard guidelines. The separation of both the analytes and internal standard was achieved on Discovery HS C18 column (250 mm x 4.6 mm, 5 µm) using Acetonitrile and TFA (0.025%) in the ratio of (65:35 v/v) as the mobile phase in isocratic mode at a flow rate of 1 ml/min, with a wavelength of 245 nm and at a column oven temperature of 25ºC. The limits

of detection (LLOD) were 5 and 10 ng/ml while the limits of quantification (LLOQ) were 10 and 15 ng/ml for Sorafenib and Paclitaxel, respectively. Sorafenib, paclitaxel and piroxicam (IS) were extracted from biological samples by applying acetonitrile as a precipitating and extraction solvent. The method is linear in the range of 15-20,000 ng/ml for Paclitaxel and 10-5000 ng/ml for Sorafenib, respectively. The method is sensitive and reliable by considering both of its intra-day and inter-day co-efficient of variance. The method was successfully applied for the quantification of the above mentioned drugs in plasma. The developed method will be applied towards Sorafenib and Paclitaxel pharmacokinetics studies in animal models.

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Poster Presentations

1. Phytochemical evaluation of *Garcinia mangostana* (purple mangosteen) fruit rind

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Abstract

Garcinia mangostana is a common tropical fruit famed as "queen of tropical fruit" and found in Malaysia, India, Myanmar, Philippines, Sri Lanka and Thailand. It is used in the treatment of inflammations, diarrhea and dysentery. Its pericarp, fruit, stem, leaves, seeds, arils and heartwood is a rich source of xanthones and their derivatives which have significant antioxidant, antimicrobial, cytotoxic, anti-inflammatory and anti-HIV activities. Phytochemicals such as phenolic acids, flavonoids, xanthones, benzophenones, tannins, alkaloids and triterpenoids are generally assumed to be the active secondary and non-nutritive constituents contributing to protective and pharmacological effects. This study aimed to evaluate the fruit rind extracts for various phytochemicals such as flavonoids, tannins, saponins, carbohydrates, reducing sugar, phytosterols and terpenoids according to the procedures of simple laboratory tests, and UV, FT-IR, NIR, and NMR spectroscopic techniques. The results showed the presence of alkaloids, carbohydrates, glycosides, terpenes, phytosterols, phenolics, flavonoids and tannins. Ethyl acetate, and methanol extracts showed abundance of the polyphenolic constituents, whereas *n*-hexane extract was rich in triterpenoids and phytosterols. Furthermore, *G. mangostana* chloroform fruit extract showed the presence of a potent anticancer constituent "α-mangostin".

Keywords: *Garcinia mangostana*, Fourier-Transformer infrared, α-mangostin

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2. Phytochemical analysis of *Garcinia indica* (Kokum) fruit rind

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Abstract

Garcinia indica (kokum) is used as a savory for curry and also in traditional medicine. Its fruit juice used for the treatment of piles, hemorrhoids, colic problems, ulcers, diarrhea, dysentery and digestive disorders. This study aimed to evaluate phytochemicals such as triterpenoids, phytosterols, phenolic compounds, flavonoids, xanthones, benzophenones, anthocyanins, carbohydrates, cardiac glycosides and tannins in *G. indica* fruit rind fruit extracts by ultra-violet (UV), Fourier-Transformer infrared (FT-IR) and near infrared (NIR) spectroscopy. The phytochemical screening results of different extracts revealed the presence of carbohydrates, glycosides, phenolics, flavonoids, terpenes, phytosterols and tannins. Carbohydrates, glycosides, phenolics and flavonoids were detected in ethyl acetate, acetone, methanol, and aqueous extracts, whereas *n*-hexane and chloroform extracts showed the presence of triterpenoids and phytosterols. Analyses by UV, FT-IR and NIR techniques showed the wavelengths and absorption bands of phenolic compounds in the polar extracts. The absorbance around 3550–3250 cm^{-1}, 1750 to 1600 cm^{-1}, and 1500 to 700 cm^{-1} in FT-IR spectra could be attributed to the O-H stretching band, C=O (ester, aldehydes, and ketones), and C-H (methylene) bending (scissoring), C=O (esters and alcohol), and CH_2 bending. The NIR and FT-IR spectra of the non-polar extracts represented the presence of lipids, phytosterols and terpenoids.

Keywords: *Garcinia indica*, Fourier-Transformer infrared, near infrared, phenolics, anthocyanin

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3. Synthesis, antimicrobial activities and catalytic applications of *acacia nilotica* based silver nanoparticles

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Abstract

Nanoparticles (NPs) have small size (1-100nm) and large surface area per unit volume. They are more reactive than macromolecules. It has wide range of applications in various fields of science. Chemically synthesized NPs have various flaws due to the use of dangerous, toxic chemicals

during their synthesis as various poisonous materials are obtained by product from them. There was an urgent need of economic and environmental green methods for the synthesis of NPS [1]. Previously different medicinal plants extracts were binded with different metals for NPs synthesis and among them, silver is the most commonly used metal for such synthesis.

Due to these advantages, our present work is based on synthesis and characterization of silver nanoparticles using *Acacia nilotica* stem extract, which is a member of sub family Mimosaeca and faimly leguminacae. It is indigenously known as 'Babul' or 'Kikar'. It is medium sized tree with a dispersed crown and distributed in temperate and arid regions of Asia [2]. Previous investigation shows that many secondary metabolites such as saponins, tannins, poly phenols, resins, androstene, D-pinitol and ethyl gallate have been isolated from this plant [3]. Most of the secondary metabolites isolated from this plant have anti-inflammatory, antioxidant activity, atherosclerotic, anti-tumor, anti-carcinogenic, anti-bacterial and anti-viral activités to a greater or lesser extent [4]. In our study, we have synthesized AgNPs using *Acacia nilotica* aqueous stem extract. These AgNPs were tested for antimicrobial activities as well as their catalytic applications such as degradation for organic pollutants or dyes.

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4. Analysis of adulteration of open milk in district Mardan, Pakistan

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Abstract

Pakistan is the second country in the world where more than 70% of the milk is contaminated due to adulteration. Adulteration of milk may reduce the quality of milk and can even make it health hazards. Adulterated milk is carcinogenic, cause allergies, kidney diseases, diabetes, hypertension, high blood pressure and heart attack. Formalin solution is added as preservative which affects kidney and liver tissues. Boric acid effect stomach, liver, brain and may even lead to death. Benzoic acid is carcinogenic. Salicylic acid causes severe headache, vomiting, diarrhea and create problem with hearing. Different additives such as formalin, boric acid, benzoic acid, detergents etc are reported in open milk of various parts of Pakistan. The present study aims to study the possible

adulteration in milk available in local markets of district Mardan, KP, Pakistan. Mardan is one of the most agricultural districts of Pakistan where large amount of open milk is sold in local markets as well as sent to other nearby districts. In this regard samples from different areas of district Mardan were collected and the presence of different possible additives used for adulteration of milk were analysed using the standard methods. It was found that most of the samples contained the preservatives while other additives were absent or present in small amount. The present study concluded the fact that proper monitoring and counseling is needed to prevent adulteration of milk in district Mardan.

Keywords: Open milk, adulteration, analysis

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5. Computer guided design and synthesis of dihydropyrimidine c-5 acylhydroxamic acid derivatives as potential urease inhibitors

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Abstract

In order to maximize the chance of finding new therapeutic agents, a rational approach is needed. Computer guided drug design strategies are now effectively providing speedy and rational outcomes to discover drug candidates with reduced costs. A variety of computational tools has been applied to design a drug i-e docking strategy, pharmacophore model and MD simulation. A combination of docking and molecular dynamic simulations (MDS) are more reliable approaches to predict the lead compounds. Urease is a nickel containing enzyme. It results in a number of disorders in the body like hepatic coma, struvite, catheters blocking and gastric carcinogenesis. Acetohydroxamic acid (AHA) is the only drug approved for the treatment of gastric related diseases. In present work, we focused on the design of hydroxamic acid derivatives of dihydropyrimidines by using a synergistic combination of docking, pharmacophore model and molecular dynamics simulations (MDS). Compound **88** showed good stability up to 100ns on the basis of affinity of enzyme-ligand complex and movements of protein. After the results obtained *via* MD Simulation, we synthesized the compounds showed good results. The synthesized

inhibitors were then evaluated for their potential against Jack beans urease (JBU) inhibition and all compounds showed good activities. Among all, compounds **88** and **93** showed best results with IC_{50} 0.31±0.01 and 0.27±0.01 respectively.

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6. Bioisosteric approach in designing new monastrol derivatives: An investigation on their ADMET prediction using *in silico* derived parameters

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Abstract

Medicinal chemists are facing an increasing challenge to deliver safer and more effective medicines. An appropriate balance between drug-like properties such as solubility, permeability, metabolic stability, efficacy and toxicity is one of the most challenging problems during lead optimization of a potential drug candidate. Insoluble and impermeable compounds can result in erroneous biological data and unreliable SAR in enzyme and cell-based assays. The weak inhibitory activity and non–drug-like properties of monastrol, the first small mitotic kinesin Eg5 inhibitor, has hampered its further development. In this investigation, a bioisosteric approach was applied that resulted in the replacement of C-5 carbonyl of monastrol with thio-carbonyl. Further lead optimization of drug-like properties was evaluated through *in silico* predictions by using ADMET predictor software. This minor structural modification resulted in upgraded Human effective jejunal permeability (Peff) and improved permeability in Madin-Darby Canine Kidney (MDCK) cells. Furthermore, C-5 thiocarbonyl analogue of monastrol (named as **Special-2**) was found safe to administer orally with no phospholipidosis toxicity, no raised levels of serum glutamate oxaloacetate transaminase (SGOT) and no potential towards cardiotoxicity. Molecular docking study was also carried out to understand the binding modes of these compounds. The docking study showed high binding affinity of the designed compounds against KSP. Hence a combination of in silico ADMET studies and molecular docking can help to improve prediction success and these compounds might be act as potential candidate for KSP Inhibition.

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7. Isolation and characterization of bioactive constituents from selected mushrooms

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Abstract

Medicinal mushrooms are sources of polysaccharides that prevent the cancer and increase the strength of the immune system (as immunomodulatory) properties. Therefore, mushrooms serve as an important source of drugs for modern medicine. As an example, the anticancer drug obtained from *Ganoderma lucidum* and produced in Japan by the name of **Krestin**, which is 25% of the world's total cancer drug marketing [1]. In addition, a number of mushroom species having polysaccharides with high molecular weight have been subjected through clinical trials such as phase I, phase II, and phase III. As another example, **lentinan** a polysaccharide isolated from *Lentinus edodes* has been used in a great number of cancer patients in clinical trials [2]. Isolation of biologically active compounds from various mushroom species has been increasing due to the wide range of medical activities of mushrooms. Mushrooms including their mycelium and other parts can provide many compounds with various biological activities [3].

Mushrooms are rich source of diverse secondary metabolites like sterols, terpenoids, phenols and biopolymers like polysaccharides, peptides/proteins and their complexes. Several of the polysaccharides possess anticancer properties. The northern parts of Pakistan are enriched with several mushrooms that grow during the month of August and onwards each year. We have selected two local mushrooms, the basidiomycetes *Phaeolus schweintzii* commonly known as velvet-top fungus, which is a plant parasite, and another is the edible *Morchella esculenta* (True Morels) of the Ascomycota group. We have isolated the secondary metabolites through methanolic extraction and the crude polysaccharides through hot water treatment methods. These crude extracts are further purified through column chromatographic methods. These compounds are further characterized through different spectroscopic methods like FTIR, H-NMR and ^{13}C-NMR. We have studied the antioxidant, anti-inflammatory; antibacterial; anticancer; antidiabetic; anti-hepatotoxic activity and other biological properties of the methanolic extract and the crude polysaccharides fractions of these mushrooms [4].

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8. Bioassay-guided extraction and evaluation of polysaccharides from the ariel parts of *Moringa oleifera*

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Abstract

Moringa oleifera, is a woody tree, distributed in the tropical and subtropical regions of the world [1, 2]. It is mainly distributed in the Philippines, Cambodia, Central America, North and South America and the Caribbean Islands. In Pakistan, M. oleifera is locally known as 'Sohanjna' and is grown and cultivated all over the country [3]. Almost all the parts of this plant: root, bark, gum, leaf, fruit (pods), flowers, seed and seed oil has traditionally been used in the treatment of malaria, parasitic diseases, skin diseases. (along with the treatment of inflammation and infectious diseases, also used for cardiovascular, gastrointestinal, hematological and hepatorenal disorders [2, 3]. It is used as potential anticancer, antioxidant, anti-inflammatory, antidiabetic and antimicrobial anti-hyperglycemic and anti-hyperlipidemic agent [1, 2]. In the Philippines, it is known as 'mother's best friend' because of its utilization to increase woman's milk production and is sometimes prescribed for anemia [3].

Polysaccharides belonging to carbohydrate constitute a large and diverse class of compounds, have major roles in applications incancer related drugs. Thus, polysaccharides have attracted the interests of researchers in related fields due to their diverse pharmacological activities including immunomodulatory, antineoplastic, antioxidative, and anticoagulant activities [4]. Recently, polysaccharides have aroused great attention for their unique bioactivities and chemical structures. Many polysaccharides have been reported to exhibit a variety of useful bioactivities, such as anti-aging, antioxidant, anti-tumor, anti-inflammatory, hypolipidemic and hypoglycemic properties. However,there are limited reports available in the literature regarding the activities of polysaccharides from M. oleifera leaves [5]. A great deal of research on *M. oleifera* mainly focused on protein fractionations, flavonoids, and fatty acid and phenolic substances. Galactose and arabinose are main sugar composition of polysaccharides from M. oleifera. Arabinogalactan from several medicinal plants have been evidenced to have pharmacological activities such as

immunomodulating, antioxidant, antiinflammatory, antitumour, antiviral, antitussive, etc. Thus, we hypothesize that arabinogalactan are active polysaccharides of M. oleifera [4].

M. oleifera was collected from Horticulture department, university of Agriculture, Peshawar, khyber pakhtunkhwa, Pakistan in the month of July, 2018. Its various parts i.e (Leaves, Stem, Seeds, and Pods) were successively extracted with methanol and hot water in order to extract various secondary metabolites and Polysaccharides. These constituents were further evaluated for various biological activities to find bioactive candidates.

9. Green synthesis of gold nanoparticle from *Thevetia peruviana* and it's biomedicinal applications

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The aim of this research was to synthesize AuNPs from *T. peruviana*'s aqueous extract to enhance the activity (both anti-bacterial and anti-fungal) of the title plant. For that purpose the extract was subjected to synthesize AuNPs and synthesized AuNPs were characterized by using Uv-visible, Fourier transform (FTIR) spectroscopy and SEM (scanning electron microscope) analysis. The active phytochemical present in extract are responsible for synthesizes AuNPs. Urease and α-glucosidase enzyme inhibitory activity of the extract have also checked which had 6.98 ± 0.98 µM and 700.7 ± 2.43 µM by using Thiourea (IC_{50} µM) as standard. It is concluded that *T. Peruviana* extract is an outstanding enzyme inhibitor and is capable of making fine nanoparticles.

Keywords: *Thevetia peruviana,* intermittent, amenorrhea, reducing agent, phytochemicals.

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10. Synthesis, antimicrobial activities and catalytic applications of *Dodonaea viscosa* based silver nanoparticles

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Abstract

Nowadays researchers are interested in using plant extracts for NPs synthesis which is also called green synthetic method or biogenic method instead of physical and chemical methods. A biogenic method is environmental friendly, cost-effective, requires less energy and also generates the Nps that are safe for human therapeutic use. Due to these advantages, the synthesis of plant based NPs by green method is preferred. Among the plant based MNPs, silver nano particles (AgNPs) are very important because of their unique catalytic properties of degradation of organic pollutants or dyes and useful antimicrobial activities such as antifungal and antibacterial activities. Owing to these advantages, our present work is based on green synthesis and characterization of silver nanoparticles using Dodonaea viscosa (family Sapindaceae) stem extract. They grow in Australia, Pakistan, India, Afghanistan, Mexico and Argentina. It is used for the treatment of rheumatism, skin infections, diarrhea, pains of hepatic or splenic origin, uterine colic and other disorders involving smooth muscles [2]. This plant have some important secondary metabolites such as di- and triterpenes, saponins, flavonoids, and a complex mixture of other phenolic compounds, saponins, alkaloids, tannins, steroids, and volatile oily compounds [3]. In our study, we have synthesized AgNPs using dodonaea viscosa aqueous stem extract. These AgNPs was tested for antimicrobial activities as well as their catalytic applications such as degradation for organic pollutants or dyes methyl orange congo red and catalytic reductions of 2-nitrophenol.

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11. Green synthesis of gold nanoparticles by using aqueous extract of *S. bicapsularis*

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Abstract

The work presented in this thesis consist of “Green synthesis and characterization of Gold nanoparticles using extract of S. bicapsularis” it includes synthesis and characterization of the new metallic nanoparticles (HAuCl4 NPs) using aqueous plant extract of S.bicapsularis as a stabilizing agent.

The progression of reliable and green methods for the fabrication of metallic nanoparticles has many benefits in the field of nanotechnology. The formation of NPs was due to the active phytochemicals such as, anthraquinones, steroids, terpenes, flavonoids, tannins and alkaloids etc. The synthesis of AuNPs was examined for their pharmacological assessment in relation to the activities of the crude aqueous extracts. Good enzyme inhibition activity was exhibited by the aqueous extract and green-synthesized AuNPs. The plant use in this research is of very beneficial activities and the goal of this research is to increase the activities (esp. antibacterial and anti-fungal activity) of the title plant. For that purpose we produced the Gold nanoparticles of the title plant and we did the three common techniques for the confirmation of Gold nanoparticles. The results were very satisfying. I hope that this work will provide a strong base for upcoming work on the title plant.

Keywords: apocynaceae, intermittent, phytochemicals, amenorrhea, aqueous extract, reducing agent, antibacterial, anti-fungal.

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12. Green/biochemical synthesis of gold nanoparticles by using aqueous extract of t.peruviana.

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Abstract

The aim of this research was to synthesize AuNPs from T. Peruviana's aqueous extract to enhance the activity (both anti-bacterial and anti-fungal) of the title plant. For that purpose the extract was subjected to synthesize AuNPs and synthesized AuNPs were characterized by using Uv-visible, Fourier transform (FTIR) spectroscopy and SEM (scanning electron microscope) analysis. The active phytochemical present in extract are responsible for synthesizes AuNPs. Urease and α-Glucosidase enzyme inhibitory activity of the extract have also checked which showed 91.2% urease inhibition (at 6.98 ± 0.98 on IC50µM) and 97.6% α-Glucosidase inhibition (at 700.7 ± 2.43 on IC50µM) by using Thiourea (IC50 µM) (at 0.2% concentration) as standard. It is concluded

that T. Peruviana extract is an outstanding enzyme inhibitor and is capable of making fine nanoparticles.

Keywords: Thevetia peruviana, aqueous extract, apocynaceae, intermittent, amenorrhea, reducing agent, phytochemicals, antibacterial, anti-fungal.

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13. Isolation and phytochemical screening of physicoactive compounds from *Nerium oleander*

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Abstract

The aim of the current investigation was to explore the phytochemical analysis and urease inhibition potential of Nerium oleander .The crude methanolic extract and its fraction shows that the presence of bioactive secondary metabolites such as alkaloids, steroids, tennine , flavonoids, saponins, carbohydrates , glycosides, terpenoids,phenole and phlobatannins . The crude methaolic extract showed the urease inhibitory potential. The current investigation which led to the isolation of new , novel and bioactive phytochemical which possesses urease inhibition potential

Keywords: Nerium oleander , phytochemical screening , urease inhibition activity

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14. Peptide based adsorbents designed for the masking of mutangenic and carcinogenic agents in water effluents

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Abstract

Dye molecules are non-biodegradable and their presence in water bodies are directly or indirectly linked with human health. They can cause severe diseases such as genetic mutation, allergic

problems, vomiting and cyanosis. That is important to treat these dye molecules prior to their discharge into water bodies. There are various physico-chemical and biological methods are used but among various methods, Peptide adsorption using suitable solid adsorbents has found great attractions due to its simplicity and nontoxicity.

Keywords: Solid Phase Peptide Synthesis (SPPS), peptide adsorbent for ionic dyes,

Selective removal of cationic and anionic dyes.

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15. Application of gold nanoparticles as sensor for compounds with lower optical properties

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Abstract

Application of gold nanoparticles as photometric sensor have been proposed for determination of compounds with lower optical properties (small absorptivity). The method is highly selective and sensitive and does not require chemical derivatization for quantification.

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