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## **Lipidomics study in liver metabolic diseases**

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## **Curriculum Vitae**

Madhulika Singh was born on the 5<sup>th</sup> of October, 1990, in Uttar Pradesh, India. Following her school education, she pursued a bachelor's degree in pharmacy (B.Pharm.) at Babu Banarasi Das National Institute of Technology and Management (BBDNITM) in Lucknow, Uttar Pradesh, India, from 2009 to 2013, and graduated with distinction. She received the award for being the top-ranking student throughout all four years of her B.Pharm. Subsequently, she was admitted to one of India's leading institutes for pharmacy education, the National Institute for Pharmaceutical Education and Research (NIPER) in Mohali, where she pursued a Master's in Medicinal Chemistry (M.S. Pharm.). During her master's program, Madhulika conducted her thesis research under the guidance of Prof. Asit K. Chakraborti. In her thesis, titled "*Design and Synthesis of 2-(2''-Arylphenyl) Benzoxazole Derivatives as Potential COX-2 Inhibitors*" Madhulika conducted molecular docking studies on various aryl phenyl benzoxazole derivatives to assess their binding affinity to COX-2. Subsequently, she synthesized these compounds and evaluated their *in vitro* enzymatic activity as potential COX-2 inhibitors. This comprehensive approach allowed her to establish a Structure-Activity Relationship (SAR) model. Madhulika received a scholarship from the Government of India during her M.S. studies. She was granted a patent titled "2-(2-aryl/alkyl phenyl) benzazole as selective COX-2 inhibitory scaffolds" for her M.S. (Pharm.) research Project (Patent Application No.: 2540/DEL/2015, Indian Patent Number: 387998). Following the completion of her master's degree, Madhulika ventured into industrial research where she worked as bioanalytical and metabolite identification scientist, in drug metabolism and pharmacokinetics (DMPK) field until June 2019. During this period, she worked in the discovery biology division of the biopharma company Syngene International Ltd., (daughter company of Biocon currently ranked 8<sup>th</sup> among Global Biotech Employers for 2022 by Science magazine).

In June 2019, she started her PhD under the supervision of Prof. dr. Thomas Hankemeier and Dr. Amy Harms at 'Metabolomics and Analytics Centre' (MAC), in the Leiden Academic Centre for Drug Research (LACDR). Madhulika worked as an early-stage researcher in the PoLiMeR consortium and her PhD research was funded through the European Union's Horizon 2020 research and innovation program under the Marie Skłodowska-Curie grant agreement. During her PhD, she developed lipidomics platforms, utilizing highly sensitive LC-MS/MS methods, aimed at investigating the role of lipids in liver metabolic diseases and gaining insights into the underlying pathophysiological mechanisms involved. Her academic involvement extended to active participation in various national and international conferences.

## Appendix

She delivered both oral and poster presentations during PoLiMeR consortium meetings, which occurred semiannually. Furthermore, she presented her research findings through poster presentations at events such as CHAINS (2021), Euroanalysis (2023), the International Conference on the Bioscience of Lipids (2023) and the LACDR Spring Symposium (2020, 2021, 2023).

## **List of Publications**

1. Zhang Z\*, **Singh M\***, Kindt A, Wegrzyn AB, Pearson MJ, Ali A, Harms AC, Baker P, Hankemeier T. Development of a targeted hydrophilic interaction liquid chromatography-tandem mass spectrometry-based lipidomics platform applied to a coronavirus disease severity study. *Journal of Chromatography A*, Volume 1708, 11 October 2023, 464342.  
<https://doi.org/10.1016/j.chroma.2023.464342>.
2. Bonanini F\*, **Singh M\***, Yang H, Kurek D, Harms AC, Mardinoglu A, Hankemeier T. A comparison between different human hepatocyte models reveals profound differences in net glucose production, lipid composition and metabolism *in vitro*. *Experimental Cell Research*, Volume 437, Issue 1, 1 April 2024, 114008.  
<https://doi.org/10.1016/j.yexcr.2024.114008>
3. **Singh M**, Elfrink HL, Harms AC, Hankemeier T. Recent developments in the analytical approaches of acyl-CoAs to assess their role in mitochondrial fatty acid oxidation disorders, *Molecular Genetics and Metabolism*. (2023) 107711.  
<https://doi.org/10.1016/j.ymgme.2023.107711>.
4. **Singh M**, Kiyuna LA, Odendaal C, Bakker BM, Harms AC, Hankemeier T. Development of targeted hydrophilic interaction liquid chromatography-tandem mass spectrometry method for acyl-Coenzyme A covering short- to long-chain species in a single analytical run. *Journal of Chromatography A*, Volume 1714, 11 January 2024, 464524.  
<https://doi.org/10.1016/j.chroma.2023.464524>.
5. Odendaal C\*, Kiyuna LA\*, **Singh M\***, Gerding A, Langelaar-Makkinje M, Zwaag M van der, Drachman A, Cetkovská V, Kioen GLF, Martines ACMF, Huijkman NCA, Schepers H, Sluis B van de, Reijngoud DJ, Oosterveer MH, Sibon OCM, Harms AC, Hankemeier T, Bakker BM. An old new player in MCADD: reduced free coenzyme A availability in medium-chain acyl-CoA dehydrogenase deficiency. (*In preparation*)

(\* authors contributed equally)

## **Others (not part of this thesis)**

1. Horcas-Nieto JM, Kiyuna LA, Langelaar-Makkinje M, Gerding A., Broekhuis MJC, Bonanini F, **Singh M**, Kurek D, Harms AC, Hankemeier T, Foijer F, Derks TGJ, Bakker B. iPSC-derived liver organoids as a tool to study Medium Chain Acyl-CoA Dehydrogenase deficiency. (*Submitted*)
2. Zhang Z, Karu N, Kindt A, **Singh M**, Lamont L, van Gammeren AJ, Ermens AAM, Harms AC, Portengen L, Vermeulen RCH, Dik WA, Langerak AW, van der Velden VHJ, Hankemeier T. Association of Altered Plasma Lipidome with Disease Severity in COVID-19 Patients. *Biomolecules* **2024**, *14*, 296  
<https://doi.org/10.3390/biom14030296>.
3. Tanwar B, Kumar D, Kumar A, Ansari MI, Qadri MM, Vaja MD, **Singh M**, and Chakraborti AK. Friedlander annulation: Scope and limitations of metal Lewis acid catalysts in selectivity control for the synthesis of functionalised quinolines. *New J. Chem.*, 2015,39, 9824-9833.  
<https://doi.org/10.1039/C5NJ02010G>

## Appendix

4. **Patent:** “2-(2-aryl/alkylphenyl)benzazoles as selective COX- 2 inhibitory scaffolds” M.S. Pharm. Research Project Patent Application No.: 2540/DEL/2015 (Granted). **Indian Patent Number: 387998.**

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The journey of my PhD has been truly unforgettable, as it has transformed me both on a personal and professional level. However, this journey would not be complete without the support of many people who have contributed in the completion of this thesis.

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