Joint Event

Euro Pharma Chemistry

&

Future Pharma

June 27-28, 2019 | Amsterdam, Netherlands

SCIENTIFIC TRACKS & ABSTRACTS

DAY 01

Joint Event
4th Pharmaceutical Chemistry Conference | 12th World congress on Future Pharma
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The Pt(II)-based Lx® linker technology for development and production of antibody-drug conjugates (ADCs) with distinguished features

Antibody-drug conjugates (ADCs) are a cutting-edge modalities in the pharmaceutical field because they allow targeted delivery of drugs, which are otherwise too potent/toxic to be applied systemically, selectively to cancer cells. However, a greater control is desirable in the stochastic conjugation technology used to synthesize ADCs. We have recently introduced a metalorganic platinum(II) linker, an ethylenediamineplatinum(II) moiety called Lx, that allows to provide ADCs with some unique features, such as targeting the histidine residues of native unmodified antibodies and an improved hydrophilicity of synthetic intermediates and presumably metabolites. The general concept of this novel linker technology (shown in the scheme below) for the preparation of stable and efficacious ADCs will be presented. The milestones of the Lx platform development as well as the key features of thus produced Lx-based ADCs such as serum stability, biodistribution, *in-vitro* cytotoxicity, and in-vivo efficacy data, along with some recent highlights such as dual radiolabeling of Lx ADCs with 195mPt and 89Zr radioisotopes, will be presented. Finally, first results will be shown regarding the manufacturing of our lead ADC, with the corresponding "semi-final" product being successfully produced at a multi-gram scale and the original Lx ADC conjugation method successfully technology-transferred to a CMO for a near-future upscaling and manufacturing.

Biography

Eugen Merkul has completed his PhD with Summa Cum Laude from the University of Düsseldorf/Germany, and Post-doctoral studies from the University of Antwerp/Belgium, followed by industrial experience at German and Dutch Companies. He is the Head of Chemistry of LinXis B.V., an innovative Dutch Biotech Company developing a proprietary ADC (antibody-drug conjugates) platform technology. He is an author/coauthor of 23 papers in reputed peer-reviewed journals and inventor/coinventor of 10 patent applications.

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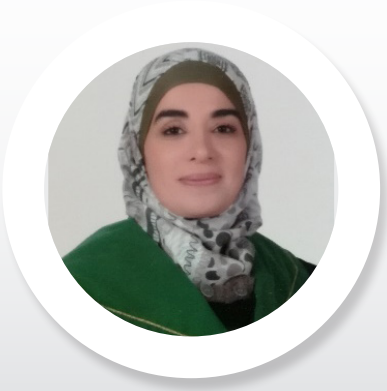
Synthesis, structural characterization and docking studies of sulfamoyl-phenyl acid esters as dipeptidyl peptidase-IV inhibitors



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Diabetes mellitus is a major worldwide health concern that has several serious complications including retinopathy, neuropathy, nephropathy and macrovascular diseases. Dipeptidyl peptidase-IV (DPP-IV) inhibitors, gliptins, are a new class of antidiabetic agents that potentiates the action of incretins in decreasing the blood glucose levels. In the present study, synthesis and characterization of a series of 10 N4-sulfonamido-acrylic and phthalamic acid methyl esters (3a-e and 5a-e) were achieved. *In vitro* anti-DPP-IV activity of the synthesized compounds was evaluated, where compound 3b demonstrated the best activity with a percent (%) inhibition of 41.7 at 10 μM concentrations and an IC50 of 23.9 μM. Moreover, Glide docking experiments revealed that our targeted compounds accommodate the binding site of DPP-IV and tend to form H-bonding with the backbones of R125, E206, S209, D545, K554, W629, Y631 and G632. Modeling findings recommend the attachment of bulky hydrophobic group on the ester side of the structure in addition to harboring extra aromatic rings that might be beneficial for better binding interaction and biological activity.

Biography

Reema Abu Khalaf currently is an Associate Professor of Medicinal Chemistry and Drug Discovery, at Faculty of Pharmacy, Al-Zaytoonah University of Jordan. She has completed her BSc in Pharmacy, MSc in Pharmaceutical Sciences, and PhD in Medicinal Chemistry and Drug Discovery at The University of Jordan. She got the Distinguished Researcher Award from Al-Zaytoonah University of Jordan, Jordan, 2012. Currently, her researches focus on the design and synthesis of new dipeptidyl peptidase-IV inhibitors that can serve as potential hypoglycemic agents. Furthermore, the design and synthesis of new inhibitors of cholesteryl ester transfer protein as anti-hyperlipidemic agents. She has published more than 20 papers in reputed journals.

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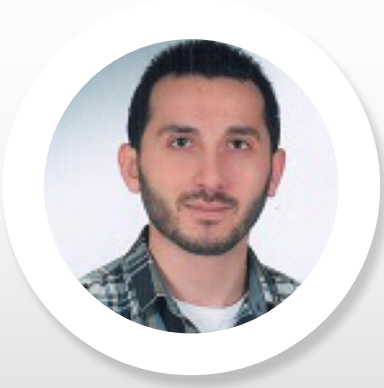

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Novel stability indicating LC methods for determination of tasimelteon

Tasimelteon (TAS) is a melatonin receptor agonist compound, which is currently in use for the treatment of non-24-hour sleep–wake disorder in totally blind people. In this study, novel stability-indicating LC methods have been developed for the determination of TAS besides its degradation products. Three different LC set-ups were used within this study. Initially, an LC-PDA instrument was developed for quantification of TAS; the separation of TAS from its degradation products was achieved on an Ascentis® Express F5-bonded fused-core silica particle column using the mobile phase of acetonitrile: acetate buffer (0.025 M, pH 4.5): water (40:10:50, v/v/v); the elution was performed in isocratic mode at 0.8 mL min^{-1} flow rate, detecting the analytes at 281 nm. In addition, an alternative method was developed by using an LC-DAD-MS/MS instrument; the responses of DAD and MS/MS detectors were used as separate analytical signals for TAS and other compounds. A second-generation C18-bonded monolithic silica column was used as stationary phase in this method, while the mobile phase was a mixture of 0.1% (v/v) formic acid in water and 0.1% (v/v) formic acid in acetonitrile (60: 40 (v/v), pH=2.5). The instrumental and analytical performances of all three set-ups were compared in terms of validation parameters mentioned in ICHQ2(R1) guideline. On the other hand, a new degradation product was identified using an LC/MS-IT-TOF instrument. In conclusion, determination of TAS besides its degradation products and identification of a novel degradation product was successfully performed using the protocols reported in this study.

Biography

Serkan Levent is a Lecturer in Anadolu University and also a PhD student at the Department of Analytical Chemistry of the same university. He has published more than 30 papers in highly reputed journal, which are mostly indexed in Science Citation Index of Thomson-Reuters.

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