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Faiza Abdu et al., Polym Sci 2017, 3:4
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The anticancer activity of the combination therapy of Gemcitabine and Doxorubicin encapsulated in a nanoemulsion

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Doxorubicin (DOX) is a chemotherapeutic drug used for the treatment of a wide variety of cancers. It is known to cause cardiotoxicity. Gemcitabine (GEM) is an anticancer drug, but it has certain limitations like short biological half-life. A new paradigm to improve DOX and GEM therapeutic index is to administer them in nanoparticles (NPs). Nanoemulsions (NEs) are well-characterized NPs drug carriers that have been broadly implemented in the delivery of anticancer therapeutics. In this study, the antitumor activity of the combination formulas of GEM and DOX, either loaded in water (GEM+DOX-Sol) or NEs (GEM+DOX/LNE), were evaluated in Ehrlich ascites carcinoma (EAC) bearing swiss albino mice. The anticancer assessment of the NEs formulas in 200 mice divided into 10 groups included the detection of the change in body weight, hematological and serum biochemical profiles and studying the histopathological alterations of the heart, liver and kidney tissues. Results showed that mice treated with GEM+DOX/LNE, which has z-average 155.38 nm and zeta potential of -38.5 mV, recorded a decrease in the mean tumor weight and significant increase in the cumulative mean survival time (MST), which was 60 days, as compared to the EAC control group, which has MST of 28 days. It also showed no significant changes in hematological and serum biochemical profiles compared to the normal group. In conclusion, the present study suggested that GEM treatment may significantly reduce cardiotoxicity induced by DOX in EAC-bearing mice. Also, GEM enhances the antitumor properties of DOX by increasing its inhibitory effect on tumor growth.

Biography

Faiza Abdu is a Professor and the Vice Dean of Faculty of Sciences, Biology Department, King Abdulaziz University, Saudi Arabia. She is also a Supervisor of Neuroscience Unit in King Fahad Medical Research Center. Her experimental approach is on physiology and neuroscience. She has collaboration with many scientists in many fields mainly in cancer and nanotechnology.

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Matheus Marques Torres et al., Polym Sci 2017, 3:4
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Comparison of the bio stimulating capacity of degradation of Poly(3-hydroxybutyrate) by forage plants and microorganisms in simulated soil

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Polyhydroxybutyrate [P(3HB)] is a microbial polyester and possess characteristics adequate to petrochemical plastics substitution as polypropylene. It is completely biodegradable and the speed of degradation depends on environmental characteristics as microbiota, temperature and humidity. So, we measured the degradation rate of P(3HB) synthesized by the bacterium *Ralstonia solanacearum* [P(3HB) RS] in a simulated soil model. The aim of the study was to evaluate the degradation capability effectiveness of the bacteria *Ralstonia solanacearum* and *Bacillus megaterium* CN3 and the bacterial degradation bio stimulating capability of the foraging plants *Lolium multiflorum* (Ryegrass) and *Lotus corniculatus* (Birdsfoot trefoil). With P(3HB) RS, produced by bacterium *Ralstonia solanacearum* RS and commercial P(3HB) Biocycle® [PHB Industrial S.A., Brazil] (control), films were produced by solubilizing up 1g in 40 mL of chloroform for 30 min at 58 °C and evaporation in petry plate to film formation. Samples were cut, weighed and separated into polyester bags with three samples each and buried in the soil to be removed at intervals of 20, 40, 60, 80 and 100 days. Trays for plant germination, containing individual cells full of commercial organic soil were used. The soil treatments were: (1) Natural soil grown with both plants, (2) natural soil grown with ryegrass, (3) natural soil grown with Birdsfoot trefoil, (4) natural soil without plants, (5) sterilized soil, (6) sterilized soil inoculated with R. *solanacearum*, (7) sterilized soil inoculated with B. *megaterium*, and (8) only natural soil. The plants used did not stimulate the biodegradation, but despite that, they helped in the fragmentation of the sample. For bacterial treatments, it was possible to affirm that B. *megaterium* is a more effective polymer degrader. Moreover, we can attest that polymer degradation is more effective in a microbiologically more favorable environment, since the treatment of unsterile soil without plants (trat.8) obtained the highest rate of degradation (100%).

Biography

Matheus Marques Torres is currently pursuing Bachelor's degree in Biotechnology at the Federal University of Pelotas, Brazil. He has developed his research activities in the Laboratory of Biopolymers where he works with studies related to the production, characterization and biodegradation of the bioplastic polyhydroxybutyrate (P(3HB).

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Drug discovery of FLT-3/c-KIT inhibitors as anticancer drugs

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Acute Myeloid Leukemia (AML) is an aggressive disease in which the rapid growth of abnormal leukemic cells in bone marrow inhibits the production of normal blood cells. Genetic mutations, such as FLT3 and c-KIT, play their roles in the stepwise leukemogenesis. The most frequent mutations among AML are FLT3 mutations. However, c-KIT mutations account for predicted higher relapse rate and less overall survival. Because development of point mutations or gene amplification of target proteins results in resistance of tyrosine kinase inhibitors, the use of a multi-targeted therapeutic approach is of potential clinical benefit. Several multi-targeted tyrosine kinase inhibitors have been developed toward clinical uses for treating AML, pancreatic cancer, non-small cell lung cancer, etc. They showed inhibitions of ABL, FLT3, c-KIT, RET, PDGFR, SRC and VEGFRs and an activity spectrum similar to tyrosine kinases-targeted drugs on the market. In the present study, a novel small molecular multi-targeted tyrosine kinase inhibitor DBPR487 was examined in *in vitro* kinase inhibition and cytotoxicity assays and evaluated for *in vivo* tumor growth inhibition efficacies. Furthermore, the plasma samples collected from the rats orally administered with DBPR487 were measured to determine the pharmacokinetic profile of DBPR487. Further preclinical toxicology and safety pharmacology studies are undergoing toward clinical development.

Biography

Min-Hsien Wang is a Research Assistant in Institute of Biotechnology and Pharmaceutical Research, National Health Research Institutes (NHRI). Her research interest is on drug discovery and development. Her work focuses on in vivo efficacy evaluation in rodents, establishment of disease animal models and toxicology study in rats. She has experiences on animal handling, compounds dosing in different routes and blood collection in animals. She has discovered lead compounds for a diabetes drug candidate (DBPR108) and anti-cancer drug candidates (DBPR112, DBPR114, DBPR115). She has publications in reputed journals which include *Bioorganic & Medicinal Chemistry Letters Journal, Journal of Medicinal Chemistry and European Journal of Medicinal Chemistry.*

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Novel and validated spectrophotometric estimation of Indomethacin in bulk and solid dosage formulation using mixed hydrotropic solubilization technique

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Around 40% of New Chemical Entities (NCE's) are poorly water soluble and not well absorbed after oral administration. To overcome the problems associated with oral absorption and bioavailability of these poorly soluble drugs, various strategies have been utilized out of which hydrotropic solubilization has shown promising results. The present study was undertaken on Indomethacin-a water insoluble drug to enhance its solubility using mixed hydrotropic solubilization technique followed by development and validation of UV spectrophotometric method for quantitative estimation of Indomethacin in bulk and pharmaceutical dosage forms. Preliminary solubility studies were carried out with different molars of hydrotropic agents and from the solubility studies performed, proper blend (1.5 M Sodium citrate and 1.5 M Sodium benzoate) of hydrotropic agents was selected for further study. UV spectrum and calibration curve of Indomethacin was established in selected blend of hydrotropic agents and it was found to exhibit λmax of 320 nm. Analysis of bulk drug of Indomethacin and marketed samples in chosen blend of hydrotropic agents was done and total drug content was calculated. The developed method was then validated as per ICH guidelines for linearity and range, accuracy, precision, limit of detection (LOD) and limit of quantification (LOQ). There was significant increase in solubility of Indomethacin with increase in molarity of hydrotropic agents and a blend of 1.5 M Sodium citrate and 1.5 M Sodium benzoate showed good results. Thus, it is concluded that the mixed hydrotropic solubilization can be effectively used for solubility enhancement of poorly water-soluble drugs and the proposed UV method which is new, simple, accurate and reproducible can be successfully employed for the routine analysis of Indomethacin in bulk samples as well as other pharmaceutical dosage forms.

Biography

Nisar Ahmad Khan is presently working as Senior Assistant Professor in the Department of Pharmaceutical Sciences, University of Kashmir, India. He has obtained his Bachelor's degree in Pharmacy from University of Kashmir and Master's degree in Pharmaceutics from SGSITS Indore, India. He has obtained his Doctorate degree in Pharmaceutics from University of Kashmir in the field of novel drug delivery systems. He has his expertise in formulation of hydrodynamically balanced drug delivery systems in the form of single unit or multiple units and has expertise in the Gastroretentive DRUG delivery systems (GRDDS). He has also worked in the field of solid dispersion technology, hydrotropic solubilization and cosmetology.

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Preparation and evaluation of gastro-retentive floating tablets of bromhexine hydrochloride using thermoplastic granulation method

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Bromhexine hydrochloride thins and loosens mucus to help clear stubborn chest congestion and breathing difficulties due to excess mucus in cold, flu and respiratory tract infections. The need for its gastro-retention is that it is dissolved in the pH range of 1-4 and after that its dissolution almost ceases because of the low solubility in the lower region of the gastrointestinal tract. The oral bioavailability of Bromhexine HCl is 20%. Thus, the floating drug delivery system may help Bromhexine HCl to stay in the acidic pH for long time and improve its oral bioavailability. Floating tablets of Bromhexine HCl were prepared by using Thermoplastic Granulation technique. Different hydrophobic retardants were used namely carnauba wax, hydrogenated castor oil and a hydrophilic polymer HPMC E15V were used in different combinations at different ratios for the preparation of the tablets. They were evaluated for tablet thickness, hardness, weight variation, friability, floating lag time and in vitro drug release. Compatibility of the drug and polymers was assessed by Fourier transform infrared spectroscopy. Differential scanning calorimetry studies were also conducted. The λmax of Bromhexine HCl was found to be 248 nm. FT-IR spectroscopy showed no interaction between the drug and polymers. DSC thermogram showed a sharp endothermic peak at 246 °C which is corresponding to melting point of the drug. The *in vitro* drug release study of the gastro-retentive floating tablets of Bromhexine HCl was found to be 89.3% at the end of 12 hours for formulation 10. All the 12 formulations remained buoyant and showed drug release up to 12 hours. The use of hydrophobic retardants and hydrophilic polymer in combination had its own advantages of maintaining integrity and buoyancy of tablets. It could be concluded that for the proper floating duration and *in vitro* release, the hydrophobic retardants and hydrophilic polymer must be used in proper ratio. Formulation 10 was considered as the optimized formulation.

Biography

Kelvin Bucktowar has obtained his BPharm and currently pursuing MPharm in Pharmaceutics at T John College of Pharmacy affiliated to Rajiv Gandhi University of Health Sciences, India. He has published numerous review and research articles in reputed journals.

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Preparation of hydrogels using various starch Aldehydes

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Hydrogels are hydrophilic, three-dimensional, and expandable matrices that are produced through chemical and/or physical crosslinking of certain polymers. In some cases, polysaccharide-based hydrogels have been prepared from a single polysaccharide such as Carboxy Methyl Cellulose (CMC) and starch. CMC is an anionic water-soluble natural polymer derivative, which is widely used in detergents, oil exploration, and in the food, paper, and textile industries because of its viscosity-increasing properties. Starch is widely used in different fields such as food, environmental-friendly plastics, and medicine due to its low cost, biodegradability, and renewability. In this study, the polysaccharide hydrogels were prepared by esterification between hydroxyl groups of CMC and aldehyde group of modified starch. Epichlorohydrin and citric acid were used for crosslinker. The starches used in the experiments were corn starch, potato starch, and soluble starch. Sodium periodate was used as the oxidizing agent. The degree of aldehydes substitution (DS) of hydroxyl groups was varied with the amount of oxidizing agent, and the DS showed a minimum of 0.87 to a maximum of 2.79. As a result of analysis of the hydrogels, epichlorohydrin crosslinker showed a high swelling ratio when reacted with native starch. On the other hand, citric acid crosslinker showed good results when reacted with starch aldehydes. The maximum swelling ratio of hydrogel was about 50.

Biography

Jungmin Lee graduated from Seoul National University in 2008. He received a master's degree from Seoul National University in 2013. He is a PhD student of Department of Biosystems and Biomaterials Science and Engineering, Seoul National University. He has published more than 5 papers in reputed journals.

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Study of Thermal Properties of Poly(phenylene sulfide)/Multi-Walled Carbon Nanotubes/Aluminum Nitride Composite

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The PPS/MWCNTs/AlN composite was prepared with poly (Phenylene Sulfide) (PPS), Covalent Functionalized Multi-Walled Carbon Nanotubes (fMWCNTs), and Aluminum Nitride (AlN) via melt-blending techniques. The AlN is a non-oxidizing ceramic material having the highest thermal conductivity among the ceramic materials. A silane coupling agent was used to introduce the functional groups on the surface of the AIN, as it is able to graft with the functional groups on the covalent functionalized MWCNTs. The salinization reaction of the AlN was characterized qualitatively and quantitatively by FT-IR (Fourier Transform Infrared Spectroscopy), and XPS (X-ray Photoelectron Spectroscopy). The grafting reaction of the AlN particles on the MWCNTs was observed using UV–Vis (Ultraviolet-Visible Spectroscopy), FE-SEM (Field-Emission Scanning Electron Microscopy) and FE-TEM (Field-Emission Transmission Electron Microscopy) images. The grafting reaction was accomplished by observing the change of the transmittance, the morphology of the AlN particle bonded to the MWCNTs. For the morphological changes of the fractured surface of the PPS/MWCNTs/AlN composites by FE-SEM, the hybrid filler was homogeneously dispersed on the PPS matrix when the AlN particle was grafted on the MWCNTs. The homogeneous distribution of the hybrid filler acts as a heat transfer path, which led the improved thermal properties, such as thermal conductivity, thermal resistance, and melting temperature than those of not grafted MWCNTs.

Biography

Min Goo Jee graduated from Kyungpook National University in 2017. He is master course student of Department of biosystems and biomaterials science and engineering, Seoul National University.

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Preparation of Carboxymethyl cellulose based-hydrogels using polycarboxylic acids

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Starch is one of the most abundant polysaccharides in the nature, which is composed of a mixture of amylose and amylopectin. Sodium Carboxymethyl Cellulose (CMC) is an anionic water-soluble polymer derivative. In this study, the preparation of superabsorbent hydrogels has been investigated with sodium carboxymethyl cellulose and Dialdehyde Starch (DAS). The dialdehyde starch was synthesized from the oxidation of the starch using sodium periodate to improve the functionality of the starch. In addition, hydrogels were prepared by using citric acid and succinic acid as a non-toxic and biodegradable crosslinking agent at various ratios. When heated, citric acid will dehydrate to form an anhydride, which will react with hydroxyl group of polysaccharide. The chemical structure of hydrogels was characterized using FT-IR spectroscopy. The swelling behavior of hydrogels was investigated in distilled water and 0.9% NaCl solution.

Biography

Dahyun Kim graduated from Seoul National University in 2016. She is Master course student of Department of biosystems and biomaterials science and engineering, Seoul National University.

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Preparation of polysaccharide hydrogels with different process methods

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Polysaccharides derived from natural resources are widely used to develop superabsorbent polymers. Previous studies were grafting petroleum-based synthetic polymers onto polysaccharides. But, these products have a disadvantage that complete biodegradation is impossible. In this study, modified starch and CMC were used as main materials, and chemical bonding of two polysaccharides was tried by esterification. Starch modification and hydrogel preparation were conducted as follows. First, the oxidation of starch was carried out in order to improve the functionality of compound. The hydroxyl groups, primarily at C-2, C-3, and C-6 positions, were transformed to aldehyde and carboxylic acid by oxidation. And then, the polysaccharide hydrogels were prepared by esterification between hydroxyl groups of CMC (or CMC-g-itaconic acid) and aldehyde group of modified starch. The final product was prepared in the form of powder or film, and various characteristics were analyzed. FT-IR spectrometer was used to confirm the chemical structure of products. The FT-IR spectra of starch aldehydes showed the characteristic IR bands at ~1735 cm-1, which confirm the oxidation of starch. In FT-IR analysis of hydrogels, the peaks related to ester bonding were observed. When hydrogel was prepared in powder form, it was confirmed that all samples showed two peaks at 1750 cm-1 and 1660 cm-1. In film form, two peaks were observed at 1710 cm-1 and 1610 cm-1 in all samples using CMC-g-itaconic acid. The maximum swelling ratio of hydrogel was about 25.

Biography

Jihyun Yeo has completed her bachelor at the age of 22 years from Kyung Hee University and is taking a master's degree at Department of biosystems and biomaterials science and engineering, Seoul National University.

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Preparation and characteristics of PPS composites using glass fiber and reduced Graphene Oxide

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These days, a research that related to automobile and advanced electro materials has been concentrated on weight reduction of materials. In particular, a competition in the development of lightweight materials is intensifying due to various issues such as responding to environmental regulations and electric cars. In addition, various materials such as light metal materials are being replaced by carbon-based materials and high-performance plastic materials In this study, Polyphenylene Sulfide/ Glass fiber/ reduced graphene oxide Composites were prepared by Twin screw extruder and injection molding processes. And then, we have investigated surface properties by Scanning electron microscopy (SEM). Thermal stabilities and Thermal conductivities were analyzed by Thermo gravimetric analysis and C-Therm TCi. Mechanical properties were examined by Universal Testing Machine (UTM). These results indicated that PPS/GF/RGO composites were enhanced thermal properties and mechanical.

Biography

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Efficiency of Brazilian xanthan encapsulation and associations in the microencapsulation of probiotics (*Lactobacillus acidophillus*)

Patricia Diaz de Oliveira, Júlia Borin Fioravante, Izadora Almeida Perez, Rosane da Silva Rodrigues, Ângela Maria Fiorentini and Angelita da Silveira Moreira
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Probiotic microorganism's consumption generates several benefits when they are significantly viable in the products in which they are applied. However, some processing conditions are unfavorable to their survival, as well as the food's own characteristics and storage conditions. Due to the low viability of probiotics when added as free cells, different technologies have been used in order to increase their survival in food. Our study aimed to evaluate of *Lactobacillus acidophilus* encapsulation efficiency by the spray dryer using xanthan pruni, which is produced by a Brazilian strain of *Xanthomonas arboricola* pv pruni, as encapsulating agent and Aerosil® as dispersant. Different encapsulating solutions were prepared in according to a rotational central composite design (RCCD) ($p<0.05$), using a full factorial 2^2 with triplicate at the central point, totaling 11 treatments. Glycerol was added at 20% relative to the total polymer mass. The microcapsules were produced in spray dryer (LabMaq MSD 1.0), with inlet temperature of 120 °C and outlet of 60 °C, with an air flow rate of 3 $L.h^{-1}$ and inlet speed of 0.4 $l.h^{-1}$. The microcapsules were stored in a desiccator at 25 °C. The survival percents were determined by comparing the concentration of viable microorganisms after the dryer process with the initial microbial concentrations. Xanthan pruni exerted positive effect on the microorganism viability within the studied range ($r=0.9423$). The mathematical model generated (viability (%)=75.10+1.90X2-1.62A) was predictive and significant within the studied range ($r=0.667$). A positive influence of the concentration of xanthan pruni in the microbial viability after dryer process was observed; which was caused, probably, by thermal protection due to the microorganism's encapsulation. These results denote xanthan pruni as potential encapsulating agent to probiotics microorganisms.

Biography

Patricia Diaz de Oliveira is an Adjunct Professor at Federal University of Pelotas, Rio Grande do Sul, Brazil. She holds a degree in Chemical Engineering from the Federal University of Rio Grande and a Doctorate in Biotechnology from Federal University of Pelotas. Presently, she is doing research at the Biopolymers Laboratory of UFPel.

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Raman analysis and morphological studies of lignin-based carbon / sepiolite hybrid materials prepared by mechanical methods

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Lignin is a kind of biopolymer from woody plants and has complex and heterogeneous aromatic structure with aliphatic moieties. Industrial lignins including lignosulfonate and kraft lignin are abundant as by-product of pulping process. Because most of lignin was used for low-cost fuels, high-value utilization of lignin has been studied in many ways. Lignin carbonization is one way of the high-value utilization of lignin. Due to its low cost, carbon neutrality and relatively high carbon contents among biomass, lignin receiced attentions as a renewable carbonaceous resource. Sepiolite is a kind of silicate clay minerals. It has fibrous texture and porous structure with 'channels' and 'tunnels'. In this study, lignin-based carbon / sepiolite hybrid materials are prepared by carbonization of lignin / sepiolite hybrid materials up to 1000 ^{0}c. Lignin and sepiolite are hybridized by mechanical mixing method. Raman anlaysis and morphological studies for the hybrid materials were investigated. Lignin-based carbon / sepiolite hybrid materials are expected to be applied as reinforcement filler or as an absorbent material.

Biography

Hyun-gyoo Roh graduated from Seoul National University in 2012. He is a PhD student majored in Biomaterials Engineering, Seoul National University. He has studied for lignin-based materials including lignin based thermoplastic polyurethane and lignin based carbon hybrid materials.

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Combined use of zoledronic acid augments ursolic acid-induced apoptosis in human osteosarcoma cells through enhanced oxidative stress and autophagy

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Ursolic Acid (UA), a naturally occurring pentacyclic triterpene acid found in many medicinal herbs and edible plants, triggers apoptosis in several tumor cell lines but not in human bone cancer cells. Most recently, we have demonstrated that UA exposure reduces the viability of human osteosarcoma MG-63 cells through enhanced oxidative stress and apoptosis. Interestingly, an inhibitor of osteoclast-mediated bone resorption, Zoledronic Acid (ZOL), also a third-generation nitrogen-containing bisphosphonate, is effective in the treatment of bone metastases in patients with various solid tumors. In this present study, we found that UA combined with ZOL to significantly suppress cell viability, colony formation, and induce apoptosis in two lines of human osteosarcoma cells. The pre-treatment of the antioxidant had reversed the oxidative stress and cell viability inhibition in the combined treatment, indicating that oxidative stress is important in the combined anti-tumor effects. Moreover, we demonstrated that ZOL combined with UA significantly induced autophagy and co-administration of autophagy inhibitor reduces the growth inhibitory effect of combined treatment. Collectively, these data shed light on the pathways involved in the combined effects of ZOL and UA that might serve as a potential therapy against osteosarcoma.

Biography

Chia-Chieh Wu is currently pursuing his PhD degree at the Institute of Biomedical Sciences, National Chung Hsing University in Taiwan.

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Optimization of Alpinia galanga oil loaded self-nanoemulsifying drug delivery system using design of experiments for fish anesthesia

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Ethanol used for enhancing water miscibility of the essential oils for fish anesthesia provides undesirable side effects to the fish. The aim of this study was to develop a water dispersible formulation of Alpinia galanga oil (AGO) self-nanoemulsifying drug delivery systems (SNEDDS) in order to minimize the amount of ethanol in the formulation and to investigate the effects of the AGO and AGO-SNEDDS for fish anesthesia. Response surface methodology was used to investigate how excipients affect the droplet size on AGO-SNEDDS formation. The fish anesthetic activity of AGO-SNEDDS with different droplet sizes was evaluated by the time it took for zebrafish (Danio rerio) to go into surgical anesthesia stage which fish stopped swimming activity, showed loss of equilibrium and responsiveness and subsequent recovery. The predicted contour plots of droplet size indicated that cremophor RH 40 provided smaller droplet size than tween 80. The goodness of model fitting ($R2>0.89$), prediction power ($Q2>0.72$) and the droplet size values between prediction and real measurement showed similar values (% error <10%). Therefore, these models had a good prediction power. Cremophor RH 40, miglyol 812:capmul MCM EP=1:1 and AGO concentrations showed the most influential variables affecting the droplet size. The droplet size plays an important role in fish anesthesia. The larger droplet required longer time to take fish to enter surgical anesthesia stage. SNEDDS3 with a droplet size around 200 nm sedated the fish into the anesthetic stage within 270 sec, significantly slower than SNEDDS1 and SNEDDS2 (218 and 212 sec) with droplet sizes around 60 and 110 nm ($p<0.03$). All formulations had significantly increased anesthetic activity compared to AGO in an ethanolic solution. In conclusion, the SNEDDS are promising nano delivery systems of AGO for anesthetic use in zebrafish.

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Nanoformulations for Hsp90 inhibitors for cancer therapy

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Heat shock protein (Hsp) 90 plays an important role in maintaining protein homeostasis and helps in cancer proliferation. Molecules targeting Hsp90 in multiple cancers have entered advanced clinical trials. However, Hsp90 targeted cancer therapy faces a major problem of the aqueous dispensability of drugs due to their hydrophobic nature. Nanoformulation using soft polymers has played an important role in the aqueous delivery of hydrophobic anticancer drugs. Hence, to address the formulation issue of hydrophobic-Hsp90 targeted drugs, we have developed Hsp90 inhibitors loaded polymeric nanoformulations, which can be dispensed using aqueous phase (devoid of organic solvents). We have developed 17AAG (first generation Hsp90 inhibitor) and Fe_3O_4 loaded PLGA magnetic nanoparticles (MNPs). We had developed two types of formulations (1:1:10 and 1:1:20) by relatively varying the concentration of PLGA polymer. Our study showed that ratio of 1:1:10 for (17AAG, Fe_3O_4 and PLGA) provided relatively better physicochemical and pharmacological response. The size of drug loaded polymeric MNPs from 1:1:10 nanoformulation were found to be 204 nm (confirmed with SEM and TEM images). These NPs provided dual mode of Pancreatic Cancer (MiaPaCa-2) cells destruction under in vitro conditions; rendered by magnetic hyperthermia (provide by Fe3O4) and Hsp90 inhibition (rendered by 17AAG). We have also developed novel albumin conjugated Hsp90 inhibitor loaded nanoparticles. We used standard desolvation method for the synthesis of drug conjugated albumin nanoparticles. Our studies showed that nab-Hsp90 inhibitor nanomedicine was found to have average particle size of around 222 nm (confirmed with high-resolution SEM and TEM images). Our study shows that the synthesized drug loaded albumin nanoparticles were found to be effective under in vitro condition against both pancreatic (MiaPaCa-2) and breast cancer (MCF7) cell lines. Our studies indicate that our nanomedicine platform, which consists of both synthetic and natural (protein based) polymers that can play a significant role the delivery of Hsp90 targeted anticancer drugs for next-generation anticancer therapy.

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Efficient delivery of structurally diverse protein cargo into mammalian cells by a bacterial toxin

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Given the vast array of applications for protein-based tools and therapeutics inside cells, there is great interest in developing safe and efficient protein delivery platforms that direct biologics into cells. To date, numerous approaches been investigated to facilitate protein entry into the cytoplasm of cells, however, though each capable of delivering protein cargo into cells to varying degrees, general mechanism-based limitations exist for these platforms. In particular, selectivity and/or efficiency remain elusive features for most platforms owing to their shared nonspecific mode of interaction with membranes. Protein toxins, which use host cell-surface receptors to initiate entry into cells, are attractive vectors to consider given their natural tendency to delivery proteins into specific cells with high efficiency. The paucity of development efforts for toxins as protein delivery vectors stem from early studies, which suggested that delivery was restricted to a select few cargo that were largely unfolded prior to translocation and that the cargo itself greatly diminished the efficiency of translocation of the system. Through careful engineering of the platform, we show that neither of these assertions is true. We show that the diphtheria toxin platform is capable of delivering proteins that are over 100 kDa in size and of varying structures and stability with exquisite efficiency. In fact, to our surprise, we found that diphtheria toxin could deliver the hyper-stable passenger protein mCherry, which we calculated to have a melting temperature greater than 90 degrees under the translocation conditions, suggesting that even folded proteins could be delivered into cells. Through a rigorous set of experiments we trace the misleading early results to effect of cargo on the readout of translocation, rather than the efficiency of translocation. We also provide functional evidence that the delivered cargo is functional. Using a-amylase as cargo we show that cytosolic glycogen is degraded in a dose and time dependent manner.

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Drug delivery across the brain protective barriers

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There are approximately 400 known neural disorders some of which being due to a disruption or failure of the blood brain barrier (BBB) such as, for example: meningitis (an inflammation of the meninges or membranes surrounding the brain and spinal cord), epilepsy (chronic or acute seizures caused by inflammation), multiple sclerosis (MS-a disease of the immune system or/and the breaking down of the BBB in a section of the brain or spinal cord), Alzheimer disease (AD-a disease in which amyloid beta contained in blood plasma enter the brain and adhere to the surface of astrocytes), possibly prion and prion-like diseases such as Parkinson disease (PD) and AD, HIV encephalitis (a precursor of HIV-associated dementia in which latent HIV can cross the BBB inside circulating monocytes in the blood stream) and systemic inflammation (sterile or infectious) that may lead to effects on the brain, cause sickness behavior and induce or/and accelerate brain diseases such as MS and PD. There are currently active investigations into treatments for a compromised BBB. As a consequence of the growing aging population, many such neurodegenerative diseases, cancer and infections of the brain will become more prevalent. Of interest here are those disorders requiring treatment by delivery of drugs across the brain protective barriers. I will review the difficulties inherent in the delivery of drugs across the BBB in the treatment if the above neurological disorders and discuss the mechanisms for drug targeting both "through" and "behind" the BBB. I will also suggest approaches for the enhancement of drug delivery including physiological approaches, chemical and biological delivery and disruption of the BBB system, the use of molecular Trojan horse systems and the various nanoparticle and nano delivering devices.

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Development and transportation pathway of Alpinia galanga oil loaded Self-Micro Emulsifying Drug Delivery Systems (SMEDDS) for fish anesthesia

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Alpinia galangal, an important edible plant in family Zingiberaceae is commonly used in Asian folk medicinal remedies. The essential oil of A. *Galanga* Rhizomes (AGO) has many biological activities e.g., antioxidant, antibacterial, antifungal and anti-inflammatory actions. However, the poor water miscibility of AGO causes the limitation of its clinical use in both human and animals. The alcohol used to dissolve AGO for fish anesthesia always causes hyperactivity in fish. The aim of this study was to solve this problem by developing Self-Micro Emulsifying Drug Delivery Systems (SMEDDS) of AGO. Pseudoternary phase diagrams of AGO were constructed to identify the best AGO-SMEDDS formulation. It was found that the AGO-SMEDDS composed of 20.0% AGO and 53.3% tween 80 and 26.7% ethanol had a mean droplet size of 82 nm after dispersing in distilled water. The anesthetic activity of the developed AGO-SMEDDS in koi (*Cyprinus carpio*) was evaluated in comparison with an AGO ethanol solution on the induction time required to reach the surgical anesthetic stage in which the fish stop all swimming activity and show loss of equilibrium and responsiveness. Results showed that the induction times of the fish receiving 200, 300 and 400 mg/L AGO-SMEDDS were 233, 130 and 112 seconds, respectively. Importantly, AGO-SMEDDS showed significantly higher anesthetic activity than the AGO ethanol solution which showed the induction times of 303, 207 and 167 seconds, with the same dose of AGO, respectively. The transportation pathway of AGO was investigated using a fluorescence microscope. AGO was labeled with Nile red. The brain, gills and skin of fish showed red fluorescent spots without auto fluorescence phenomena compared to unlabeled AGO. This result suggests that the AGO entered the fish via gills and skin and was transported to the brain where the anesthetic effect took place.

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Ultra structural study of the pathogenesis of liver fibrosis in rats

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Liver fibrosis is a significant health problem developed as a response to a wound-healing process in injured liver characterized by excessive deposition of fibers and extracellular matrix. Despite extensive studies, the ultra-structural events are not well elucidated in liver fibrosis. The aim of this study was to clarify the ultra-structural events that govern the ECM deposition and fibrosis progression using dimethyl nitrosamine DMN induced liver fibrosis in rat's model. Two groups of male rats were assigned in this study: Control and DMN. Rats were administered DMN intra-peritoneally (10 mg/kg, 3 days/week for 21 days). Administration of DMN induced significant body weight loss and severe pathological alterations in hepatic cells. All hepatic cells suffered specific changes. The hepatocytes were injured and went through apoptosis. The sinusoidal endothelial cells lost their fenestrae. The Kupffer cells as well as the lymphocytes proliferated and contributed to the inflammation. In addition, the quiescent hepatic stellate cells (HSCs) activated; they lost their retinoid and acquired large nucleus, attained large amount of fibers around it. HSCs were transformed into myo-fibroblasts phenotype synthesized extracellular matrix (ECM) proteins and produced fibrous scar. Furthermore, portal fibroblast PFs proliferated and produced large amount of fibers in portal and periportal area. Lymphocytic infiltration, necrosis, hepatocyte steatosis, cholangiocyte proliferation all these contributed to liver fibrosis in this study. In conclusion, the most distinctive features of the cellular events of hepatic fibrosis in this study were focal deposition of ECM and collagens, primarily in portal and periportal areas as well as bizzare and extensive fibrous appearance of mitochondria in hepatocytes. This guides us to believe that activated portal fibroblasts contributed highly to fibrosis.

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Formulation and pharmacological evaluation of metallic nanoparticles

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In recent research and development there has been prodigious excitement in the nano pharmacological area for the study of nanoparticles synthesis using some natural products. Biological methods have been used to synthesize zinc oxide nanoparticles in presence of medicinally active plants such as *Ocimum tenuiflorum, Azadirachta indica*, etc., and this intention made us to assess the biologically synthesized zinc oxide nanoparticles from the leaf of *Ocimum tenuiflorum* using 1 mM zinc oxide solution. Zinc oxide nanoparticles have been widely used for many applications. In current study the nanoparticles tested for their anti-diabetic activity. Morphology and metal composition of synthesized nanoparticles were determined by characterization techniques. Poly herbal formulation was prepared by proper addition of plant mediated zinc oxide nanoparticles that were prepared from *Ocimum tenuiflorum* and *Azadirachta indica*. The formulation tested for its in vitro anti diabetic activity using α-amylase assay. The strongest activity (at concentration: 25 mg/ml) was shown by the nanoparticles formulation (97.77%) comparatively with crude extract. The outcomes of this study show that the administration of some of metallic nanoparticles may possibly control the postprandial blood glucose ranges and confirm the use of these herbs suggested as a treatment of diabetes in traditional medicine and displayed a good inhibitory activity on amylase.

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Major challenges in formulation development: From the perspective of a developing state

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Reducing the disease burden timely and cost-effectively is one of the prime goals of every national health policy, as health and access to safe, effective, quality and affordable medicine is the basic right of people. According to the World Health Organization (WHO), the world consumption of pharmaceutical products has increased drastically from US$ 70 billion to US$ 1.1 trillion (Since 1975), with a consumption of medicines per capita growing from US$ 17 to US$ 531. Regardless of this increase in world consumption, more than 80% of all pharmaceutical products are consumed by 15% of the world population located in 'developed countries'. In order to mitigate this global health inequity, pharmaceutical industries of developing world need to accelerate the development and production of pharmaceutical products of optimal quality. Formulation development, being a very crucial and lengthy process, involves different pharmaceutical technologies and presents a number of challenges to the pharmaceutical industry of countries like Pakistan, India, Bangladesh, etc. Pakistani pharmaceutical market is of US$ 326 billion. In Pakistan, the major challenges that pharma industry faces while developing a new product are stricter and non-supportive pharma regulations of the national drug regulatory body that discourage new drug development, national insufficiency of research and development in producing active pharmaceutical ingredients (APIs), lack of bioequivalence and clinical trials facilities and inadequate commercial and economic feasibility regarding export of new drugs. Besides these, the complex science of drug designing which require novel technologies and well-trained talent is also a crucial challenge. This study recommend to promote harmonization of regulatory processes by adopting globally harmonized standards, establish targeted capacity-building for quality APIs, train the talent, improve research and development sector, develop bioequivalence and clinical trial facilities and set transparent pricing rules. For Pakistan, it is a high time to improve health and access to quality medicine. The recommendations in this presentation may prove helpful in improving the development rate of safe, effective, affordable and high quality drug formulations.

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Design, formulation and evaluation of transdermal patch of Propranolol using chamomile essential oil as permeation enhancer: *In vitro in vivo* chapter

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Statement of the Problem: Skin permeation enhancement technology is a rapidly emerging field which would expressively increase the number of drugs which is suitable for transdermal drug delivery. Transdermal drug administration route offers many benefits over oral administration of drugs and has stimulated research to find ways to overcome the barrier function of the skin by use of various enhancers' approaches. The exploration for the ideal skin penetration enhancer has been the emphasis of significant research effort over a number of eras. Many potent enhancers have been revealed, but in most of the cases, their effects are associated with toxicity.

Methodology: Physiochemical evaluations like majorly, drug content and aging, moisture uptake and thickness were performed to rationalize the suitability and pertinence of the formulation. *In vitro* and *ex vivo* and *in vivo* studies were carried out using Franz diffusion cell using albino rabbits (pharmacokinetics). In vitro permeation studies demonstrated a significant enhancement with chamomile essential oil.

Findings: Formulation with 10% chamomile essential oil exhibited the best permeation of the model drug evidenced by kinetic parameters. The pharmacokinetic parameters, such as the $C_{max,}$ $T_{max,}$ MRT, AUCo-t and T1/2 derived from transdermal administration differed significantly ($p<0.05$) from those estimated from oral administration. The C_{max} of model drug after transdermal administration of optimized patch formulation was found to be 88.37±2.3 µg/ml and the plasma concentration was maintained for 36 hours which was in good agreement with the reported plasma levels of model drug reported in published clinical studies. In variance to oral delivery well sustained activity was observed over a period of 24 hours after transdermal administration.

Conclusion & Significance: Taking together, the transdermal patch using indigenous natural chamomile essential oil can be successively used to achieve better patient compliance in contrast to the oral conventional tablets in pharmaceutical industries.

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Chitosan hydrogel based nanocomposite system with self-healing ability: Films and patches

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Introduction & Aim: Bio-polymeric hydrogel system prepared from chitosan cross-linked with glycerol possesses the self-healing ability, which enables this fantastic hydrogel material to form smooth films or coating. By successful utilization of this self-healing ability possessed by this hydrogel material we have fabricated different types of nanocomposite hybrid biomaterials.

Methods: In the first approach chitosan nanocomposite hydrogel was fabricated by using Carbon dots (CDs) synthesized from commercially available Assam CTC tea. Then a composite nanomaterial was also synthesized by coating the surface of graphene oxide by the iron oxide nanoparticle and this composite nanomaterial was used to fabricate chitosan-iron oxide coated graphene oxide nanocomposite hydrogel films. This chitosan based hydrogel system was also used to fabricate a kind of super absorbent patch using cotton wool. We also modified the patch by incorporating graphene oxide (GO) into this hydrogel system. The films and the patches were fabricated by gel casting technique and by the compression molding technique, respectively.

Results & Conclusion: The films obtained from chitosan-CDs nanocomposite hydrogel system showed UV-blocking ability along with the improved mechanical and thermal property. Chitosan-iron oxide coated graphene oxide nanocomposite hydrogel films are robust along with another interesting property, the antimicrobial activity. Cotton based patches after loading GO showed antimicrobial activity as well as efficient wound healing ability when tested in animal model and thus can serve as a bandage material. The main advantage of such patches is that any type of chemicals, drugs, nano or micro particles can be loaded in it as per requirement. Since chitosan is a bio-polymer having the inherent property of biodegradability and biocompatibility, so such type of films and patches fabricated from chitosan based hydrogel system may find high potential application in the bio-medical as well as food packaging industry. The patches may have application in the textile industry as well.

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Synthesis, characterization and functions of biomass eugenol based helical polymers

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Eugenol (4-allyl-2-methoxyphenol) is a main component (80 wt. %) of clove oil, which is mainly produced in Indonesia. It is widely used as perfumes, antioxidants, drugs, foods and taste items. Eugenol is inexpensive natural resource, which carries reactive phenolic hydroxyl and allyl group and is therefore expected as a key component for environmentally friendly organic synthetic chemistry. On the other hand, biopolymers, exemplified by proteins and DNA, adopt three-dimensionally well-ordered structures, which indispensable for the maintenance of living systems. Although the formation of such regular secondary structures is obviously entropically unfavorable, protein and DNA construct well-arranged helical structures, which are stabilized by hydrogen bonding. The energy of hydrogen bonding compensates the entropic cost. This is the strategy of nature to provide three-dimensionally well-ordered biopolymers. The incorporation of naturally derived eugenol in addition to amino acids into polyacetylene is interesting from the view point of green, sustainable chemistry and polymerization chemistry. This paper is report the synthesis of polymers from eugenol as starting material and examination of polymerization with (nbd) Rh+[η^6-C_6H_5B-$(C_6H_5)_3$] catalyst, which is effective to polymerization mono substitutes acetylene. Characterization of polymers can be soluble in common organic solvent and can be form thermo responsive material so can be function as smart or intelligent material.

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Tunable angle dependent/independent structural color of hydrogel by modulating lamellar structure

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In this paper, we report tunable angle dependence of stimuli responsive photonic hydrogels containing multi-lamellar structure of alternative rigid polymeric platelets of high refractive index and ductile polymer matrix of low refractive index. Therefore, the refractive index variation and periodic lamellar spacing satisfies the Bragg's law to diffract visible light and the gel exhibits magnificent structural color. The packing geometry of periodic multi-lamellae of the photonic crystal is fabricated from flat-lamellae to cylindrical lamellae. 1D photonic crystalline lamellar sheet domains forms a rectangular sheet hydrogel in which the lamellar sheets aligned periodically parallel to the top surface. On the other hand, cylindrical rod-like colored gel is achieved by arranging periodic multi-cylinder packing of the lamellar domains. The cylindrical photonic hydrogel exhibits angle independent color whereas the sheet hydrogel reveals strong angle dependency. A rocking curve has been constructed to justify the tunable angle dependency of the multi-lamellar hydrogel. The tunable angle dependency of this photonic material could potentially benefits light modulation, visualization, optical sensing and display technologies.

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Interfacial construction and multi-scale structural evolution in nanocomposites

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We first report the construction of hybrid shish-kebab (HSK) superstructure in low-crystallinity elastomer nanocomposites with incorporation of carbon nanotube bundles (CNTBs). With strong interfacial adhesion, the tensile strength of olefin block copolymer (OBC)/CNTBs nanocomposites was tripled from 7.34 MPa to 24.11 MPa. With innsitu synchrotron small angle X-ray scattering (SAXS) and wide-angle X-ray diffraction (WAXD) as well as in situ Raman spectra, the multi-scale structural evolution was thoroughly studied. The formation of HSK leads to lower lamellar density, exhibiting remarkably increased long period. Unlike that in neat OBC, the lower density of crystal lamellaes in nanocomposites does not dominate the evolution of long range orderness at low strain regions, the long period of nanocomposites exhibit an inversely increasing trend. With addition of CNTBs, the orientation behavior still follows the slip-link theory. With HSK acting as larger but fewer physical junctions, the chain connectivity of the soft and hard segments in OBC chains in nanocomposites is lower than that in neat OBC, it is less necessary for HSK to adjust their orientation status along the stretching direction. Thus the orientation factor of orthorhombic crystals at low strain regions is lower than that of neat OBC. The mesoscopic structural evolution of CNTBs can be directly revealed by the downshift trend of the Raman G-band of CNTBs in nanocomposites, which reveals the axial deformation of CNTBs. The downshift can reach a maximum of 10.2 cm^{-1} and the downshift under axial deformation also confirm to the slip-link theory and is consistent with the orientation status of HSK superstructure.

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Evaluation of therapeutic potential of folk plants extracts against Acanthamoeba *in vitro*

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Statement of the Problem: Acanthamoeba is an opportunistic protozoan pathogen and one of the most prevalent organisms in our natural environment (i.e., air, soil and water). It is recognized to cause fatal brain infection (*Granulomatous encephalitis*) and eye infection (blinding keratitis). Treatments for both infections are problematic because of the amoebic cysts resistance to therapeutic agents. That is why there is no effective anti-amoebic drug available to date. The purpose of the present study was to evaluate in vitro strength of plants extracts on the viability and biological properties of *Acanthamoeba castellanii* (T4 genotype) and its cytotoxic effects on human corneal epithelial cells (HCEC).

Methodology & Theoretical Orientation: Using HCEC, adhesion, cytotoxicity and amoebicidal, amoebic growth assays were performed.

Findings: Normally, Acanthamoeba exhibited >90% binding and >80% cytotoxicity to HCEC cells which was remarkably inhibited by plant extracts to >70 and 60% respectively. It was also observed that extracts (ranging from 0.1 to 1.5 mg/ml) exhibited amoebicidal effects, i.e., >50% of trophozoites were killed at 1.5 mg/ml within 1 hour. However, the residual amoeba remained static for quite some time. Furthermore, extracts also inhibited >50% amoeba numbers up to 7 days during growth assay. Furthermore, plant extracts (1 to 30 mg/ml) exhibited amoebicidal effects against Acanthamoeba cysts. Furthermore, Acanthamoeba encystment was also inhibited in concentration dependent manner with maximum inhibition at 2 µg/ml after 48 hours. Among all Peganum harmala seed extracts showed optimal activity against amoeba. Our results confirmed that extracts have toxic effects against both cysts and trophozoite.

Conclusion & Significance: Overall, we reported for the first time that selected plant extracts exhibited inhibitory effects on biological properties of Acanthamoeba without any toxic effects on HCEC cells in vitro.

Recommendations: Further experiments are required with purified fractions of plant extracts to identify the active ingredients and to elucidate the mechanism of action of the effective compounds both in vitro and in vivo which may provide a new series of chemotherapeutic agents.

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Sustained Release and Skin Permeability Enhancement of Pentazocine by Proniosome derived Niosomes and Niosomal Gel

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Proniosomes (PN) are the dry water soluble carrier systems that may enhance the oral bioavailability, stability and topical permeability of therapeutic agents. The low solubility and low oral bioavailability due to extensive first pass metabolism make Pentazocine as an ideal candidate for oral and topical sustained release delivery. The present study was aimed to formulate the PNs by quick slurry method that are converted to niosomes (liquid dispersion) by hydration, and subsequently formulated to semisolid niosomal gel. The PNs were found in spherical shape in the SEM and stable in the physico-chemical and thermal analysis (FTIR, TGA and XRD). The quick slurry method produced high recovery (>80% yield) and better flow properties (θ=28.1-37.4°). After hydration, the niosomes exhibited desirable entrapment efficiency (44.45-76.23%), size (4.98-21.3µm) and zeta potential (-9.81mV to -21.53 mV). The in vitro drug release (T100%) was extended to more than three half-lives (2-4 hrs) and showed good fit to Fickian diffusion indicated by Korsmeyer-Peppas model (n=0.136-0.365 and R¬2=0.9747- 0.9954). The permeation of niosomal gel was significantly enhanced across rabbit skin compared to the pure drug-derived gel. Therefore, the PNs are found promising candidates for oral as bioavailability enhancement and sustained release for oral and topical delivery of pentazocine.

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