EFMC-YMCS
Young Medicinal Chemists' Symposium
Nice, France
September 8-9, 2022

BOOK OF ABSTRACTS

Organised by

EFMC

EFMC Young Scientists Network

Nice, France
September 8-9, 2022
www.efmc-ymcs.org

Welcome

Dear participant,

On behalf of the European Federation for Medicinal chemistry and Chemical biology (EFMC), the EFMC Young Scientists Network and the Organising Committee, we warmly welcome you to Nice for the 9th edition of the EFMC Young Medicinal Chemists' Symposium (EFMC-YMCS).

Since the first edition of the EFMC-YMCS in 2014, the symposium has gone from strength to strength with increased participation from EFMC-National Adhering Organisations, and it is now firmly established as the premier forum in Europe for young Medicinal Chemistry and Chemical Biology researchers to promote their science.

Our principal aims are:
- Creating a network of young European investigators in Medicinal Chemistry and Chemical Biology
- Stimulating young European investigators to share their scientific work with peers, and inspiring them to become leaders in their field
- Creating competition, excellence and European Champions in Medicinal Chemistry and Chemical Biology

After two years of virtual events, we happily welcome around 200 scientists from 25 nations in Nice, France for the latest edition. The symposium will consist of: 2 keynote lectures, 19 oral communications given by prize winners from national competitions around Europe; 19 flash poster presentations; and more than 100 poster presentations showcasing the latest advances in drug discovery advances.

We also invite you to attend the different soft-skills training sessions organised in collaboration with the EFMC Young Scientists Network:
- Reaxys Workshop: A Tandem Tour to Unveil the Profile of an Active Molecule
- Reaching Out: Effective Communication and Networking for Scientists

Finally, there will be various networking opportunities hosted inside and outside the "official" programme, and we look forward to meeting you all in the informal atmosphere which characterize our event. Please help the organisers sustaining this friendly ambience.

During the closing ceremony, the following prizes will be awarded to the European Champions in Medicinal Chemistry and Chemical Biology:
- EFMC-YMCS Presentation Prize, sponsored by the EFMC
- EFMC-YMCS Poster Prizes, sponsored by Chemistry Europe
- EFMC-YMCS Public's Prize, sponsored by F. Hoffmann- La Roche

We thank our sponsors (Novartis, Janssen, Merck, MSD, F. Hoffmann- La Roche, AstraZeneca, Sanofi & Vertex), the Société de Chimie Thérapeutique (SCT) and all the participating National Adhering Organisations for their support, without which we could not run this event, and we look forward to your participation!

EFMC-YMCS Organising committee

Chair:
Maria DUCA (University of Côte d'Azur, Nice, FR)
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David ALKER (David Alker Associates, UK),
Stéphane AZOULAY (University of Côte d'Azur, Nice, FR),
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Brieuc MATAGNE (LD Organisation, BE),
Luc VAN HIJFTE (Symeres, Nijmegen, NL)

STRUCTURE-ACTIVITY RELATIONSHIP, DOCKING ANALYSIS AND ADME PROPERTIES OF NEWLY DESIGNED, POTENT SEROTONIN 5HT1A RECEPTOR LIGANDS

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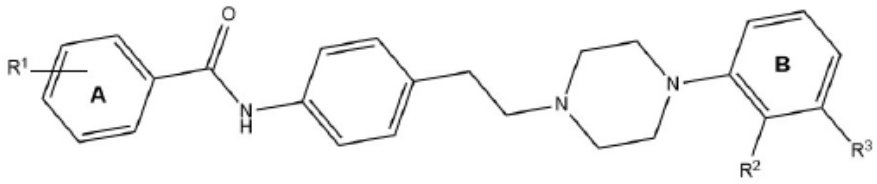
Serotonin 5HT1a receptor belongs to a class of G-protein coupled receptors and it is widely recognized as one of the targets for treating neurological disorders such as depression and schizophrenia.[1] *N*-Arylpiperazine structural motif is present in many compounds with pronounced 5HT1a activity including recently approved aripiprazole for the treatment of the major depressive disorder.[2]

As a part of our ongoing research on the development of novel 5HT1a receptor ligands, six novel compounds were designed possessing high 5HT1a binding affinity (K_i = 4.8-52.2 nM) when compared to previously disclosed lead compound **1** (K_i = 575 nM).[3] By changing the position of hydroxy group on the ring **A**, it was found that meta and para positions are more favorable for pharmacological activity than ortho. Addition of the 2,3-dichloro and 2-methoxy substituents on the ring **B** led to overall increase of 5HT1a affinity, with 2-methoxy derivatives **6** and **7** being the most potent. The relative position of the substituents on rings A and B was somewhat influential, as it can be seen on the affinity in pairs **2>3**, **5>4** and **7>6**.



1, R^1 = 2-hydroxy; R^2 = H; R^3 = H. **2**, R^1 = 3-hydroxy; R^2 = H; R^3 = H. **3**, R^1 = 4-hydroxy; R^2 = H; R^3 = H.
4, R^1 = 3-hydroxy; R^2 = Cl; R^3 = Cl. **5**, R^1 = 4-hydroxy; R^2 = Cl; R^3 = Cl. **6**, R^1 = 3-hydroxy; R^2 = OMe; R^3 = H.
7, R^1 = 4-hydroxy; R^2 = OMe; R^3 = H.

Docking analysis revealed that all six compounds bind well in the active site of 5HT1a receptor forming necessary key interactions with the active site residues. In addition, compounds **2-7** were subjected to ADME prediction, demonstrating favorable properties such as Blood Brain Barrier permeation and zero violations of Lipinski's rule of five.[4]

Due to the apposite initial results, both calculated and experimental, compounds **2-7** will be subjected to additional pharmacological experiments regarding their functional activity, kinetics and toxicity.

References

1) L. Wang, Y. Zhang, X. Dud, T. Ding, W. Gong, F. Liu. Biomed. Pharmacother. 120 (2019) 109408.
2) P. Xu, S. Huang, H. Zhang, C. Mao, X.E. Zhou, X. Cheng, I.A. Simon, D.-D. Shen, H.-Y. Yen, C.V. Robinson, K. Harpsøe, B. Svensson, J. Guo, H. Jiang, D.E. Gloriam, K. Melcher, Y. Jiang, Y. Zhang, H.E. Xu. Nature, 592 (2021) 469.
3) V. Sukalovic, A. Elena Bogdan, G. Tovilovic, D. Ignjatovic, D. Andric, S. Kostic-Rajacic, V. Soskic. Arch. Pharm. Chem. Life Sci. 346 (2013) 708.
4) A. Daina, O. Michielin, V. Zoet. Sci. Rep. (2017) 7:42717.