Poster Presentations

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Enhancement of antibacterial activity of ciprofloxacin hydrochloride by complexation with sodium cholate

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Ciprofloxacin is a broad spectrum bactericidal anti-infective agent of the fluoroquinolones class used in treatment of many bacterial infections. In recent times, there has been increasing resistance to the antibiotic. In this work, we investigated the effect of making an ion- pair complex of ciprofloxacin-hydrochloride with sodium cholate on bacterial activity. The optimal ratio of the reactants and pH were determined using UV spectrometry. The complex was characterized by octanol-water partitioning, melting point, and IR spectrometry. The antibacterial activity of the complex was determined against *Escherichia coli, Staphylococcus aureus, Klebsiella pneumoniae,* and *Streptococcus pneumoniae* by the agar-well diffusion method. The complex was whitish to off-white in color and crystalline, with a melting point of 238^{0}C. The stoichiometry of the complex shows a molar ratio of 1:1 of sodium cholate to ciprofloxacin. The best pH for complexation was pH 9. The complex partitioned 3.38 times into octanol than in water. The FTIR revealed interaction between the 4-nitrogen atom in the 7-piperazinyl group of ciprofloxacin and the carbonyl of the cholate. The drug in complex form gave double the antibacterial activity of the uncomplexed drug. This study showed that development of hydrophobic ion pair complex enhances antibacterial activity of ciprofloxacin hydrochloride.

Speaker Biography

Ugochkwu Jane I is a Lecturer in Pharmaceutical Sciences at the Enugu State University of Science and Technology, Enugu, Nigeria. Her speciality is in Microbiology and Biotechnology. She is a young dynamic Researcher. She has published many articles in both local and international journals.

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Application of nanobioinformatics in drug design and delivery systems

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Nanobioinformatics is a convergent field which integrates the science of nanotechnology with bioinformatics. Nanobioinformatics has the potential to solve problems regarding high throughput genomics data, novel biomarker discovery, complex biological systems, computer-aided drug design (CADD), and nanobiology. Also, nanobioinformatics can be used for devising and designing of different nanosystems. In this context, for instance, bioinformatics can efficiently facilitate identification of multiplexed probes in a nanoparticle. Nano drugs are capable of cell targeting, penetration, and controlled release. Today, the application of nanobiotechnology in drug delivery systems is well-known. Bioinformatics is an important predictive approach for designing nano-transport systems for specific drugs. Also, integration of the power of two chem/bioinformatic techniques, molecular dynamics (MD) and docking, with statistics can help prediction of the efficiency of drug loading in nanoparticles. In addition, in the context of in-silico drug design, nano-design through nanoscale simulation and modeling requires cheminformatic and bioinformatic techniques such as MD simulations, quantitative structure–activity relationship (QSAR), molecular mechanics and quantum mechanics. A growing number of publically available databases such as nanoparticle ontology and chemical entities of biological interest can be used to retrieve required data for nanobioinformatic drug design. Altogether, nanobioinformatics is a novel multidisciplinary field with many potential capabilities in drug design and delivery systems which may significantly accelerate the treatment many deadly diseases including cancer.

Speaker Biography

Abbas is a student currently living in Tehran, Iran. He completed his diploma in biology at the age of 18 years (2011) from Shahid Beheshti High School. Then, he obtained a B.Sc. degree in Genetics from the Shahid Chamran University of Ahvaz in spring 2015. Now, he is studying Masters of Biochemistry at the University of Kashan. His special research interests range from Bioinformatics to Drug Design focusing on melanoma and lung cancer. He is also interested in Epigenetics.

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Application of nano-sciences in modification of mechanistic/mammalian target of rapamycin signaling pathway in cancers

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Nanosciences covers a clear majority of devices derived from biology, engineering and basic sciences which contain nanovectors for the drug delivery system in anticancer drugs. There have been available nanoparticles with various characteristics for optimal drug delivery e.g. for increasing their stability in the circulation system and targeted delivery to the tumors by taking the advantage of enhanced permeability and retention effect near the tumor tissue. Evaluation of the mechanisms and therapeutic effects of nanoparticle-based mammalian mechanistic target of rapamycine (mTOR) modulation can be useful in developing safe in treatment of cancer. mTOR is a conserved serine/threonine kinase in the cellular PI3K/Akt/mTOR signaling pathway. This pathway is modified by cellular alterations such as level of energy, growth factors, stresses, as well as the increased environmental level of cancerous cytokines. In general, increase of this kinase protein function is seen in various types of cancers, especially in cancer stem-like cell. Additionally, activation of this pathway in the most common cancers like nervous system is in consideration. Recent studies have shown the relationship between different cellular signaling pathways and genetic mutations, that involved in the cancers, with mTOR pathway. Based on previous studies, different treatments like surgery, chemotherapy, radiotherapy, aren't more effective and have some side-effects. Therefore, the researchers are trying to find better ways to treat cancer. One approach to this aim is about the essence of understanding all molecular pathways, proteins and mutations.

Speaker Biography

Abbas Ebrahimi-Kalan was born in Tabriz, Iran, in 1980. He received the B.Sc. degree in Radiology from the Tabriz University of Medical sciences, Tabriz, Iran in 2004, and the MSc. and Ph.D. degrees in Anatomical sciences from the Tabriz University of Medical Sciences, Tabriz, Iran, in 2006 and 2014, respectively. In 2014, he joined the Department of Cognitive and neurosciences, faculty of advanced medical sciences, Tabriz University of Medical Sciences, Tabriz, Iran; as an assistant professor. His current research interests include neurosciences, regenerative medicine, nano medicine and animal model of Multiple Sclerosis, Spinal cord injury and Alzheimer Disease. He is a Life Member of the Iranian anatomical sciences association and Neurosciences Society.

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Nanosilicas as bioactive substances, drug delivery means and activator of pharmacological action of natural or synthetic biologically active substances

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Toxicoses caused by low-quality food, pharmaceutical treatment or environmental pollution can be successfully treated only due to the usage of different enterosorbents. Nanosilicas (fumed silica) are the most advantageous for binding toxins of protein origin. Moreover, they can deactivate pathogenic flora, act as a carrier of chemical and natural medicinal substances, and improve their biological activity. When used in combination with several types pf biopolymers, they may regulate the release rate of active substances. The above-mentioned properties make competitive advantage over products with similar purposes, currently available on the market. Last time, it creates a wide range of composite systems based on nanosilica, which possess strong detoxifying effect, adaptogenic, antioxidant and immune modulating properties, and to develop methods of action prolongation immobilized on the surface of silica-carrier biologically active substances and development of efficient methods improving biological activity of antibiotics due to specific binding of them by silicas or their composites with biopolymeric agents. The most promising is the usage of medicinal products and biologically active additives, produced based on nanosilica, in industrial areas and for people with low income. With the development of nanochemistry, the unique ability of nanooxides to participate in structuration of adjacent water layer was discovered. Because of the interactions between water and nanoparticles, interfacial water decomposes to produce a system nanosized water clusters separated by silica particles. It appears that properties of such nano-structured water are very different from the properties of bulk water. Such water is capable to have different dissolving abilities, for example it does not dissolve polar compounds such as mineral acids and hydrogen peroxide, and also it may form weakly associated water domains with non-polar compounds and not participate in formation of hydrogen bonds. As a result, upon contact of silica nanoparticles with cellular objects a strong effect on cell metabolism occurs which is probably due to retention of nutrients and stimulation of receptor system near the cell membranes. Then, due to the interaction between nanoparticles of silica-carrier and immobilized on its surface, biologically active substances stimulation of mucous membrane cells will occur, which leads to the growth of biological availability of the products. The main problem in the area of development and introduction of biologically active additives and pharmaceuticals is the conduction of pre-clinical and clinical trials. Conduction of such trials requires significant financial investments, which small and medium-sized enterprises usually can't afford. At present time Macrosorb LT company together with the Chuiko Institute of Surface Chemistry have developed a line of ready to use biologically active additives for detoxification of the body (Silasita), characterized by high antioxidant and immunostimulating activity (Balzasil), for lymph purification (Lymphodren), series of fitosils for preventive care and treatment of number of diseases.

Speaker Biography

Lyudmila Suvorova is a candidate of medical sciences, an expert in the field of nano and biotechnology in the direction of medicine. CEO of Macrosorb LT. The initiator of the creation of the direction is the UNITED GLOBAL HEALTH, the health of the environment, plants, animals, food safety and man in a closed cycle. Leader in the direction of social and inclusive business, GREEN economy for transition countries; participant of 4 projects HORIZON 2020 of the European Union. Suvorova L.A. Is a co-author of 12 scientific articles, co-author of the textbook for universities: " NANOCHEMISTRY in solving the problems of ENDO and exo ecology" and the author of 1 patent. . The company MacrosorbLT conducts experimental work and the introduction into practical application of Nanobiocomposite products in the field of nanomedicine and agriculture, water and soil purification.

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Nano sized soy phytosome-based thermogel as topical anti-obesity formulation: An approach for acceptable level of evidence of an effective novel herbal weight loss product

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Obesity has become an increasing problem over recent years. Nano lipo-vesicles thermogel of soy extract were formulated and evaluated to reduce the size of adipose tissue cells through percutaneous absorption. Phytosome formulations were prepared with three different techniques: solvent evaporation, anti-solvent precipitation and co-solvency. Optimized formulae were selected using Design Expert® (Version 7.0.0, Stat-Ease Inc. Minneapolis, MN) the means of the highest entrapment efficiency, minimum particle size and maximum drug release and then evaluated for successful complex formation by means of FTIR. Particles zeta potential was detected. Particles shape was evaluated using TEM to insure particles spherical shape and non-aggregation. Optimized phytosome formulae were involved into selected thermogel formulation after evaluation of different plain formulations for clarity, homogeneity, pH, gel transforming temperature and viscosity. Phytosomal thermogel formulation was then re-evaluated for its clarity, homogeneity, pH and gel transforming temperature and for its rheology behavior and permeation study. *In vivo* study was done to ensure anti -obesity effect of soy phytosomal hydrogel. Concisely, soy phytosomal thermogel was found to have the ability to reduce the size of adipose tissue cells of the abdomen in male albino rats.

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Development, characterization and pharmacokinetics of olmesartan-loaded solid lipid nanoparticles

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As synthetic and pharmaceutical scientists have realized that the development of new drugs alone is not sufficient to ensure progress in drug therapy, development of suitable drug carrier systems was considered a vital strategy to overcome these problems. One of those drug carrier systems is solid lipid nanoparticles (SLN), which have been developed for various routes of administration with several objectives including enhancement of bioavailability of poor water soluble drugs. In order to be effective, an orally delivered drug must avoid several potential barriers. For example, it must avoid degradation by stomach acid and gut lumen digestive enzymes; avoid metabolism by enzymes in the gut wall cell; and avoid first-pass extraction by the liver. Olmesartan medoxomil (OLM), a hypertensive drug is practically insoluble in water and has oral bioavailability of 26% and 99% plasma protein binding. It is on the basis of its physicochemical and biopharmaceutical properties, that the drug was selected as a candidate for SLN drug delivery system. The purpose of the present study was to investigate the bioavailability enhancement of OLM by solid lipid nanoparticles. OLM loaded SLN was prepared by hot homogenization and ultra-sonication method. Optimization was by particle size, polydispersity index, shape and surface morphology determination. Physicochemical and other spectroscopic parameters on optimized formulations (F_3 and F_7 respectively) were determined. *In-vitro* drug release studies were performed using dialysis bag. Bioavailability studies were done using albino rats. The *in-vitro* drug release study demonstrated that drug-loaded formulations gave higher drug release than olmesartan medoxomil. Zero-order kinetic model best described the release kinetics of the drug from the formulations based on the correlation coefficient values. When compared with the oral tablet of OLM, the pharmacokinetics of OLM loaded SLN formulations exhibited higher plasma drug concentration, larger area under the curve, and more enhanced oral bioavailability.

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Evaluation of medicine distribution, regulatory privatisation, social welfare services and liberalization

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The strategy of price liberalization and privatization had been implemented in Sudan over the last decade, and has had a positive result on government deficit. The investment law approved recently has good statements and rules on the above strategy to pharmacy regulations. Under the pressure of the new privatization policy, the government introduced radical changes in the pharmacy regulations. To improve the effectiveness of the public pharmacy, resources should be switched towards areas of need, reducing inequalities and promoting better health conditions. Medicines are financed either through cost sharing or full private. The role of the private services is significant. A review of reform of financing medicines in Sudan is given in this article. Also, it highlights the current drug supply system in the public sector, which is current responsibility of the central medical supplies public corporation (CMS). In Sudan, the researchers did not identify any rigorous evaluations or quantitative studies about the impact of drug regulations on the quality of medicines and how to protect public health against counterfeit or low-quality medicines, although it is practically possible. However, the regulations must be continually evaluated to ensure the public health is protected against by marketing high quality medicines rather than commercial interests, and the drug companies are held accountable for their conducts.

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Medicines and biology: Sustainable management of pharmacy, pharmacists and pharmaceuticals and how to bridge the gap in human resources for health?

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Worldwide, there are different systems for providing pharmacy services. Most countries have some element of state assistance, either for all patients or selected groups such as children, and some private provisions. Medicines are financed either through cost sharing or full private. The role of the private services is therefore much more significant. Nationally, there is a mismatch between the numbers of pharmacists and where are they worked, and the demand for pharmacy services. The position is exacerbated locally where in some areas of poor; there is a real need for pharmacy services, which is not being met and where pharmacists have little spare capacity. Various changes within the health-care system require serious attention be given to the pharmacy human resources need. To stem the brain drain of pharmacists, it is, however, necessary to have accurate information regarding the reasons that make the pharmacists emigrate to the private sector. Such knowledge is an essential in making of informed decisions regarding the retention of qualified, skilled pharmacists in the public sector for long time. There are currently 3000 pharmacists registered with the Sudan medical council of whom only 10% are working with the government. The pharmacist: population ratio indicates, there is one pharmacist for every 11,433 inhabitants in Sudan, compared to the world health organization (WHO) average for industrialized countries of one pharmacist for 2,300 inhabitants. The situation is particularly problematic in the southern states where there is no pharmacist at all. The distribution of pharmacists indicates the majority are concentrated in Khartoum state. When population figures are taken into consideration all states except Khartoum and Gezira states are under served compared to the WHO average. This mal-distribution requires serious action as majority of the population is served in the public sector. This study reveals the low incentives, poor working conditions, job dissatisfaction and lack of professional development programs as main reasons for the immigration to the private-sector. The objective of this communication is to highlight and provide an overview of the reasons that lead to the immigration of the public-sector pharmacists to the private-sector in Sudan. The survey has been carried out in September 2004. Data gathered by the questionnaires were analyzed using statistical package for social sciences (SPSS) version 12.0 for windows. The result has been evaluated and tabulated in this study. The data presented in this theme can be considered as nucleus information for executing research and development for pharmacists and pharmacy. More measures must be introduced to attract pharmacists into the public sector. The emerging crisis in pharmacy human resources requires significant additional effort to gather knowledge and dependable data that can inform reasonable, effective, and coordinated responses from government, industry, and professional associations.

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Nanoencapsulation of bioactive metabolites of local medicinal plants for effective drug delivery and its efficacy test using laboratory animal models

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Nano-encapsulation of drugs involves formation of drug loaded particles with diameters ranging from 1 to 1000 nm. Nanospheres have a matrix type structure with drugs being absorbed either at the sphere surface or encapsulated within the particle. Nano-capsules are vesicular systems in which the drug is confined to a cavity consisting of an inner liquid core surrounded by a polymeric membrane. In this case, the active substances are usually dissolved in the inner core, but may also be adsorbed to the capsule surface. Nano-encapsulation of drugs increases their efficacy, specificity and targeting ability and protect their payload from premature degradation in the biological environment, enhance bioavailability, and prolong presence in blood and cellular uptake. Peptide drugs are attracting increasing interest now-days with better understanding of their role in physiopathology, as well as progress in biotechnology and biochemical synthesis. However, the use of peptides and proteins in medicine has been limited by low bioavailability, which results from their poor stability to proteolytic and hydrolytic degradation, low permeability across barriers, and short biologic half-life in the circulatory system. Most therapeutic peptides are still, being administered by the parenteral route because of insufficient absorption from the gastrointestinal tract (GIT). Bioavailability of drug is defined as a measurement of the extent of a therapeutically active component that reaches the systemic circulation and is available at the site of action. It is one of the key pharmacokinetic properties of a phytochemical or drug. Phytochemicals with health benefits, such as plant polyphenols (that is, curcumin, resveratrol, epigallocatechin gallate, and so on) and carotenoids (that is, lycopene, β-carotene, lutein, zeaxanthin, and so on), have received much attention from the scientific community, consumers, and food manufacturers because they can be used to lower blood pressure, reduce cancer risk factors, regulate digestive tract system, strengthen immune systems, regulate growth, sugar concentration in blood, lower cholesterol levels, and serve as antioxidant agents. Although, the use of polyphenols in capsules and tablets is abundant, their biological effects are frequently diminished or even lost due to incomplete absorption and first-pass metabolism. Overall, the therapeutic use of drug molecule is limited due to poor solubility, poor permeability, instability and extensive first past metabolism before reaching the systemic circulation. Many researchers have attempted to improve its solubility by adding non-polar solvents (DMSO), synthesis of water soluble derivative and complexation with cyclodextrin and liposomes. However, the encapsulation of drug molecule on suitable nano-carriers is one of the promising ways to circumvent these problems. Hence, the present work focuses on various nano-encapsulation strategies for successful targeted drug delivery.

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Safety of intravenous injection of 50nm gold nanorods (AuNRS) in dogs

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There is an increasing interest in the application of gold nanoparticles in cancer therapy; however, their toxicity should be carefully assessed before its application in clinical trials. The present work was conducted to evaluate the possible toxicity of intravenous injection of 50nm gold nanorods; this included their effect on hematology, liver and kidney functions, histopathology and TEM for liver, spleen and kidney. Sixteen baladi dogs were divided into three groups; control (n=5); acute toxicity (n=5), and long term acute toxicity (n=6) groups. Dogs in the treated groups were intravenously injected with 75µg of 50nm AuNRs/kg body weight, while dogs in the control group were injected with normal saline solution. Blood samples were collected before AuNRs injection, on day-15 and on day-30 after AuNRs injection to study the acute, and up to the six months after AuNRs injection to study the long term acute toxicity, and from control group, blood samples were collected at the same times. Biopsy samples were collected from the control and after the first and six months of AuNRs injection and prepared for histopathology and TEM examination.Blood samples were analyzed for complete blood count, liver and kidney functions. Results showed no aberrant clinical changes after intravenous injection of AuNRs in dogs. Also, no gross morphological changes in size, color and texture of liver, kidney and spleen were detected at biopsy sampling. Histopathological examination of the biopsy samples revealed that, intravenous injection of AuNRs produced mild changes in liver and kidney in at long term acute toxicity group, while spleen tissues were not affected by AuNRs injection. TEM failed to detect AuNRs in spleen, kidney or liver of treated animals either in acute or long term acute toxicity groups. There were mild changes in RBCs, HGB, MCM, total protein, globulin, total bilirubin and creatinine levels in the blood samples taken from dogs in both AuNRs groups compared with control dogs. In conclusion, intravenous injections of AuNS did not elicit harmful effect on liver, kidney or spleen of dogs; therefore, it can be safely used in cancer therapy in dogs without any impairment of their physiological functions.

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Improved drug delivery and therapeutic efficacy of PEGylated liposomal doxorubicin by targeting anti-HER2 peptide in murine breast tumor model

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Statement of the problem: The most common chemotherapy regimen for treating cancer is based on the application of nonspecific cytotoxic substances which can induce toxic side effects. Targeted cancer therapy is a powerful therapeutic strategy to management of cancer. HER2 as an anticancer target has long been studied. Its overexpression plays an important role in the pathogenesis and progressiveness of breast and other cancers.

Methodology & theoretical orientation: To establish efficient and reliable drug delivery to HER2-overexpressing cells, the authors of this study have developed anti-HER2 (ErbB2) peptide-liposomal formulations of doxorubicin (DOX) by an engineered breast tumor targeting peptide ligand, AHNP, anti-HER2/neu peptide, (FCDGFYACYADV) with three glycine amino acids as spacer before its original sequencing. Towards this goal, PEGylated liposome doxorubicin (PLD) bearing different ligand densities of AHNP was prepared and characterized for their size, zeta potential and peptide conjugation. The AHNP functionalization and density effects on breast tumor cell uptake, selective cytotoxicity, prevention of tumor growth and the tissue biodistribution of encapsulated DOX were studied in mice bearing TUBO breast cancer tumor model.

Findings: The findings demonstrated that increasing the ligand density of AHNP increases cytotoxicity and cell-uptake in SKBR3 and TUBO cells which overexpress HER2 but not in MDA-MB-231 with low HER2 expression profile. The anticancer activity was also superior for targeted liposomal DOX with more AHNP densities.

Conclusion & significance: This experiment displayed the great potential of AHNP as a targeting moiety on the liposome surface and emphasized the significance of adjusting density of ligand to maximize the targeting capability of the nano drug delivery systems. Overall, the results showed that optimum AHNP density functionalization of PLD can significantly improve selectivity and the therapeutic index of liposomal DOX in the treatment of HER2 positive breast cancer and merits further investigation.

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Protocatechuic acid loaded chitosan coated iron oxide nanoparticles for cancer therapy

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Iron oxide nanoparticles (FNPs) were synthesized by co-precipitation method, followed by coating with chitosan (CS) biopolymer and used as a nanocarrier for efficient delivery of anticancer agent protocatechuic acid (PA). The Fourier transform infrared spectra revealed that the FNPs nanoparticles could be successfully coated with CS polymer and PA as an active anticancer drug. The magnetic measurements showed that the designed nanocarrier and protocatechuic acid-chitosan-iron oxide nanocomposite (PA-CS-FNP) were superparamagnetic while the release of PA from PA-CS-FNP nanocomposite was found to be in a sustained manner and significantly lower in phosphate buffered solution at pH 7.4 than pH 4.8, due to different release mechanism. The spherical shape of nanosized FNPs and PA-CS-FNP was observed by Transmission Electron Microscopy (TEM) and loading of PA in the PA-CS-FNP nanocomposite was estimated to be about 11.3 %. In addition, PA-CS-FNP nanocomposite showed higher inhibitory effect to cancer cell growth than free PA, without affecting normal fibroblast (3T3) cell growth.

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In silico study of anti-HIV and anticoagulant properties of coumarin and p-coumaric acid, fullerenes and their respective conjugates

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Coumarin and p-coumaric acid have been implicated to alleviate multiple disease conditions and nanoparticles have been known to inhibit key proteins, individually but in this study we are interested in assessing the anti-HIV and anticoagulant properties of coumarin and p-coumaric acid along with their synthesized fullerene conjugates and fullerene. We isolated coumarin and p-coumaric acid from endophytic fungi, alternaria species-1 from crotalaria pallida leaf and characterized by UV, XRD, FTIR, and C13 NMR. Subsequently, we synthesized the fullerene nanoparticles using coumarin and p-coumaric acid separately. Two coagulant proteins and nine HIV-1 proteins were selected using iGEMDOCK. We report that p-coumaric acid has greater interaction with coagulant proteins followed by coumarin and fullerenes. Among HIV-1 proteins higher interaction was observed with p-coumaric acid especially, HIV-1gp120. However, upon conjugating fullerene to coumarin and p-coumaric acid, coumarin-fullerene showed significantly greater interaction with coagulant proteins and all HIV-1 proteins, compared to p-coumaric acid-fullerene and fullerene. Our in silico study, thus identifies nanoparticles synthesized by fullerene conjugated to naturally occurring coumarin and p-coumaric acid as a safe and cost effective alternative strategy to treating HIV or its use as an anticoagulant.

Keywords: Alternaria species-1, coumarin, p-coumaric acid, molecular docking, anticoagulant, anti-HIV

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