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Maria Arkel, Drug Des 2017, 6:4(Suppl)
DOI: 10.4172/2169-0138-C1-017

Synthesis of creatine derivatives for the treatment of creatine deficiency disorders

Maria Arkel
University of Genova, Italy

Creatine plays an essential role in the energetic metabolism and serves dual purpose: under normal conditions, it provides high-energy phosphate to the cellular ATPases; under conditions of higher energy requirements or of ischemia, it provides an energy reserve to postpone anoxic depolarization. The main drawback of creatine is due to its hydrophilic nature and consists in its poor crossing of both the blood-brain barrier and the cell plasma membrane, that creatine crosses using a specific transporter, CrT1. The lack of creatine in the brain is mainly due to three severe diseases, CDS (Creatine Deficiency Syndromes), among which CrT1 deficiency is currently an incurable disease, as administered creatine is not able to reach the brain since the transporter is not functional. This project describes the synthesis and biological studies of some creatine derivative compounds which are able to cross biological membranes in an independent way from the CrT1. There can be two different approaches for this purpose: 1) creatine lipophilic derivatives able to cross lipid-rich biological membranes without using the CrT1. This strategy consists in the synthesis of a modified creatine that is more lipophilic than creatine itself, a diacetyl-creatine ethylester. 2) creatine derivatives in which creatine is linked to a carrier able to use a different transporter from CrT1. This strategy consists in the synthesis of a chimeric molecule composed of creatine and a sugar in order to utilize the glucose transporters in the brain. The following biological tests have been carried out: 1. Stability determination by means of mass spectrometry analysis; 2. Study of the neuroprotective effect; 3. Biochemical tests to measure the concentration of creatine and phosphocreatine in the tissue.

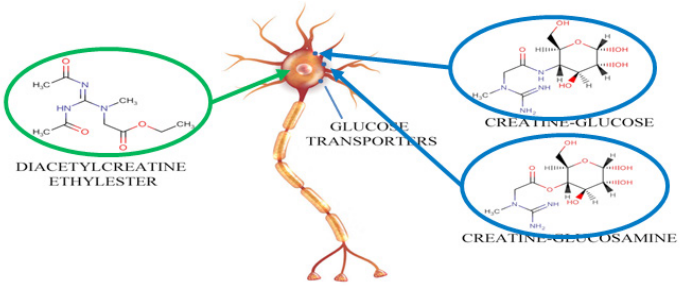

Figure : Two different kind of prodrugs have been synthesized in order to carry the creatine molecules across the neurons membranes: one exploiting its lipophilic nature and the other one utilize alternative transporters instead of SLC6A8

Biography

Maria Arkel is a 3rd year PhD student, working on organic synthesis of biomolecules, particularly creatine derivatives, and their characterization by means of HPLC and mass spectrometry. Her research fields also include biological tests on amino acid derivatives and peptide synthesis.

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Ali Asram Sagıroglu et al., Drug Des 2017, 6:4(Suppl)
DOI: 10.4172/2169-0138-C1-017

Design, optimization and characterization of coenzyme Q10 and D-panthenyl triacetate loaded liposomes

Ali Asram Sagıroglu[1], **Burak Çelik**[1] and **Samet Özdemir**[2]
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Statement of the Problem: Coenzyme Q10 (CoQ10) is a lipid soluble molecule that is found naturally in many of the eukaryotic cells that is essential for electron transport chain and energy generation in mitochondria. It has strong antioxidant, skin protecting and wound healing properties, therefore used widely in topical formulations. D-panthenyl triacetate (PTA) is an oil soluble derivative of D-panthenol, which is essential for coenzyme A synthesis in the epithelium. PTA slowly deacetylate into D-panthenol inside the skin acting as a reservoir which is necessary for cutaneous wound healing, protection and rejuvenation of the skin.

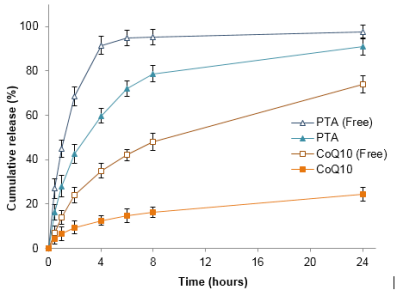
Methodology & Theoretical Orientation: Liposomal formulations that encapsulate both ingredients were prepared and optimized by applying response surface methodology, for the purpose of increased stability and skin penetration Findings: The optimum formulation composed of 4.17 mg CoQ10, 4.22 mg PTA and 13.95 mg cholesterol per 100 mg of soy phosphatidylcholine. The encapsulation efficiency (EE %) of the optimized formulation for CoQ10 and PTA was found 90.89%±3.61 and 87.84%±4.61, respectively. Narrow size distribution was achieved with an average size of 161.6±3.56 nm, while spherical and uniform shape was also confirmed from scanning electron microscopy (SEM) and transmission electron microscopy (TEM) images. Cumulative release of 90.93% for PTA and 24.41% for CoQ10 was achieved after 24 hours of *in vitro* release study in sink conditions. Physical stability tests indicated that the optimized liposomes were suitable for storage at 4°C over at least 60 days.

Conclusion & Significance: It can be concluded that encapsulating both PTA and CoQ10 is a promising way for prolonged effect and simultaneous delivery of both ingredients. Based on these findings, possible effects of our optimized liposomal formulation on wound healing mechanism will be further investigated in cell culture studies.

Figure 1 In vitro release profiles PTA and CoQ10 from the optimized liposomes along with free PTA and CoQ10 solutions as controls.

Notes: Each data represents the mean ± SD (n=3).

Abbreviations: PTA, D-panthenyl triacetate; CoQ10, coenzyme Q10.



Biography

Ali Asram Sagiroglu is PhD student in Pharmaceutical Technology. His research areas are: Nano Particle Characterization, Modification and Characterization of Polymers, Polymeric Drug Delivery Systems, and Nano Drug Delivery Systems.

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Young Bong Kim et al., Drug Des 2017, 6:4(Suppl)
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Development of a Middle Eastern respiratory syndrome coronavirus DNA vaccine using baculoviral delivery system

Young Bong Kim, Yu-Youn Jang, Hanul Choi, Han Sam Cho, Sehyun Kim and **Youn Dong Cho**
Konkuk University, South Korea

Middle East respiratory syndrome coronavirus (MERS-CoV) has emerged as a new pathogen that can transmit between humans as well as animals and humans, causing severe complications and high mortality rates. Since the MERS was first discovered at the end of 2012, it spread and has caused more than 1,800 infections and 650 deaths. No direct treatments are available yet, highlighting the importance of prevention through suitable vaccination regimes. The viral spike (S) protein has been characterized as a key target antigen for vaccines. The MERS-CoV spike (S) protein is responsible for receptor binding and virion entry into the cell and is highly immunogenic and induces neutralizing antibodies. In this study, we constructed a human endogenous retrovirus (HERV) envelope-coated, baculovirus-based, MERS-CoV DNA vaccines (S full gene, S1, and receptor binding domain (RBD) gene delivering vaccines. AcHERV-MERS (1×107 FFU) were intramuscularly injected into mice, and blood samples were collected every 10 days after immunization. The immunized sera showed high titers of MERS-Cov antibodies and neutralizing activity against MERS-CoV without adjuvant. The AcHERV-MERS could be a potential DNA vaccine candidate

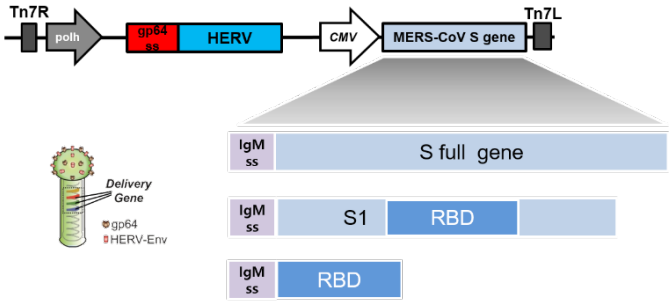

Figure: Schematic diagram of n MERS-CoV DNA vaccine constructs. Full-length Spike gene, Spike S1, and RBD gene were cloned under the CMV promoter. Each target genes contain the IgM signal peptide

Biography

Young Bong Kim received his Doctorate from Sogang University in Korea and trained at the NIAID/NIH in the United States. Since his appointment as a Professor at Konkuk University in 2003, he has been working on several vaccines against pathogenic viruses such as HIV, MERS-CoV and ZIKA virus.

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Zorica Naumovska et al., Drug Des 2017, 6:4(Suppl)
DOI: 10.4172/2169-0138-C1-017

(S)-EL-7 new selective competitive antagonists for AMPA and KA receptors

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[2]University of Copenhagen, Denmark

Ionotropic glutamate receptors (iGluRs) constitute a family of ligand gated ion channels subdivided in three classes NMDA, AMPA (iGluA1-4) and KA (iGluA5-7 and KA1,2) according to the agonist that selectively activates them. They are critically important for normal brain function and are considered to be involved on neurological disorders and degenerative diseases such schizophrenia, Alzheimer's disease, brain damage following stroke and epilepsy. Extensive studies on GluA2 receptors were performed and many crystal structures as complexes of GluA2-LBD with agonists, partial agonists and antagonists were obtained. AMPA receptor antagonists are considered to have clinical potential as neuroprotective drug candidates. In order to identify the structural determinants for receptor selectivity between homomeric AMPA and KA receptors a serial of rigid and flexible biaromatic alanine derivatives carrying selected hydrogen bond acceptors and donors has been synthesized based on published X-ray structure of competitive antagonist (S)-ATPO co-crystallized with iGluR2(S1S2J) LBD. The compounds were tested in radioligand binding studies on recombinant iGluA1-7 receptors. Based on these results and on the results obtained from molecular modeling studies, important structure-activity relationships at AMPA and GluR5 were established. A group of compounds selective for either GluR5 or AMPA receptors were identified. Suitable crystals for X-ray crystallography were obtained from (S)-EL-7-iGluR2 (S1S2J) complex. This X-ray structure provides structural information on the water-mediated interactions between the ligand and Tyr702, a non-conserved amino acid residue within the ligand binding pocket among the four AMPA receptor subunits. It has been identified as important determinant for AMPA receptor agonist subunit selectivity. This position is not responsible for the observed subunit selectivity of (S)-EL7 as it was expected from the results acquired with molecular docking which suggested direct hydrogen bonding. The domain closure achieved by (S)-EL-7 ranges between 6.9˚-9.2˚ value in between what has been observed previously for antagonists (ATPO:2.5˚-5.1˚) and partial agonist (KA:13˚).

Biography

Zorica Naumovska is working currently as an Assistant Professor in Faculty of Pharmacy in Skopje, Macedonia in the Institute for Pharmaceutical Chemistry and is involved in teaching and research in Pharmaceutical Chemistry, Drug Discovery and Development, Pharmacogenetics, Drug Information and Clinical Pharmacy. She has finished her Master's degree working on the project in collaboration with Department of Drug Design and Pharmacology in Faculty of Health and Medical Sciences in University of Copenhagen. Her fields of interest are neurodegenerative and psychiatric diseases and she has defended PhD thesis considering influence of polymorphic variation of metabolic enzymes and transporter proteins in drug responses for these diseases. She has specialization in Drug Information and is Head of the National Drug Information Centre since 2014. She is active member in ISPOR-Macedonia, Pharmaceutical Association of the RM, Pharmaceutical Chamber of the RM, and European Association of Clinical Pharmacy.

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Shan-Chi Tsai et al., Drug Des 2017, 6:4(Suppl)
DOI: 10.4172/2169-0138-C1-017

Electrophoresis of an emulsion droplet near a charged plane

Shan-Chi Tsai and **Eric Lee**
National Taiwan University, Taiwan

Middle East respiratory syndrome coronavirus (MERS-CoV) has emerged as a new pathogen that can transmit between humans as well as animals and humans, causing severe complications and high mortality rates. Since the MERS was first discovered at the end of 2012, it spread and has caused more than 1,800 infections and 650 deaths. No direct treatments are available yet, highlighting the importance of prevention through suitable vaccination regimes. The viral spike (S) protein has been characterized as a key target antigen for vaccines. The MERS-CoV spike (S) protein is responsible for receptor binding and virion entry into the cell and is highly immunogenic and induces neutralizing antibodies. In this study, we constructed a human endogenous retrovirus (HERV) envelope-coated, baculovirus-based, MERS-CoV DNA vaccines (S full gene, S1, and receptor binding domain (RBD) gene delivering vaccines. AcHERV-MERS (1×107 FFU) were intramuscularly injected into mice, and blood samples were collected every 10 days after immunization. The immunized sera showed high titers of MERS-Cov antibodies and neutralizing activity against MERS-CoV without adjuvant. The AcHERV-MERS could be a potential DNA vaccine candidate.

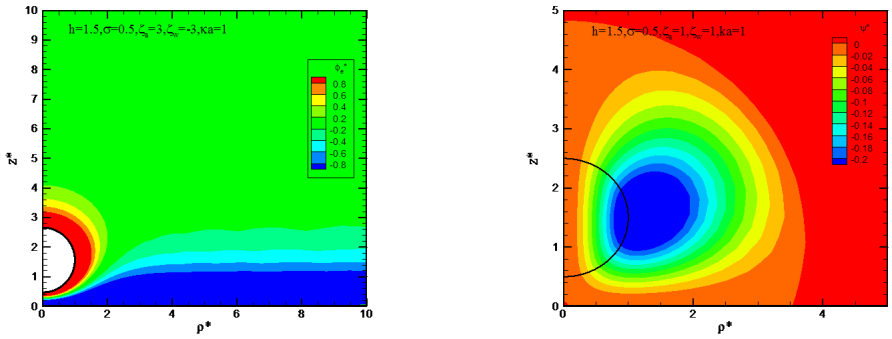

Figure: Equilibrium electric potential Contour of streamline

Biography

Shan-Chi Tsai is currently a PhD student under the guidance of Professor Eric Lee. She has a journal paper published in *Langmuir* in 2016, "Electrophoretic and Electroosmotic Motion of a Charged Spherical Particle within a Cylindrical Pore Filled with Debye–Bueche–Brinkman Polymeric Solution. Langmuir.".

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Snježana Zubčić et al., Drug Des 2017, 6:4(Suppl)
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Influence of extraction solvent in determination of selected corticosteroids in herbal dermatological products

Snježana Zubčić[1], Martina Matičević[2], Siniša Tomić[1] and **Rajka Truban Žulj[1]**
[1]Agency for Medicinal Products and Medical Devices of Croatia, Croatia
[2]University of Zagreb, Croatia

The use of herbal products has significantly increased in recent decades. One of the main factors leading to this trend is that consumers assumed that use of herbal products is safer and natural alternative to traditional medical treatments. It has been found that many of such so called natural products have been counterfeited by addition of active pharmaceutical ingredients. One of the groups of products of our interest was herbal dermatological products. The aim of the study was to find the most appropriate extraction solution for the best recovery of added synthetic corticosteroids in topical preparations before assay determination by chromatographic method. Four different extraction solutions were used and nine corticosteroids were determined, namely: alclometasone dipropionate, betamethasone dipropionate, betamethasone valerate, dexamethason, hydrocortisone acetate, clobetasol propionate, methylprednisolone acetate, mometasone fuorate and triamcinolone acetonide. For that purpose, validated analytical chromatographic method was used that was developed previously for assay determination of above mentioned compounds. Results show that 0.1% V/V acetic acid in methanol is the most appropriate extraction solution for 4 compounds namely, alclometasonezon dipropionate, clobetasol propionate, mometasone furoate and betamethasone dipropionate. Further, it can be seen that methanol gave the best recovery for 3 compounds - betamethasone dipropionate, mometasone froate and hydrocortisone acetate, and also acetonitrile was the best choice for 3 compounds - methylprednisolone acetate, betamethasone valerate and dexamethasone. Finally, in ethanol as extraction solution only 1 compound had the best recovery, triamcinolone acetonide. It can be seen from all of the obtained results that the best compromise extraction conditions, if one would like to extract most of above mentioned corticosteroids, would be accomplished by using acetonitrile as the extraction solution. Following acetonitrile, second choice for extraction more than half of mentioned corticosteroids would be both methanol or 0,1 % V/V acetic acid in methanol. The results suggest that addition of acetic acid changes the type of compounds that are extracted and efficiency of extraction procedure.

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Fatmi Sofiane et al., Drug Des 2017, 6:4(Suppl)
DOI: 10.4172/2169-0138-C1-017

Formulation and evaluation of camptothecin suppository as drug delivery for colorectal cancer

Fatmi Sofiane [1, 2], **M Iguer-Ouada**[2], **M Lahiani-Skiba**[1] and **M Skiba**[1]
[1] Rouen University, France
[2] Abderrahmane-Mira University, Algeria

The aim of the present work is to design and evaluate suppositories of camptothecin, an anticancer agent. Rectal suppositories of camptothecin alone, in binary systems (dispersed in PEG 6000 and complexed with cyclodextrin) and ternary systems (camptothecin complexes dispersed in PEG 6000) were prepared using various hydrophobic and hydrophilic polymeric bases like Semi-synthetic glyceride (Suppocire® AM Pellets) and polyethylene glycols (PEGs) mixtures. The obtained formulations were evaluated by various physical parameters like weight variation, drug content, hardness and liquefaction time. *In-vitro* release study was performed in USP type I apparatus using phosphate buffer pH 7.2 as dissolution media. The suppositories prepared were within permissible range of all physical parameters. *In vitro* drug released from water soluble base (PEG) was greater than that from oil soluble base, to reach ninety percent (90%) of drug dissolution. It is also established that the drug release from all the formulations is by diffusion mechanism (r = 0.9547 to 0.9967) according to Higuchi's equation. This work offers a new approach to colorectal cancer treatment.

Biography

Fatmi Sofiane has completed his PhD at the age of 34 years from Abderrahmane-Mira University and postdoctoral studies from Abderrahmane-Mira University. He has published more than 7 papers in reputed journals.

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R. Ketrane et al., Drug Des 2017, 6:4(Suppl)
DOI: 10.4172/2169-0138-C1-017

Dosage method validation using UV for prednisone active ingredient in 5 mg, PRECORTYL® generic pill- Princeps dissolution kinetic study

R. Ketrane and **N. Bouchara**
Université de Bejaia, Algeria

PRECORTYL® 5 mg is a generic presented as pills where CORTANCYL is its princeps. It consists of an active ingredient, which is Prednisone, and five excipients. PRECORTYL® 5 mg is a glucocorticoid drug. It is used to treat a large spectrum of immunologic, allergic and inflammatory diseases, including asthma and arthritis this is what makes its financial interest. To optimize the production costs a new method that consists on UV spectrophotometry is validated to be used in routine tests. The aim of this study is to validate an assay method of the active ingredient using a UV spectrophotometry as well as doing a comparative dissolution kinetic study. The obtained results of both tests are compliant according European pharmacopeia standards.

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Adam Master et al., Drug Des 2017, 6:4(Suppl)
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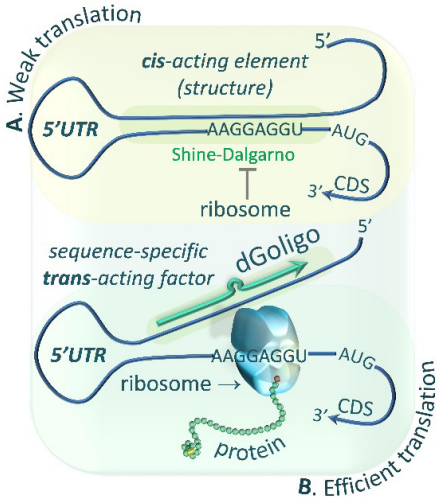
Gene-specific enhancement of protein synthesis by targeting 5'UTRs -A novel oligonucleotide-based strategy for translational control of selected tumor suppressors

Adam Master[1], **Anna Wojcicka**[2,3] and **Alicja Nauman**[2]
[1]DNAi - The Center of Genetic Information, Poland
[2]University of Warsaw, Poland
[3]Medical University of Warsaw, Poland

Background: The frequently reported lack of correlation between various mRNA and protein levels in cancers suggests that translational control can be an important target for new therapeutics regulating mechanisms of protein biosynthesis. Naturally occurring microRNAs and synthetic siRNAs are the most recognized regulatory molecules acting via RNA interference. Surprisingly, recent studies have shown that the interfering RNAs may also activate gene transcription via the newly discovered phenomenon of small RNA-induced gene activation (RNAa), triggered by promoter-specific small activating RNAs (saRNAs).

Findings: Here we show that oligonucleotide-based trans-acting factors termed dGoligos (dGs), which were designed by our dGenhancer calculator, can also specifically enhance gene expression at the level of protein translation by acting at sequence-specific targets within mRNA 5'-untranslated regions (5'UTRs) of THRB suppressor. The *in vitro* translation efficiency of reporter constructs containing alternative TRβ1 5'UTRs was increased by up to 55.8-fold following exposure to specific dGs. Complementary *in vivo* study showed that dGs can enhance TRβ1-5'UTR-mediated translation up to 4.8-fold. This method was successfully applied to enhance translation of another *CDKN2A* suppressor. Moreover, we show that the most folded 5'UTR has higher translational regulatory potential when compared to the weakly folded TRβ1 variant suggesting that the strategy may be especially applied to enhance protein synthesis from translationally non-active or less-active transcripts containing long complex 5'UTRs. dGs can serve as molecular switches to translationally active conformation of folded 5'UTRs leading to efficient translation of target mRNAs.

Significance: This study represent the first strategy for gene-specific translation enhancement using selective trans-acting factors designed to target specific 5'UTR cis-acting elements. This developmental strategy may complement other available methods for gene expression regulation including gene silencing and may find its use in enhancement of genes frequently silenced in cancers and other genetic disorders, especially at the level of translational control.



Biography

Adam Master has completed his Ph.D in medical sciences from The Center of Postgraduate Medical Education in Warsaw (medical biology), M.sc. from The Jagiellonian University in Krakow (molecular biology), Eng. from Krakow University of Technology (chemical technology, biotechnology of recombinant proteins). He has published 28 papers, more than 22 abstracts and 3 patents. In his work he has focused on translational control in cancer research, forensic sciences and genetic diagnostics in personalized molecular medicine. He is a member of The Polish National Chamber of Laboratory Diagnosticians, The American Society of Gene &Cell Therapy, and The British Society for Endocrinology.

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Ensure quality assurance for companies and institutions

Boyd L. Summers
Weber State University, USA.

Outside or inside quality assurance representatives are trained and chartered to partner with companies and/or institutions and instill quality, maintain process and product requirement compliance through in-house audits and evaluations and to provide oversight. Quality is inclusive for creating a community working together and establishes an inspired future for business management, employees and customers. Drive the growth of our people and our business through personal and professional development focused on disciplined execution and quality. At the start of each review period, auditors prepare for audit and evaluation planning by identifying contracts and those processes that will be evaluated during that specific review period. The purpose of the audits and evaluations ensure that activities and/or tasks are completed as planned and are compliant with approved company and/or institution plans and procedures. Companies and/or institutions maintain historical records (electronic or paper) such that they accurately reflect the activities and status they represent. Manage configuration and control of audit and evaluation records as required by company requirements are retained records for compliance and use for future improvements. There are other and effective methods for audits and evaluations, but the number one method is to ensure "Quality Assurance is First" and the other methods come in second!

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Electromembrane extraction combined with capillary electrophoresis for the determination of metoclopramide and ondansetron in urine samples.

Ehsan Sadeghi
Shahid Beheshti University, Iran

Electromembrane extraction (EME) is a sample preparation technique in pharmaceutical, chemical, clinical and environmental analysis. This technique uses electromigration across artificial liquid membranes for selective extraction of analytes and sample enrichment from complex matrices. This method has many advantages such as simplicity, rapid, low-cost, low LOD, high preconcentration factor and high recovery. In the present work, simultaneous preconcentration and determination of two basic drugs namely metoclopramide (MCP) and ondansetron (OSN) were studied using EME as a suitable extraction method, followed with capillary electrophoresis (CE) using ultraviolet (UV) detection as separation technique. The drugs were extracted from 4 ml sample solutions, through a supported liquid membrane (SLM) consisting 2-nitrophenyloctylether (NPOE) impregnated in the walls of a polypropylene hollow fiber, and into a 20 µL acidic aqueous acceptor solution resent inside the lumen of the hollow fiber with a potential difference applied over the SLM. The variables of interest, such as chemical composition of the organic liquid membrane, stirring speed, extraction time and voltage, pH of donor and acceptor phases and salt effect in the EME process were investigated and optimized. Under optimal conditions NPOE as SLM, stirring rate of 1000 rpm, 200 V potential differences, 20 min as the extraction time, acceptor phase HCl (pH 1.0) and donor phase HCl (pH 1.5). After the microextraction process, the extracts were analyzed by CE with optimum conditions phosphate running buffer (pH 2.0), applied voltage of 20 kV and 25°C. Under the optimum conditions, limits of detection (LOD) and quantification (LOQ) for MCP and OSN were 2.31-2.68 and 7.72-8.91 ng mL-1 respectively. Preconcentration factor and RSD for five replicates of each drugs were calculated to be 200 and 4.06-3.93 respectively. Finally, the applicability of this method was studied by the extraction and determination of these drugs in urine samples with recovery percentages of 87–92%

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Extraction and characterization of phytochemicals from white seringa (*Kirkia acuminata*) bark extracts

R M Chinheya, A Wakandigara and **J Kugara**
University of Zimbabwe, Zimbabwe

The intention of this study was to extract and characterize phytochemicals with analgesic effect from *Kirkia acuminata* bark extracts. Soxhlet extraction and steam distillation were used for the extraction of compounds. Methanol, dichloromethane and hexane were used as solvents. Classes of phytochemicals were identified by qualitative tests and thin layer Chromatography using UV light. The qualitative tests of the phytochemical screening indicated the presence of alkaloids, anthraquinones, glycosides, flavonoids, phenols, tannins to name a few. Alkaloids, flavonoids, phenols and tannins were also observed on thin layer chromatography. Menthol, catechol, 1,2 benzenediol-4-methyl, nitro phenyl salicylate, phenol dimethoxy, tau-cadinol, isopropenyl-8-dimethyl, menthone and levomenthone were identified using gas chromatography-mass spectrometer. The hexane fraction which is highly a non-polar solvent showed that very few phytochemicals were taken up in it. The polar solvents showed compatibility with the various chemical classes. The presence of these compounds gives *Kirkia acuminata* its characteristic property of being an analgesic. It thus finds application in the field of medicine.

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Indication of vascular endothelial growth factor binding components from herbal extracts by HerboChip: A platform for drug screening on a chip

Weihui Hu[1], **Gallant K L Chan**[1], **Huaiyou Wang**[2], **Michael Y T Cheng**[1], **Tina T X Dong**[1] **Zhongyu Zhou**[1,2] and **Karl W K Tsim**[1]
[1] Hong Kong University of Science and Technology, China
[2] Chinese Academy of Sciences, China

HerboChip is an array of different fractions deriving from herbal extracts, which could be applied in drug screening. Here, we aimed to identify effective components from traditional Chinese medicines (TCMs) that interact with vascular endothelial growth factor (VEGF) as a target using HerboChip. The extracts of TCMs were chemical standardized and fractionated by a standard HPLC profiling. The biotinylated-VEGF was hybridized with chips coated with different HPLC-separated fractions from the herbal extracts. Straptavidin-Cy5 was used to identify the VEGF-bound fractions. Over 100 chips were screened, and 8 positive hits were identified. The interaction of identified herbal extracts/phyto-compounds with VEGF was further confirmed in cultured human umbilical endothelial cells. As a result, the identified herbal extracts/compounds interfered (i.e. binding) with VEGF-induced cell proliferation and cell migration. The amounts of phosphorylated eNOS, phosphorylated Akt and phosphorylated ERK 1/2 were markedly altered in the co-application of the herbal extracts/compounds with VEGF. In addition, the phosphorylation of eNOS, Akt and ERK 1/2 could be modulated by the identified extracts/compounds. Six compounds from TCMs showed activating activities on the VEGF response, and two TCM compounds showed inhibiting activities. In conclusion, the current result supported the applicability of HerboChip for screening VEGF binding components from herbal extracts.

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Combinational strategy via co-delivery of drugs and siRNA by layered double hydroxide-based nanocomposites in cancer therapy

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Chemotherapy is one of most common cancer treatments in clinics. In most cases, the clinical responses show that the efficacy of chemotherapy is limited by the development of multidrug resistance (MDR) in cancer cells during a long period of treatment. Target-specific delivery and sustained release of anticancer agents and siRNA has attracted considerable research interest in cancer chemotherapy. It is clear that the single treatment by either anticancer drug or siRNA delivered by nanocarriers can only achieve limited success in overcoming the MDR of cancer cells. Thus, the development of an effective strategy to overcome the multidrug resistance in chemotherapy remains a major challenge in the treatment of cancers, where co-delivery of anticancer drugs and siRNA would be a promising strategy. For this purpose, layered double hydroxides (LDHs), a family of anionic clay materials, have been examined as an example for simultaneous drug and gene delivery by using their unique properties. Our strategy is to combine two different types of anticancer therapeutics for effective cancer treatment. For example, 5-fluorouracil (5-FU) and siRNAs were co-loaded and then co-delivered to treat cancer cells, as illustrated in Scheme 1. Our data clearly indicate that LDH nanoparticles (NPs) can efficiently co-deliver 5-FU and siRNA into MCF-7 and U2OS cells and combination treatment with siRNA and 5-FU leads to significantly higher cytotoxicity to three cancer cell lines (MCF-7, U2OS and HCT-116), compared to the single treatment with either siRNA or 5-FU. Therefore, co-delivery of siRNAs and anticancer drugs by LDHs synergistically enhances the efficacy in these cancer treatments and has great potential as a novel approach for effective cancer treatment.

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Pharmaceutical impurity analysis of raw materials and final product by using analytical techniques

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Isolation and identification of unknown components and impurities: The evaluation of pharmaceutical raw materials and finished products for impurities and degradation products is an essential part of the drug development and manufacturing testing process. Additionally, toxicological information must be obtained on any drug-related impurity that is present at a concentration of greater than 0.1% of that of the active pharmaceutical ingredient (API). In pharmaceutical QC and manufacturing, impurity analysis has traditionally been performed by HPLC with UV, PDA, or MS detection. As it is essential to detect and measure all of the impurities in the sample, it is necessary to have a high resolution separation process. This usually involves long analysis times resulting in low throughput. As candidate pharmaceutical compounds become more potent and are dosed at lower and lower levels, ever more sensitive assays are needed to detect and measure impurities. The low throughput of HPLC can become the rate-limiting step in product release testing or process evaluation. Since much of the process of impurity identification involves the coupling of LC to sophisticated MS, any reduction in analysis time will result in a more efficient use of these significant investments. Analytical technology advances such as UPLC and UPC offer significant improvements in throughput and sensitivity, with benefits to the process of product release and identification of drug-related impurities. The most characteristic feature of the development in the methodology of pharmaceutical and biomedical analysis during the past 25 years is that HPLC became undoubtedly the most important analytical method for identification and quantification of drugs, either in their active pharmaceutical ingredient or in their formulations during the process of their discovery, development and manufacturing.

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Use of calculated indexes for prioritization of medicinal plants in the preparation of improved traditional medicine (itm)

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Several medicinal plants have a known chemical composition and pharmacological effects. Using their traditional uses across Cameroon, Africa and other continents and their chemical and pharmacological properties, we have defined for each species its convergence index, its index of efficiency and its index of sustainable use. The objective of this work was to classify the identified plants in order of priority for the preparation of the improved traditional medicines (ITM) according to the index of efficiency and sustainable exploitation (Ie-se) calculated from the previous indices. The fieldwork consisted, with the help of 37 traditional healers, in identifying the plants and in detailing their ethnopharmacological preparation. In order of importance, there are 9 efficacy parameters taking values 1 to 9. The average for a given plant corresponds to its Efficiency Index (Ie). Sixteen (16) parameters of sustainable exploitation taking values 1 to 16 were established. The average for a plant is its Sustainable Use Index (Ise). Finally, the sustainable efficiency index is the sum of the two indices (Ie + Ise = Ie-se) taking values 1 to 9. It allows plants to be classified into three groups. The production of ITMs with Group I [9-5] plants is recommended because of their chemical, pharmacological and conservation properties more available than Group II [4-3] and Group III [2-1] plants. *Pausinystalia yohimbe* (5) and *Euphorbia hirta* (7) belong to this group. This classification may be favorable for the inexpensive preparation of the IT Ms and for the use of plant species that are more efficient and available in nature.

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