10th World Congress on

Medicinal Chemistry and Drug Design

June 14-15, 2018 | Barcelona, Spain

Scientific Tracks & Abstracts

Day 1

Sessions:

Day 1 June 14, 2018

Medicinal Chemistry | Analytical Chemistry | Applications of Organic and Medicinal Chemistry in Drug Discovery | QSAR (Quantitative Structure-Activity Relationship) Fragment-Based Drug Design | Drug Design and Drug Development | Pharmacology and Toxicology

Session Chair
Letizia Giampietro
University "G. d'Annunzio", Italy

Session Co-Chair
Youssef I Moharram
Tanta University, Egypt

Session Introduction

Title: **Electrochemical behaviour of duloxetine HCl drug in formulation and spiked human serum at a carbon paste electrode**
Youssef I Moharram, Tanta University, Egypt

Title: **Synthesis and structure-activity relationship of a new derivatives of 14- and 15-membered macrolide antibiotics containing rebuilt saccharide arms**
Anna Janas, Adam Mickiewicz University in Poznań, Poland

Title: **Pyrazoline containing malonyl CoA decarboxylase inhibitors: Design, synthesis and in vitro evaluation**
C S Ramaa, Bharati Vidyapeeth's College of Pharmacy, India

Title: **Multicomponent access to conjugate vaccines**
Yanira Méndez Gómez, Leibniz Institute of Plant Biochemistry, Germany

Title: ***In vitro* and *in vivo* activity of opioid cyclopeptide with mu/delta agonist profile**
Katarzyna Gach-Janczak, Medical University of Lodz, Poland

Title: **Recombinant ricin nanoparticles design for CXCR4+ cancer cell therapy**
Raquel Díaz, Universitat Autònoma de Barcelona, Spain

Title: **Levels of selected metals in commercially available rice in Ethiopia**
Bisratewongel Tegegne, Addis Ababa University, Ethiopia

Title: **Discovery and structure - activity relation study of small-molecule as CB2 selective ligand**
Amer Tarawneh, Tafila Technical University, Jordan

Youssef I Moharram, Med chem (Los Angeles) 2018, Volume 8
DOI: 10.4172/2161-0444-C1-039

Electrochemical behaviour of duloxetine HCl drug in formulation and spiked human serum at a carbon paste electrode

Youssef I Moharram
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The electrochemical behavior of duloxetine HCl (DXT.HCl) drug was investigated. Two precise linear sweep and square wave adsorptive anodic stripping voltammetry methods have been described for its trace quantitation in pharmaceutical formulation and human serum. A mechanism of its oxidation was reported and illustrated. The method shows the development of a sensor for selective and sensitive determination of DXT.HCl. DXT.HCl has been oxidized at a CPE via 2-electron due to oxidation of its secondary amino group. The strong adsorption phenomenon of DXT.HCl can be used as an effective preconcentration step prior to the actual voltammetric quantification of the analyte. Two precise linear sweep and square wave adsorptive anodic stripping voltammetry methods have been described for its trace quantitation in pharmaceutical formulation and human serum. The methods were simple, rapid, and in expensive and sophisticated apparatus or expensive solvents, in comparison with other methods used previously for the study of DXT.HCl. So the proposed method can be used for the routine analysis of DXT.HCl, either alone or in its pharmaceutical formulations. However, the proposed SW-AdASV method has a better detection limit in spiked human serum (LOD=2.1×10^{-8} mol L^{-1}), therefore it is sensitive enough for assay of DXT.HCl in human plasma of real samples and for pharmacokinetic studies. It can be also recommended for its quantification in quality control and clinical laboratories.

Biography

Youssef I Moharram has completed his PhD at Tanta University in Egypt and Leeds University in UK (Channel System). He has published more than 25 papers.

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Anna Janas et al., Med chem (Los Angeles) 2018, Volume 8
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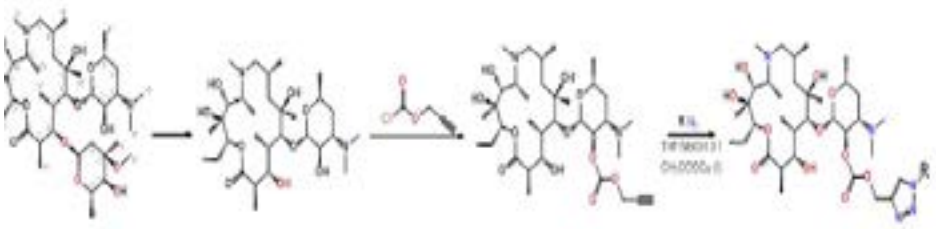
Synthesis and structure-activity relationship of a new derivatives of 14- and 15-membered macrolide antibiotics containing rebuilt saccharide arms

Anna Janas, Krystian Pyta and **Piotr Przybylski**
Adam Mickiewicz University in Poznań, Poland

Macrolide antibiotics are large group of natural products produced by various Streptomyces strains. They are used against various infectious diseases. Macrolides can be classified by a lot of different criteria. One of them is type and size of the macrolide ring and type of saccharide moieties joined to the aglycone ring as e.g. mycaminose, mycarose, cladinose, forosamine, desosamine. These classifications includes mainly lactone macrolides antibiotics, such as 14-membered erythromycins, 15-membered azithromycins and 16-membered leucomycins. The macrolide lactone antibiotics mechanism of action is based on the inhibition of bacterial protein biosynthesis at different stages by reversible binding to the bacterial 50s subunit at the ribosome. In our laboratory we work on new modifications of lactone macrolide antibiotics, of an improved binding profile to biological target and of increased antibacterial potency. Our modifications are performed using cascade and click approaches to enable better matching between antibiotic and target enzyme/protein. Previously, some changes at aglycone ring via complete reconstruction of saccharides parts using regio- and diastereoselective cascade combination of intramolecular esterifications followed by tandem E1cB eliminations and subsequent 1,2-addition to carbonyl followed by 1,6-conjugate addition α, β, γ, δ –unsaturated aglycone led to entirely new series of macrolide antibiotics of antibacterial and anticancer potential. Currently, with the support of Polish National Science Centre (decision number UMO-2015/19/B/ST5/00231), we applying this approach to modification of another group of natural macrolide antibiotics - 15-membered azalides, by rebuilt saccharide arms using Huisgen reactions, to obtain efficient alternatives to the currently used antibiotics (azithromycin) in clinical therapy.



Biography

Anna Janas was born in Gniezno, Poland, in 1992. She obtained her B.Sc. from Adam Mickiewicz University in Poznan in 2014 and received her M. Sc. degree at the same institution in 2016. She is currently carrying out her PhD studies in chemistry under the supervision of Prof. Piotr Przybylski at Department of Chemistry, Adam Mickiewicz University. To this date she is a co-author of 2 publications. Her research interests include the synthesis of new derivatives of 14- and 15-membered antibiotics with rebuilt sugar arms, determination of their structures in solution and physicochemical parameters.

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C S Ramaa et al., Med chem (Los Angeles) 2018, Volume 8
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Pyrazoline containing malonyl CoA decarboxylase inhibitors: Design, synthesis and in vitro evaluation

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Introduction: Cardiovascular disease is one of the leading causes of death in the modern world. Impaired cardiac efficiency is an important contributor to the severity of cardiovascular disease. Impaired cardiac efficiency is caused by an inadequate supply of oxygen to the heart. Malonyl-CoA decarboxylase (MCD) decarboxylates malonyl-CoA to acetyl-CoA. Therefore, the inhibition of MCD increases the level of malonyl-CoA, which further reduces fatty acid oxidation and increases glucose oxidation in the mitochondria. A shift in the mitochondrial metabolism from fatty acid to glucose oxidation increases Adenosine tri phosphate production. Thus, the heart may receive more energy even if the oxygen supply is less. In addition, increased glucose oxidation reduces pyruvate in cellular fluids, improving the pH balance of heart cells. Recently, researchers have synthesized MCD inhibitors based on this novel approach of increasing energy supply to the heart.

In the present work series of small molecules (5a–5m, 6a–6j) were schematically designed and synthesized using simple chemical procedures. Their structures were confirmed based upon findings from infrared, 1H nuclear magnetic resonance (NMR), 13C NMR, and mass spectra. The derivatives were evaluated for their in vitro malonyl CoA decarboxylase inhibition activity by using fluorimetric assay. Pyrazol-1-yl-1, 3-thaizol-4(5H)-one derivative (5a–5m) showed better activity than pyrazol-1- yl-1-ethanone derivatives (6a–6j). Compounds 5e, 5j, and 6f showed an excellent in vitro malonyl CoA decarboxylase inhibition activity with IC50 value 0.10, 0.27, and 0.26 μM, respectively. These most active compounds 5e, 5j, and 6f were docked into malonyl-CoA decarboxylase (HsMCD, PDB ID: 2YGW) to study ligand–protein interaction.

Biography

C S Ramaa is a Professor and Head of Department of Pharmaceutical Chemistry at Bharati Vidyapeeth's College of Pharmacy, Navi Mumbai. She received her PhD in Pharmaceutical Chemistry from University Department of Chemical Technology. She has been working at Bharati Vidyapeeth's College of Pharmacy, Navi Mumbai. She has received several grants from renowned funding agencies like Department of Science and Technology, Basic Research in Nuclear Sciences, Lady Tata Memorial Trust and University of Mumbai. She has published more than 35 research and review articles in international and national esteemed journals. She has also presented more than 30 presentations at national and international conferences. She has been awarded as Best Research Guide for national level PharmInnova Award.

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Yanira Méndez Gómez, Med chem (Los Angeles) 2018, Volume 8
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Multicomponent access to conjugate vaccines

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Though the discovery of antibiotics in the 20th century discouraged the application of carbohydrate based vaccines, the appearance of bacterial resistance and the cuasi prohibitive access to really new antibiotics have turned the interest toward new carbohydrate based vaccines. This work describes the development of a new synthetic strategy towards antibacterial glycoconjugate- and specially multivalent vaccines. The conjugation of functionalized capsular polysaccharides of *Streptococcus pneumoniae* and *Salmonella enterica* serovar Typhi to carrier proteins such as diphtheria and tetanus toxoids was caried out via the Ugi 4-component reaction, giving access to mono and multivalent unimolecular glycoconjugates by conjugating them to immunogenic proteins. This gives rise to opportunities toward multivalent and self-adjuvanting vaccines, which will be reported.

Biography

Yanira Méndez Gómez received her academic education from the University of Havana. Currently, she is a PhD student in the group of Prof B Westermann, IPB, Germany and the group of Prof D G Rivera, CEPN, Cuba. She is dealing with the synthesis and bioconjugation of capsular polysaccharides to carrier proteins and adjuvants to obtain conjugate vaccine candidates. Simultaneusly, she is working as Lecturer in Department of Organic Chemistry at University of Havana.

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Raquel Díaz et al., Med chem (Los Angeles) 2018, Volume 8
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Recombinant ricin nanoparticles design for CXCR4+ cancer cell therapy

Raquel Díaz, Victor Pallarès, Olivia Cano-Garrido, Naroa Serna, Laura Sánchez-Garcia, Aïda Falgàs, Mireia Pesarrodona, Ugutz Unzueta, Alejandro Sánchez-Chardi, Julieta M. Sánchez, Isolda Casanova, Esther Vázquez, Ramón Mangues and **Antonio Villaverde**
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Biomedical Research Institute Sant Pau (IIB-Sant Pau) and Josep Carreras Research Institute Hospital de la Santa Creu i Sant Pau, Spain

The potent ligand T22, that specifically binds the CXCR4+ receptor, overexpressed in some cancer cells, was engineered to be attached to the N-terminus of the mutated A chain of the plant toxin ricin fused to a 6xHis tag in the C-terminus. The soluble recombinant protein T22mRTAH6 spontaneously self-assembled as protein-only regular nanoparticles of about 12nm in size, capable of CXCR4 dependent cellular internalization and effective cytotoxic effect *in vitro*. Meanwhile, the insoluble version of the protein presented moderate free-protein release inducing to a partial cytotoxic effect in the cells. The T22mRTAH6 nanostructured construct was also tried in mouse models of acute myeloid leukemia, where it proved to reduce dramatically the disease affectation of clinically relevant organs. The functionalized protein nanoparticles are then proposed as suitable prototypes for antitumor carcinogenic therapies based on self-mediated intracellular drug delivery.

Biography

Raquel Díaz is studying her PhD program at Univerity Autonomous of Barcelona .

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Bisratewongel Tegegne et al., Med chem (Los Angeles) 2018, Volume 8
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Levels of selected metals in commercially available rice in Ethiopia

Bisratewongel Tegegne, Bhagwan Singh Chandravanshi and **Feleke Zewge**
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This study reports the levels of metals in commercially available imported (Oryza sativa) and Ethiopian rice(Oryza glaberrima). The levels of thirteen metals (Ca, Mg, K, Na, Fe, Mn, Zn, Cu, Co, Ni, Cr, Cd and Pb) were determined in six varieties of raw rice collected from Addis Ababa supermarkets, Fogera town and Amahara Regional Agricultural Research Institute and in one selected cooked rice by flame atomic absorption spectrometry (FAAS) after digesting the powdered rice samples with HNO_3, $HClO_4$ and H_2O_2 mixture. The validation of optimized digestion procedure was evaluated using spiking method and an acceptable percentage recovery was obtained. The levels of metals found in the imported and Ethiopian rice, respectively, were in the ranges (mg/kg): Ca 75.8-630, 205-427; Mg 90.6-150, 99.5-2250; K 1680-2150, 1100-3020; Na 70.6-78.6, 26.7-80.9; Fe 48.9-117, 41.3-113; Mn 4.1-15.5, 3.7-16.6; Zn 16.4-25.7, 15.6-140; Cu 2.7-4.9, 3.3-15; Co 12.6-14.6, 8.8-10.4; Ni 2.5-75.1, 41.5-69.7; Cr 2.2-3.12, 2.32-4.82; Cd <0.34, 0.45-2.54; Pb 2.1-5.3, 0.8-3.8. Comparison between levels of metals in the imported and Ethiopian rice showed significant differences for most of the metals. The results indicated that Ethiopian rice is comparatively rich in essential metals than imported. A statistical analysis of variance (ANOVA) at 95% confidence level for metal determination indicated significant difference between the means of each variety of samples. Comparison between levels of metals in cooked and raw rice showed that the difference in the level is not significant.

Biography

Bisratewongel Tegegne Alemu done her PhD & MSc. from Analytical Chemistry; Addis Ababa University, she done her BSc. in Applied Chemistry from Haramaya University, she is currently working as teacher in higher education at Bahir Dar University, Bahir Dar (Ethiopia). she received certificate of oral presenter on 4th Annual conference of Society of Ethiopian Women in Science and Technology, and workshop on Empowering Women in Leadership Skill in Science and Technology, April 2018. she also received certificate on Environmental Risk Assessment Management from Africa Center of Excellence for Water Management (ACEWM) Addis Ababa University, Ethiopia. she won Gold Cup award for being the From Haramaya University, Ethiopia, first from the graduated batch in July 2010.

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Amer Tarawneh et al., Med chem (Los Angeles) 2018, Volume 8
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Discovery and structure - activity relation study of small-molecule as CB2 selective ligand

Amer Tarawneh[1, 2], Lo'ay Al-Momani[1], Francisco León[2], Janet Lambert[2], Anastassiya V Gadetskaya[3] and **Stephen J Cutler[2]**
[1]Tafila Technical University, Jordan
[2]The University of Mississippi, USA
[3]Al-Farabi Kazakh National University, Kazakhstan

The CB1 receptor was originally called the cannabinoid receptor before the CB2 receptor was discovered, but CB1 did not explain the immunomodulatory effects of cannabis, which were already well-documented at this time. In 1993, this effect was accounted by the finding of the CB2 receptor in a human promyelocytic leukemia cell line. Both CB1 and CB2 are G-protein coupled receptors, which share a 48% sequence identity. There have been numerous studies on the pharmacology of CB2, giving it the name receptor with an identity crisis. Because CB2 (unlike CB1) is largely not expressed in the central nervous system, but rather in the spleen and immune cells, it is known as the peripheral cannabinoid receptor soon after its discovery. When CB2 expression was found in the neurons and in the microglial cells of the brain, this terminology was determined to be inaccurate, and CB2 expression has since been shown to be correlated with neuroinflammation. A 2005 study showed a 200-fold up regulation of the CB2 receptors in the microglial cells in an *in vitro* model of autoimmune encephalomyelitis many of these studies are now considered questionable because further research has shown that the anti-CB2 antibodies used in these Immunohistochemical methods have non-specific binding with other proteins. However, the immunomodulatory effects of CB2 remain unchallenged. In addition, CB2 expression has more recently been associated with neurodegenerative diseases such as Huntington and Alzheimer. CB2-selective Positron Emission Tomography (PET) tracers in Alzheimer's mice have demonstrated increased expression of CB2, concomitant with the formation of amyloid-beta plaques. This suggests that CB2 PET tracers may have potential as a diagnostic tool for neuro-inflammation. In order to counteract these effects, studies are underway to develop selective CB2 ligand. This research began with testing of a series of isoxazole and triazole derivatives, which lead to discovery of a novel ligand highly selective for cannabinoid receptor 2. Compound ATJ-31 produced a concentration-dependent inhibition of specific [3H] - CP55, 940 (CB2) binding with a Ki value of 105 nM, while no binding affinity toward CB1 receptor was observed. The current study aims to design, synthesize and biologically evaluate potential CB2 receptor ligand.

Recent Publications

1. Savonenko A V, Melnikova T, Wang Y, Ravert H, Gao Y, Koppel J, Lee D, Pletnikova O, Cho E, Sayyida N, Hiatt A, Troncoso J, Davies P, Dannals R F, Pomper M G and Horti A G.(2015) Cannabinoid CB2 Receptors in a Mouse Model of Aβ Amyloidosis: Immunohistochemical Analysis and Suitability as a PET Biomarker of Neuroinflammation. PLoS ONE 10(6):e0129618.
2. Baek J H, Darlington C L, Smith P F and Ashton J C. (2013) Antibody testing for brain immunohistochemistry: Brain immunolabeling for the cannabinoid CB2 receptor. Journal of Neuroscience Methods 216(2):p. 87.
3. Marchalant Y, Brownjohn P W, Bonnet A, Kleffmann T and Ashton J C (2014) Validating Antibodies to the Cannabinoid CB2 Receptor: Antibody Sensitivity Is Not Evidence of Antibody Specificity. Journal of Histochemistry & Cytochemistry. 62(6): p. 395.
4. Di Marzo V, Stella N and Zimmer A (2015) Endocannabinoid signalling and the deteriorating brain. Nat Rev Neurosci. 16(1): p. 30.
5. Savonenko A V, Melnikova T, Wang Y, Ravert H, Gao Y, Koppel J, Lee D, Pletnikova O, Cho E, Sayyida N, Hiatt A, Troncoso J, Davies P, Dannals R F, Pomper M G and Horti A G (2015) Cannabinoid CB2 Receptors in a Mouse Model of Aβ Amyloidosis: Immunohistochemical Analysis and Suitability as a PET Biomarker of Neuroinflammation. PLoS ONE. 10(6): p. e0129618.

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Young Researchers Forum Day 2

Tuvshinjargal Budragchaa, Med chem (Los Angeles) 2018, Volume 8
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Synthesis of α-acylamino and α-acyloxy amide derivatives of desmycosin and evaluation of their antibacterial activities

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Bacterial resistance to the existing drugs requires a constant development of new antibiotics. Especially compounds active against gram-negative bacteria are difficult to target. Most effective in terms of time, effort and success rate is the medicinal chemistry driven development (evolution) based on existing antibiotics. Towards this end, macrolide antibiotics were modified to give new derivatives, aiming for enhanced antibacterial activities and physicochemical profiles. This work describes the structural diversification at the C-20 aldehyde moiety of desmycosin into α-acylamino and α-acyloxy amide functionalities in a very efficient and simple way, using isonitrile mediated multi component reactions. The desired compounds were obtained in 45–93% yield under mild conditions. Antibacterial activities were determined against gram-negative Allivibrio fischeri. The test revealed that the activity is highly dependent on the amine component introduced. Thus, methylamine derived desmycosin bis-amide displayed an enhanced inhibition rate vs. desmycosin (99% vs. 83% at 1 μM). In Ugi reaction, amine and isocyanide components with longer acyclic or bulky substituents reduced potency. In contrast, the carboxylic acids with increased chain length substituents afforded conjugates with increased bioactivity. In Passerini (P-3C) reaction, butyric acid derived α-acyloxy amide showed much better result displaying higher activity (90% at 1 μM) than the reference desmycosin.

Biography

Tuvshinjargal Budragchaa has completed her PhD at the University of Vienna, austria concentrating in Asymmetric synthesis and application of bronsted acid catalysis and their applications. Currently, she is doing her postdoctoral research at the Department of Bioorganic Chemistry, Leibniz Institute of Plant Biochemistry, and Halle Saale. She focuses on modification of exisiting macrolide moieties to enhanced antibacterial activities and fine tune the physicochemical profiles as well as modification of plant derived bioactive compounds.

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Neha Upadhyay et al., Med chem (Los Angeles) 2018, Volume 8
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5-naphthylidene-2,4-thiazolidinediones: *In silico* studies, synthesis and primary cytotoxicity evaluation in leukemic cell lines

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[2]Medical University of Warsaw, Poland
[3]D Y Patil University, India
[4]Amity University, India

Introduction: Contribution of antidiabetic Thiazolidinediones (TZDs) to cancer therapy has been evidenced by numerous *in-vitro* and *in-vivo* studies. While TZDs are known to stimulate PPAR-γ receptor, they also have multiple PPARγ independent effects and the specific role of PPARγ activation in the anticancer effects of TZDs is still under investigation. Also, several reports show the correlation between full activation of PPARγ and associated adverse effects. This prompted us to develop TZD analogues as partial PPARγ agonists and evaluate their anticancer potential.

Methods: We designed series of novel TZDs based on, QSAR model, Docking analysis and Molecular properties study. Further we synthesized and structurally characterized them by 1H-NMR, ^{13}C-NMR, FTIR and Mass spectroscopy.

Results & Discussion: In the present work, a QSAR model was developed and validated using 25 TZD derivatives synthesized in our laboratory earlier, showing antiproliferative activity against K 562 cell lines, by using experimental and computational study and analysis. The predicted activities by our QSAR models were very close to those experimentally observed, indicating that these models can be safely applied for prediction of more effective hits having the same skeletal framework. We used this model to design new series of 5-naphthylidene-2,4- TZDs and predicted their antiproliferative activity. The molecules from the series, obeying Lipinski's rule of five were subjected to docking analysis using VLife protocol. The molecules displaying desired interactions as that of partial agonists of PPARγ were further taken for synthesis and evaluated for primary cytotoxic effects on several cancerous cell lines.

Biography

Neha Upadhyay has completed her Post-graduation in Pharmaceutical Chemistry from Bombay College of Pharmacy, Mumbai. She is working as a Junior Research Fellow (JRF) on a project funded by DST, India. She has registered for PhD in Pharmaceutical Sciences at Bharati Vidyapeeth's College of Pharmacy, Navi Mumbai, India.

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Targeting epigenetics: Synthesis and biological evaluation of difluorinated propanediones as HMTase inhibitors

Kalpana Tilekar[1], Neha Upadhyay[1], Tanushree Pal[1], Sanjay Gupta[2] and **C S Ramaa[1]**
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Introduction: Pharmaco-epigenomics constitute the hope for a new strategy in cancer treatment owing to epigenetic deregulation, a reversible process, suspected of playing a role in malignancy 30 years prior to the sequencing of the human genome. In this field, several enzymes like HDACs, DNA methyl transferases (DNMTs) and histone methyl transferases (HMTase) have been studied extensively for their capability to be inherited by natural or synthetic compounds. To date, HDAC and DNMT inhibitors are used in cancer therapy are tested in clinical studies. In contrast to this, the search for inhibitors of HMTase is still in its infancy and *in-vivo* data of most of the agents are not available.

Methods: In this research work, we synthesized few difluorinated propanediones and their structures were determined by analytical and spectral (FTIR, 1H NMR, ^{13}C NMR) methods. The newly synthesized compounds were first evaluated for their antiproliferative activity and then for HTMase inhibitory potential in leukemic cell lines. We have also performed cell cycle analysis to study cell growth arrest.

Results: Amongst all the synthesized compounds, PR-4 was found to be most active. In the cytotoxicity assay, it showed cell growth of 42.6 % and 53.4% comparable to that of adriamycin; 44.5% and 53.2% in U937 and JURKAT, respectively. At a concentration of 1 and 10μM, it had shown to alter the methylation levels in two leukemic cell lines of histiocytic lymphoma (U937) and acute T-cell leukemia (JURKAT). Cell growth arrest was found in the G0/G1 phase in both the cell lines.

Discussion: The apoptosis pattern suggests that the molecule PR-4 could emerge as a potential anticancer agent by targeting HMTases.

Biography

Kalpana Tilekar has completed her Post-graduation in Pharmaceutical Chemistry, from Bharati Vidyapeeth's College of Pharmacy, Mumbai. She worked as an Assistant Professor at NCRD's Sterling Institute of Pharmacy, Navi Mumbai, India. Currently, she is working as Junior Research Fellow (JRF) on a project funded by DST, India and she is registered for PhD in Pharmaceutical Sciences at Bharati Vidyapeeth's College of Pharmacy, Navi Mumbai, India.

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Development of 3, 5-dinitrophenyl containing heterocycles: Structure-antimycobacterial activity relationships studies

Galina Karabanovich
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Our research focuses on the design and synthesis of novel nitro group containing heterocyclic compounds with high and selective antimycobacterial efficiency and on the study of relationships between their structure and antimycobacterial activities/toxicities. Previously described 1-alkyl-5-(3,5-dinitrobenzyl)sulfanyl-1H-tetrazoles and 2-alkyl-5-(3,5-dinitrobenzyl) sulfanyl-1,3,4-oxadiazoles showed outstanding activities against drug-susceptible and drug-resistant strains of *Mycobacterium tuberculosis (M. tuberculosis.)*. Their minimum inhibitory concentrations reached 0.5 μm and 0.03 μm, respectively. Moreover, 1, 3, 4-oxadiazole derivatives were active against replicating and nonreplicating strains of *z*. Described compounds demonstrated selective effect on mycobacteria as were inactive against tested fungi and bacteria and exhibited low *in vitro* genotoxicity and toxicity in mammalian cell lines. Current work continues to study the role of individual fragments of previously described molecules in their biological properties. We focused on influence of the heterocycle and Benzylsulfonyl linker on antimycobacterial activity. Results of *in vitro* evaluation showed that both fragments play a significant role in the antimycobacterial efficacy of target compounds. Moreover, alkyl/aryl substituents on heterocycle could also affect compounds efficacy.

Biography

Galina Karabanovich has completed her PhD at the Faculty of Pharmacy in Hradec Kralove, Charles University. Currently, she occupies the Postdoctoral position at the same University. She has published 12 papers, majority of them in medicinal chemistry journals. Her research interests are focused on the design and synthesis of compounds with potential antimycobacterial activity; study of the relationships between structure and antimycobacterial activity of prepared substances; synthesis of dexrazoxane analogues.

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Amr Elagamy, Med chem (Los Angeles) 2018, Volume 8
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Synthesis of highly functionalized spirocyclic butenolides via ring contraction of fused 2H-pyran-2-ones

Amr Elagamy
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Butenolides are a class of lactones, considered as oxidized derivatives of furan with structure made of four carbon heterocyclic ring called furan-2(5H)-ones. A broad range of natural products and biologically active compounds contain butenolides structural as subunits. These compounds exhibit various biological activities such as anti-inflammatory, anticancer, antimicrobial, antifungal, and anti-viral HIV-1. A new method for synthesis of highly functionalized spirocyclic butenolides was achieved through ring opening and relactonization at C5 of fused 2H-pyran-2-ones using nitroalkane as a carbanion source. Nitroethane provides (E)-and (Z)-isomer of spirocyclic butenolides in a ratio of almost 2:1 with relatively better yields than in case of nitromethane which provides only one isomer. Moreover, spirocyclic butenolides obtained from nitroethane undergoes decarboxylative rearrangement in presence of sodium ethoxide to give only one isomer of triene and might be used as a valuable intermediate for synthesis of various triene compounds.

Biography

Amr Elagamy has completed his Bachelor of Science in Chemistry at the Faculty of Science, Tanta University, Egypt, and Master degree in Organic Chemistry at Kirori Mal College, University of Delhi, New Delhi, India. He was awarded DBT-TWAS Postgraduate Fellowship in 2015 to complete his PhD in Organic Chemistry at the University of Delhi, New Delhi – India.

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