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POSTERS

Violina T Angelova et al., Clin Pharmacol Biopharm 2018, Volume:7
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Molecular dynamics model of melatonin and MT1 receptor

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Melatonin receptor (MT1) is an attractive target for elaboration of new drug candidates, but unfortunately is known to be unstable out of the membrane lipid bilayer, which makes the obtaining of a crystal structure by X-Ray diffraction (XRD) an elusive goal. Up to now, there is no published real structure suitable for docking of new ligands targeting this receptor. However, there are lots of model based on the data from crystallized rhodopsin, but they are too artificial for reasonable docking of drug-like candidate molecules. To overcome these drawbacks, we built an *in silico* molecular model of a melatonin receptor in membrane bilayer in water cell, with explicit water molecules. For that purpose, we used GROMACS molecular mechanics software with GROMOS force field and TYP3P water model. Calculations were carried out in periodic boundary conditions at 300 K and one bar pressure, physiological NaCl content and pH7. By the simulation, we caught the act of melatonin entering the receptor which enlightened a wide variety of interactions that can facilitate or to disturb the movement of melatonin to the hardly accessible active site of MT1. Molecular docking of the drug like candidates was performed on receptor model. The information can be used along with data obtained from the structure of melatonin-receptor complex to construct new analogs of melatonin, capable not only to activate the receptor but also to successfully manage their way to the MT1 binding site.

Biography

Violina T Angelova has completed her PhD in Organic Chemistry from Institute of Organic Chemistry with Centre of Phytochemistry, Bulgarian Academy of Science, in 2004. She has 22 years of research experience and published more than 29 papers in reputed journals. Currently, she is an Associate Professor at the Faculty of Pharmacy, Medical University of Sofia.

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Neuropharmacological studies of novel melatonin derivatives

The majority of available literature on experimental animals revealed that melatonin has anticonvulsant action in acute seizures tests with different mechanism of action. An important advantage of melatonin as an add-on option in a therapy of epilepsy is associated with its low toxicity, antioxidant activity as well as its ability to synchronize disturbed circadian rhythms in epileptic patients. A series of melatonin analogues, containing indole scaffold, were synthesized and their anticonvulsant activity was tested on ICR mice by measuring the time of three different seizure phases (myoclonic, clonic and tonic) induced by intravenous infusion of pentylenetetrazol (PTZ). The novel melatonin derivatives were synthesized according to the classical method by condensation of hydrazones with 5-methoxyindole-3-carboxaldehyde or 5-benzyloxyindole-3-carboxaldehyde. The hydrazide-hydrazones with indole moyeties were purified by recrystallization and the molecular weights were determined, using ES-MS. The compounds were injected intraperitoneally at doses of 30, 60 and 100 mg/kg 30 min before PTZ. The most potent compounds, with significantly increased thresholds for myoclonic, clonic and tonic seizures compared to vehicle were the derivatives with 2-thienyl and p-Cl-phenyl fragments at a dose of 60 mg/kg, which effects was comparable to that of melatonin at the same dose of 60 mg/kg, used as a positive control. None of the compounds displayed neurotoxicity in the rota-rod test. *In silico* assessment of their BBB permeability indicated them as CNS active agents. Molecular docking was performed into a human gamma-aminobutyric acid ($GABA_A$) receptor and depicted good binding properties of melatonin derivatives, considered in this study. Based on anticonvulsant screening results, these newly synthesized melatonin derivatives will be explored in other seizure tests with different mechanism of action as well as in models of epilepsy.

Biography

Jana Tchekalarova has completed her PhD in Pharmacology in 2004 from Institute of Physiology, BAS. She has 22 years of research experience. She is currently working as an Associate Professor at the Institute of Neurobiology, BAS and as the Head of Behavioral Neurobiology Dept. She is an Adjunct Professor at the Section of Biochem., Physiology and Pathophysiology in the Med. Dept. of Sofia University. According to Mendeley profile her h-index=12, publications 51 with IF; citations=385. She has more than 500 citations. She has been serving as an Editorial Board Member of *Drug Development Research, Journal of Neurological Disorders and Stroke* and Asian Council of Sci Editors.

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ACCEPTED ABSTRACTS

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Nanobiotechnology-based drugs for treatment of neurological disorders

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There are approximately 400 known neural disorders, some being due to a disruption or failure of the blood brain barrier (BBB) such as, *e.g.,* meningitis, epilepsy, multiple sclerosis, prion and prion-like diseases (Parkinson's, Alzheimer's), HIV encephalitis, and systemic inflammation (sterile or infectious). As a consequence of the growing aging population, many such neurodegenerative diseases, cancer, and infections of the brain will become more prevalent. Unfortunately, the developmental process for new drugs has not kept pace with progress in molecular neuroscience because most of the new drugs discovered are unable to cross the BBB. This clinical failure may be largely attributed to a lack of appropriate drug delivery systems. Of interest here are those disorders requiring treatment by delivery of nanobiotechnology (NBT)-based drugs through the BBB-one of the most promising applications in clinical neuroscience. Nanoparticles, utilized as drug delivery agents, could potentially carry out multiple tasks in a predefined sequence. They can be effective careers in delivery of conventional drugs, recombinant proteins, vaccines, *etc.* The following nanotechnologies are available: liposomes, peptides, radiolabeled polyethylene glycol coated hexadecylcyanoacrylate nanospheres, polyalkylcyanoacrylate or poly-lactic-co-glycolic acid (PLGA) nanoparticles with polysorbate 80 or poloxamer, and magneto-electric nanoparticles (MENs). Localized and controlled delivery of drugs at their desired sites of action is preferred because it reduces toxicity and increases treatment efficiency. I will discuss the various strategies that have been explored to increase drug delivery into the brain and their attending difficulties, with particular emphasis on NBT-based drug delivery systems. However, although the use of nanotechnology is expected to reduce the need for invasive procedures for delivery of therapeutics, some devices such as implanted catheters and reservoirs will still be needed. Further, there is some concern about the safety of nanoparticle entry in the brain and these needs to be resolved before human use.

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Nanotechnology in the creation of new antibacterial drugs

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The influence of basic physical factors caused by magnetite nanoparticles (constant magnetic field and sorption) on microorganisms by examining the reactions of the intensity of free radical lipid peroxidation (FRLP) and bacteriostatic action was studied. It was well established that the magnetite nanoparticles caused unequal reaction in intensity of FRLP on different groups of microorganisms. It was determined that the most significant factor that influenced the ultimate indicator of the intensity of luminescence on *Candida albicans*, Escherichia coli and Pseudomonas aeruginosa was constant magnetic field which induced by nanoparticles. On the contrary, sorption was the most significant factor on *Staphylococcus aureus.* It was found that the rate of consumption of free radicals lipid reduced reliably on all microorganisms after their processing by magnetite nanoparticles. The results of microbiological studies of *Escherichia coli, Klebsiella pneumoniae* and *Staphylococcus aureus* showed that bacteriostatic effect was detected after exposure by magnetite nanoparticles. Visually, it was detected by decreasing the number of colonies on the nutritious medium in comparison with the control. It revealed an interesting fact that saline NaCl, which had previously been processed by magnetite nanoparticles also significantly, had a marked bacteriostatic effect on the studied microorganisms. This effect could be explained by mechanism of change in the polarization structure water of microorganisms by magnetite nanoparticles. It was discovered that degree of expression of bacteriostatic action which induced by magnetite nanoparticles had correlation with marks of reactions intensity of FRLP. Maximum bacteriostatic effect on *Staphylococcus aureus* was expressed in second variant application of magnetite nanoparticles where mechanism of sorption was more significant than action of the magnetic field. On the contrary, maximum bacteriostatic effect on *Escherichia coli* and *Klebsiella pneumoniae* was revealed in third variant, where time exposition of contact with microorganism's nanoparticles and, consequently, action of a constant magnetic field was determinative.

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Physicochemical characterization of the starch from Ethiopian potato *(Plectranthus edulis)*: a potential pharmaceutical excipient

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Starch from the tubers of Ethiopian potato *(Plectranthus edulis) (Fam. Lamiaceae)* has been isolated and examined for its chemical composition, amylose content and physicochemical properties. The yield of starch was about 80.4% on dry weight basis. The proximate composition of the starch on dry weight basis was found to be 0.14% ash, 0.21% lipid, 0.43% protein, and 99.22% starch. The amylose content was 30.6%. Its true density and moisture content values were 1.47 g/ml and 11.2%, respectively. Scanning electron microscopy (SEM) of the starch granules showed characteristic morphology that was by large oblong (elliptical) with some oval-shaped granules. The starch has normal granule size distribution with a mean particle size of 36.20 µm. The DSC thermograms of P. *edulis* starch obtained from starch-water mixtures (1:1), exhibited higher T_o (69.2°C), T_p (74.3°C) and T_e (83.3°C) values than those of potato starch. X-ray diffraction pattern of the starch was typical B-type with a distinctive maximum peak at 17.5o2θ. The starch possesses higher swelling power and moisture sorption pattern, but lower solubility values than those of potato starch at all temperatures studied. Considering the high yield value and some similar physico-chemical properties to those of potato starch, P. *edulis* (Ethiopian potato) can be explored as an alternative source of starch for various applications.

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1D and 2D materials, flexible electrodes and tunable surfaces

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I will present three of our primary research topics, as each relates to 1D/2D materials, substrates and surfaces. First, I will focus on our investigation of chemical vapor deposition (CVD)-growth of transition metal dichalcogenides (TMDs) as well as their heterostructures, and characterization to illuminate the role of dissimilar 2D substrates in the prevention of interior defects in TMDs. We further demonstrate the epitaxial growth of TMDs on hBN and graphene, as well as vertical/lateral heterostructures of TMDs, uniquely forming in-phase 2D heterostructures. This research provides a detailed observation of the oxidation and anti-oxidation behaviors of TMDs, which corroborate the role of underlying 2D layers in the prevention of interior defects in TMDs. If the technique could be developed to be highly reliable and high fidelity, it could have a large impact on the future research and commercialization of TMD-based devices. The second research area concerns our development and application of flexible electrodes and energy storage toward wearable and multifunctional electronics. Here, we develop a facile fabrication technique utilizing vertically aligned carbon nanotubes (VACNTs), which enables high-throughput fabrication of flexible electrodes. For example, our structure shows a high flexibility and stability during stretching up to 20% and bending up to 180 degrees, promising for various flexible electronics applications. Lastly, we investigate and utilize smart polymer functional surfaces using dodecylbenzenesulfonate-doped polypyrrole (PPy (DBS)); we demonstrate a novel *in situ* control of droplet pinning on the polymer surface, enabling the control of droplet adhesion from strongly pinned to extremely slippery (and vice versa). The pinning of organic droplets on the surfaces is dramatically controlled *in situ*, presenting great potential for manipulation and control of liquid droplets for various applications including oil separation, water treatment and anti-bacterial surfaces. We believe that our work represents a major advance in materials science and engineering, especially pertaining to those topics that involve functional and tunable surfaces.

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Development of a novel drug delivery system comprising biopharmaceuticals for dermal and nail delivery

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Predominantly, the majority of fungal infections (dermal and nail) are caused by dermatophytes, such as *Trichophyton rubrum* known as one of the most prominent. Among fungal infections, nail infections or onychomycosis exhibit the most difficulties and limitations in their treatment. Onychomycosis affects around 5-10% of the population in the world. Onychomycosis is a common infection of the nail caused by dermatophyte affecting mostly toenails in adults being associated with limited treatment options. In this study novel dosage forms were prepared and evaluated for their suitability in treatment of onychomycosis. Films were prepared comprising polymeric excipients such as chitosan, (hydroxypropyl) methyl cellulose, hydroxyethyl-cellulose, carboxymethylcellulose according to solvent evaporation method. Developed formulations were evaluated in terms of physical appearance, stability and adhesiveness. Furthermore skin and nail irritation studies were conducted. Five potential formulations (F1-F5) were designed while F1 and F4 exhibited the most promising results in terms of stability with 26 min and 40-67 min, respectively, and suitability in nail application. F1 as the most favorable dosage form revealed with 2.9438 kg/m/s in terms of adhesive force the most adhesive properties in contrast to the other preparations. All formulations were found to be non-skin irritating and safe to use. Taken together, these findings suggest novel designed films containing polymeric excipients as a fruitful platform for the treatment in onychomycosis.

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Anti-rhinovirus activity of ethyl 4-(3-(2-(3-methylisoxazol-5-yl) ethoxy) propoxy) benzoate (EMEB)

Giulio Tarro
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The compound EMEB has got a definite anti-rhinovirus activity on both HRV14 (group A) and HRV39 (group B). The specific activity is lower than that found for pirodavir used as a positive control, but, since the cytotoxic activity of EMEB on human HeLa cells is more favourable than that of pirodavir (50 µg/ml against 3 µg/ml), the final protection index is higher for EMEB (>700) as compared to pirodavir (250). EMEB seems to be stable in aqueous solutions, since its activity after 10 days was unchanged. When EMEB is challenged with Rhinovirus infected HeLa cells during the whole reproduction cycle, its antiviral activity remains evident and strong even after 18 hours from infection. This fact is important because it means that the compound keeps functioning even when the viral infection is already in progress; this finding makes us to hypothesize that the compound EMEB could act not only as a prophylactic agent against the common cold, but also as a therapeutic drug in patients who already show the disease symptoms (at least within the first 24 hours from the start of symptoms). These last statements must be confirmed with assays on the mechanism of action of the compound, by analyzing its adhesion to the cell virus internalization into the cells, the viral uncoating, transcription and translation, and finally on viral morphogenesis.

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Fast dissolving drug delivery systems

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Fast-dissolving formulations represent excellent opportunities for life cycle management to the pharmaceutical companies. Fast dissolving technologies have many advantages like ease of swallowing, administration without water, quick onset of action for improving both patient convenience and compliance as benefits for the patient; extended life cycle, product differentiation, patent protection as benefits for pharmaceutical companies. But there are some challenges for formulation development studies like taste -masking, disintegration time, moisture sensitivity, friability, packaging and intellectual property issues, especially for the generic companies. The technologies are under patent protection like Zydis®, Flashtab®, OraSolv® and DuraSolv™, and WOWTAB®. One of the major issues is a taste-masking problem may be overcome with using cyclodextrins, polymer coating, flavoring and sweetening agent, microencapsulation techniques. There are some modified excipients for providing both taste-masking and product ability properties in the formulation like Ludiflash® and Pharmaburst®. From the analytical development point of view, there are several different methods from conventional dosage forms which are determined in the Pharmacopoeias. And for comparison and assessment of taste masking, electronic tongue may be a good opportunity, which was developed by Alpha MOS. In the sense of generic companies, developing a fast dissolving tablets version of an existing immediate-release product means that the two formulations must be bioequivalent, and this can be challenging for in-vivo studies, especially if the method of taste masking retards the dissolution rate of the active ingredient after disintegration. What about the future of fast dissolving technologies? Orally disintegrating extended Release (ODT-ER) dosage forms are providing all of the benefits of these two drug delivery technologies in a single pharmaceutical product. And oral rapid films also may be a good alternative, especially for the OTC market.

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Essential considerations for selecting clinical research organizations (cross): Pragmatic guidance for biotech companies based on case-studies in Europe, Japan, and the US

Hiroko Tadano

Trans World Clinical Alliance, Netherlands

Senior management in biotechnology organizations span the gamut of industry expertise from deep academic and research backgrounds to corporate, global biopharma skills, and everything else in between. This internal collective corporate experience and history often drives how a clinical research organization (CRO) partners are eventually selected, and often without considerations to other key imperative elements that determine the best fit, for the immediate as well as the long-term needs of a clinical development program. The presenters will utilize case-study examples from biotechnology companies in Europe, Japan, and the US to describe how biotechnology companies can increase their chances of success in choosing an appropriate external clinical development partner. Understanding where blind-spots often occur, how to navigate internal corporate mind-sets, and individual biases will be discussed through case-examples. Various approaches and solutions will be highlighted, and specifically tailored for the small- to mid-size biotechnology companies. The presenters will also discuss critical issues in the selection process such as fees, deliverables, timelines, and managing disappointments.

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Recent applications of nanotechnology in advanced drug delivery systems

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Nanotechnology is attracting great attention worldwide in biomedicine. Targeted therapy based on drug nanocarriers systems enhances the treatment of tumors and enables the development of targeted drug delivery systems. In recent years, theranostics are emerging as the next generation of multifunctional nanomedicine to improve the therapeutic outcome of cancer therapy. Polymeric nanoparticles with targeting moieties containing magnetic nanoparticles as theranostics agents have considerable potential for the treatment of cancer. The use of directed enzyme prodrug therapy (DEPT) has been investigated as a means to improve the tumor selectivity of therapeutics. Magnetic DEPT involves coupling the bioactive prodrug-activating enzyme to magnetic nanoparticles that are then selectively delivered to the tumor by applying an external magnetic field. Gene therapy is an attractive method for meeting the needs for curing brain disorders, such as Alzheimer's disease and Parkinson's disease. On the other hand, due to the fact that hepatocellular carcinoma (HCC) is resistant to standard chemotherapeutic agents, gene therapy appears to be a more effective cure for HCC patients. Ultrasound-mediated drug delivery is a novel technique for enhancing the penetration of drugs into diseased tissue beds noninvasively. This technique is broadly appealing, given the potential of ultrasound to control drug delivery spatially and temporally in a noninvasive manner.

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Finding pharmaceutical agents by assembling chemotypes

Jun Xu, Mengyang Xu, Liangyue Wang, Chao Zhao and He Peng
Sun Yat-sen University, China

This talk introduces *a de novo* chemotype (substructure) generation algorithm (DSGA) that derives frequent substructures in order to avoid the subjectivity of empirical method, and avoid the meaningless substructures generated from algorithmic approaches by statistical analyses. DSGA derives frequent chemical substructures (FCS) from a large compound library. In an FCS, substructures are not inter-included. When the library is big enough to represent the chemical diversity, such as ZINC database (27 million medicinal compounds), the resulting FCS is termed as the FCS dictionary (FCSD) for drug-like compounds. For a focused compound library (FL), DSGA can derive a focused FCS (fFCS) from FL. (fFCS) can be used as structural descriptors for focus library SAR studies. Six focused libraries against targets PDE4D, mTOR, HDAC1, DPP4, BACE and ALR2 were tested with DSGA approach. Using the (fFCS) as structural descriptor sets, six virtual screening models were generated to predict ligands against the targets; the prediction accuracies are greater than 90%. Three methods were proposed to assembly drug-like molecules from substructures: Using the laws in the nature, such as isoprene rule; organic synthesis rules, such as retro-synthon rules proposed by E J Corey; pharmaceutical rules derived from a focused compound library against a specific target. We use DSGA to figure out rules that are used to compose privileged scaffolds by assembling FCS. It can be chemically challenging to make the compounds proposed by these assembling approaches. By combining DSGA method, bioisosterism method and click chemistry, we generated privileged chemome (substructures/chemotypes) from Hsp90 inhibitor library, and then found out available chemical fragments with bioisosterism rules. With SPR technology, we confirmed the fragments that interacted with Hsp90. Finally, we used “click chemistry” to assemble the substructures and produced nanomolar selective Hsp90 inhibitors.

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Involvement of D1/D2 dopamine receptors within the nucleus accumbens and ventral tegmental area in the development of sensitization to antinociceptive effect of morphine

Leila Zarepour
Iran University of Medical Science, Iran

The nucleus accumbens (NAc) and the ventral tegmental area (VTA) are two major areas for the mesolimbic dopaminergic system, which are strongly involved in the development of behavioral sensitization. In the present study, we investigated the role of D1/D2 dopaminergic receptors within the NAc or VTA in response to sensitization to morphine by the tail-flick test as a model of acute pain. Sensitization was induced by subcutaneous (SC) injection of morphine (5 mg/kg), once daily for three days followed by five days free of drug. After the sensitization period, antinociceptive responses induced by an ineffective dose of morphine (1 mg/kg; SC) were obtained by the tail-flick test and represented as maximal possible effect (%MPE). In experimental groups, D1 and D2 receptor antagonists, SCH-23390 and sulpiride (0.25, 1 and 4 µg/rat), were separately microinjected into the NAc or VTA, 10 minutes before morphine administration during the sensitization period, respectively. Results showed that, injection of morphine during the sensitization period (development of sensitization) increased %MPE of the ineffective dose of morphine from 2.43±1.4% in naive to 47.75±4.01% in sensitized animals ($P<0.001$). Unilateral microinjections of different doses of the D1/D2 receptor antagonists, SCH-23390 and sulpiride, into the NAc dose-dependently decreased %MPEs in morphine-sensitized animals. Nonetheless, %MPEs were only affected by intra-VTA administration of SCH-23390 in morphine-sensitized animals ($P<0.05$). Our findings suggest that both the D1/D2 dopamine receptors in the NAc and the D1 receptors in the VTA may be of more important in the development of sensitization to in rats.

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A novel class of parenteral anticoagulant agents for percutaneous coronary intervention (PCI) based on tick thrombin inhibitors

R Manjunatha Kini

National University of Singapore, Singapore

Hematophagous insects depend on potent anticoagulant and antiplatelet agents for securing their blood meals. We identified a novel class of thrombin inhibitors, named as ixothrins, from the salivary gland extracts of ticks. We isolated and characterized variegin and avathrin from the salivary gland extracts of tropical bont tick *(Amblyomma variegatum)*. They are among the smallest thrombin inhibitors found in nature. We examined the structure-function relationships of variegin, avathrin and ultravariegin using a number of mutants. We also determined the X-ray crystal structure of thrombin-variegin and thrombin-avathrin complexes. They interact with exosite I, prime subsites and active site of thrombin. Based on the structure as well as the prior knowledge on thrombin inhibitors, we designed several peptides to understand the interaction between thrombin and these inhibitors. These peptides cover a diverse spectrum of potency, kinetics and mechanism of inhibition, including peptides with affinities ranging from low picomolar to nanomolar values, with fast and slow tight binding, displaying competitive and non-competitive inhibition. We evaluated the antithrombotic efficacy (carotid artery thrombosis and stent thrombosis models) and bleeding side effects (tail incision and ear bleeding models) of variegin in rats and pigs, respectively. The results strongly support the superior antithrombotic efficacy of variegin with minimal bleeding in comparison with comparator drugs, heparin and hirulog (Bivaluridin or Angiomax®). Thus, ixothrins may have the potential in developing parenteral anticoagulant agents for percutaneous coronary intervention (PCI).

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Inhibition of aortic calcification by policosanol in dyslipidemic rabbits is enhanced by pentoxifyllin: Potential role of PCSK9

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Policosanol (POL) is a hypocholesterolemic drug of natural origin and has been shown to reduce circulating levels of proprotein convertase subtilisin/kexin type 9 (PCSK9) in healthy subjects. Recently, we have reported that POL can attenuate aortic calcification in diabetic dyslipidemic rats; however, the underlying mechanism is not fully elucidated. We aimed to investigate the effect of POL on aortic calcification and if PCSK9 has a contributory role, and also to examine whether combination of POL with pentoxifylline (PTX), as antitumor necrosis factor alpha (TNFα) would offer additional benefits. Thirty adult male New Zealand rabbits weighing 1.5–2 kg were randomly assigned into five groups. One group received standard chow diet and served as normal control group (NC). The other four groups received 0.5% w/w cholesterol rich diet for 12 weeks and concurrently treated with placebo, POL, PTX or combination of POL and PTX. Sera samples and aortic tissue were collected for biochemical measurements and histological assessment. Rabbits fed cholesterol rich diet demonstrated dyslipidemia, increased inflammatory state and elevated serum levels of PCSK9, compared to NC group. Aortic calcification was evident in dyslipidemic rabbits, represented by increased calcium deposition and osteopontin (OPN) expression in aortic tissue, along with elevated serum levels of alkaline phosphatase (ALP) and osteocalcin (OCN). Dyslipidemic rabbits showed a significant up regulation of wingless type MMTV integration site family 3A (Wnt3a) and bone morphogenetic protein 2 (BMP 2) genes in their aortic tissue. POL significantly reduced circulating PCSK9 levels, suppressed calcification markers and attenuated aortic calcification. Combination of POL with PTX alleviated aortic calcification to greater extent than either monotherapy, which may be attributed to further suppression of PCSK9 and calcification markers. These findings suggested that POL exerted anti-calcifying effect partly via inhibition of PCSK9. Combination of POL and PTX offered additional benefits and might represent a promising therapeutic option for aortic calcification.

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Fluorescent and T1 MRI active multilayer nanoparticle for imaging and targeting cellular delivery

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Multifunctional plasmonic nanostructures have enormous potential in the treatment of solid tumors; however, tracking particles with drug cargo and triggering the release of the cargo in mapped tumors is still impossible. To overcome this challenge we have developed an MRI and fluorescent active nanostructure nanomatryoshka. This new nanostructure with IR plasmonic signatures is composed of a 50 nm Au core surrounded by dye molecules and Gd (III)-DOTA chelate doped SiO_2 inner-shell and an outer Au shell. The experimental result demonstrates an enhanced T_1 relaxation (r_1~24 mM^{-1} s^{-1} at 4.7 T) compared to the clinical Gd (III)-DOTA chelating agents (r_1~4 mM^{-1} s^{-1}). Further, this design preserves the fluorescence signal (65%) after 24 hours of exposure, leading to enhanced fluorescence photostability (23x). This dual-imaging functionality nanosystem increases MRI sensitivity by concentrating Gd (III) ions into the Gd-NMs, reduces the potential toxicity of Gd (III) ions and dye molecules by preventing their release *in vivo* through the outer Au shell protection, and the terminal gold layer surface can then be functionalized to increase cellular uptake, circulation time, or thermal drug-release properties.

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Antivenom immunoglobulin

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Envenomation by snake and scorpion bite is a real public health problem in North Africa. Algeria alone records 50000 scorpion bites per year and between 50-100 deaths, of which 80% are unfortunately children. The therapeutic management of severe forms of envenomation is based, among other things, on the administration of specific immune sera. We will see in this illustration, the process of preparation of these anti-venoms, obtained by harvesting and then purifying the antibodies from plasma produced by the donor animal (horse) at the Pasteur Institute of Algeria.

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6th European Biopharma Congress

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Modulating drug release from sustained release polyethylene oxides: effect of vitamin E, mannitol and dicalcium phosphate

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Introduction & Objective: Different molecular weight forms of polyethylene oxide can be used successfully in controlled release drug delivery due to their excellent matrix forming properties. The objective of this study is to investigate the effect of vitamin E succinate and different fillers on release rate stability of highly soluble drug diltiazem HCl containing polyethylene oxides.

Results & Discussion: The effect of storage conditions showed that the release rate of the drug was significantly increased from tablets that were stored for longer periods at 40°C. That is to say, drug release was faster at longer storage times (8>4>2>0 weeks).The increase in drug release is expected to be due to oxidative degradation primarily in the amorphous region of the polymers that there was significant decrease in the drug release rate of the formulations that contained mannitol and DCP. The results in indicated the use of vitamin E stabilized PEO and decreased the rapid drug release occurring as a result of the storage time (2, 4, 8 weeks) at 40°C. The reason behind this phenomenon could be when vitamin E was dispersed in the PEO containing drug; it delayed the penetration of oxygen into the PEO matrix during the storage time.

Conclusion: The results indicated that PEO can successfully be used in controlled release drug delivery; vitamin E and fillers stabilized drug release from aged matrices containing PEO.

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The key to Manufacturing Viral Vaccines for individual Human Population

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Nowadays, subunit viral vaccine becomes the major choice for manufacturing viral vaccine with a thought of safety reason to prevent side effects. However, the success to use subunit viral vaccine to prevent a particular viral infection is very limit. This is different from the time when Cowpox virus was originally used for vaccination to prevent the smallpox viral epidemic over a century ago. Although the knowledge of immunity has been discovered a lot more than the Edward Jenner's period, the effectiveness of viral vaccine could not reach our accomplishment. Accordingly, we need to revise our knowledge and manipulate in the right direction for the viral vaccine production. Basically, to induce an immunity to prevent a viral infection, our body must produce a specific antibody which needs induction not only by a particular viral antigen but also the molecules called major histocompatibility complex (MHC). Each molecule of MHC alleles plays a key role in the immune response by forming a specific complex with its appropriate epitope to induce a specific T cell clone thru its specific receptor. MHC class I is required for inducing cytotoxic T cell while MHC class II is for helper T cell. Helper T cell plays a key role to induce an effective stage of acquired immunity especially a specific antibody which is believed to be a gearwheel to prevent an invasion of the particular viral particle. To produce the viral-specific antibody, MHC class II plays a key role to induce helper T cell and then B cell to synthesize a specific antibody. Since the MHC gene alleles are highly polymorphic so the possibility that individuals have the same gene alleles might be one in a million which, mostly, can be found in those who are an identical twin. Accordingly, a subunit viral vaccine, which contains a limit number of epitopes, would reduce a capacity of an antigen presenting cell, such as a dendritic cell, to process some epitopes to induce the particular helper T cell clones. Subsequently, the corresponding B cell clones cannot synthesize the specific antibody to neutralize the particular infectious viral particle. Accordingly, this presentation will present a different notion and principle to develop a viral vaccine for an individual human population.

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From traditional materials to modern drug: How Chinese medicines contribute to new drug discovery

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Facing complicated diseases and unmet medical needs, drug discovery and development from Chinese medicines should have new strategy. There are about 25% modern drugs inspired from traditional medicine including Chinese Medicine. The way of drug discovery and development in past 100 years is from natural resources to chemical synthesis, but no matter whether it is natural compound or synthesized compound drug discovery and development are more and more difficult. Not only experience in natural materials, but also wisdom and knowledge in traditional medicine may help form new strategy to discover new drug. It is known that 25% modern drugs were inspired from traditional medicine. It has been intensively studied a lot about natural resource in terms of chemical and pharmacological profiles. So far, over 10000 single compounds were isolated from Chinese medicines (Chinese medicinal plants, animal parts and minerals) among which some have been identified as new drugs such as ephedrine, artemisinin and arsenic trioxide etc., while others are promising drug candidates suggesting that Chinese medicines are still an important resource for new drug discovery. It is more amazing, if we watch composite formulae, they are over 100000 in total. Clinically, Chinese medicines mainly use composite formulae to treat various diseases, especially complicated diseases. Recently, both experimental and clinical studies showed Realgar-indigo naturalis, qili qiangxin capsules and compound danshen dripping pills are promising formulae for treatment of acute promyelocytic leukemia, chronic heart failure and coronary heart disease. Actually, Western medicines also often use combination therapy for disease treatment in clinical setting, such as cancer, hypertension and AIDS etc. To this goal, we developed a comprehensive, dynamic and specific strategy for drug discovery for cancer and metabolic diseases as one attempt. This presentation will talk about drug discovery from single compounds to multiple components as drug candidates in Chinese medicine by recent developed technologies.

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