

FIXED-BED AND SIMULATED MOVING BED CHROMATOGRAPHY USING ACHIRAL AND CHIRAL ADSORBENTS FOR THE COMPLETE PREPARATIVE SEPARATION OF A QUATERNARY MIXTURE

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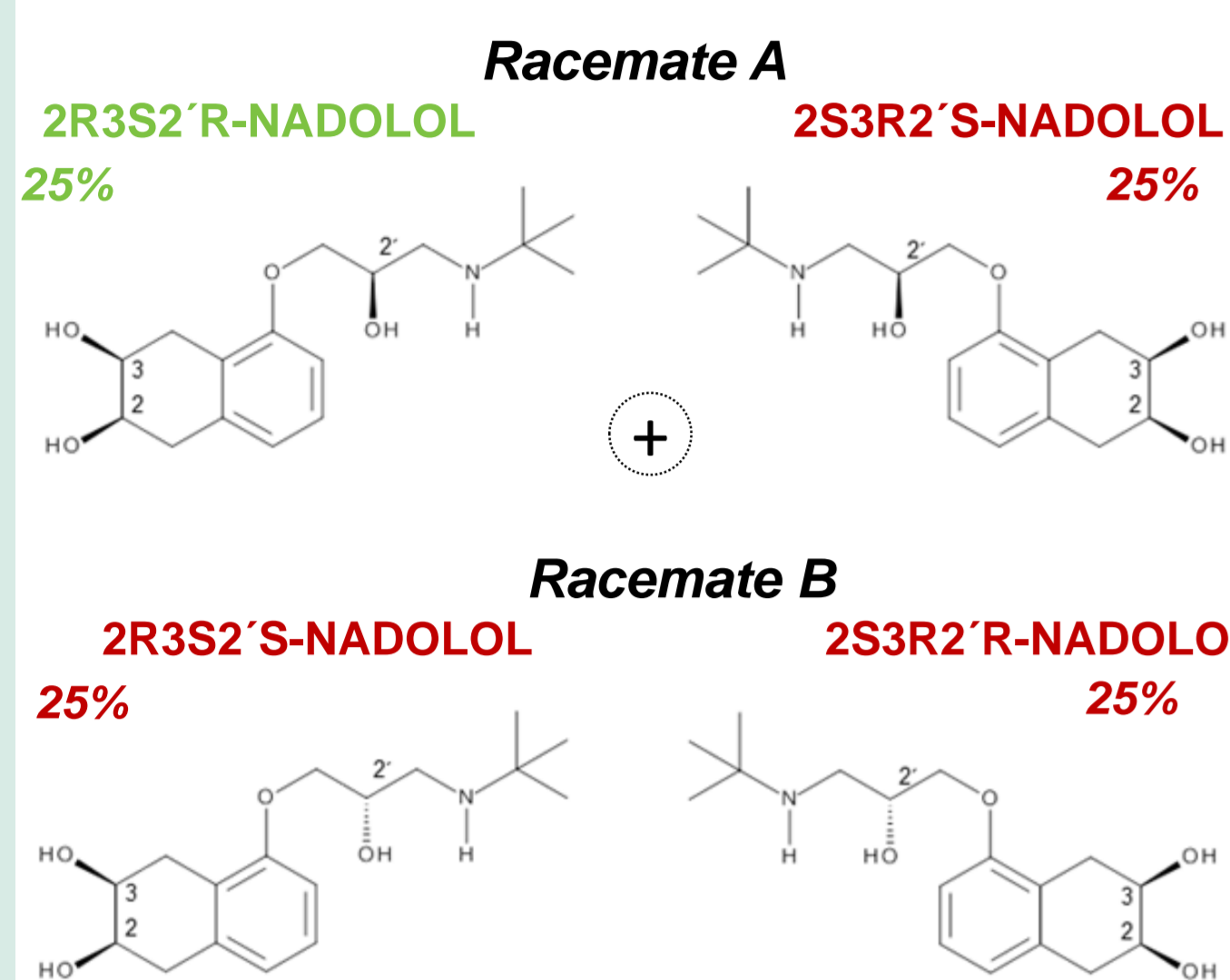
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Case Study: Nadolol Stereoisomers | Objective

NADOLOL is one representative pharmaceutical β -blocker drug marketed as a chiral mixture of 4 stereoisomers or “a mixture of 2 racemates”



BENEFITS

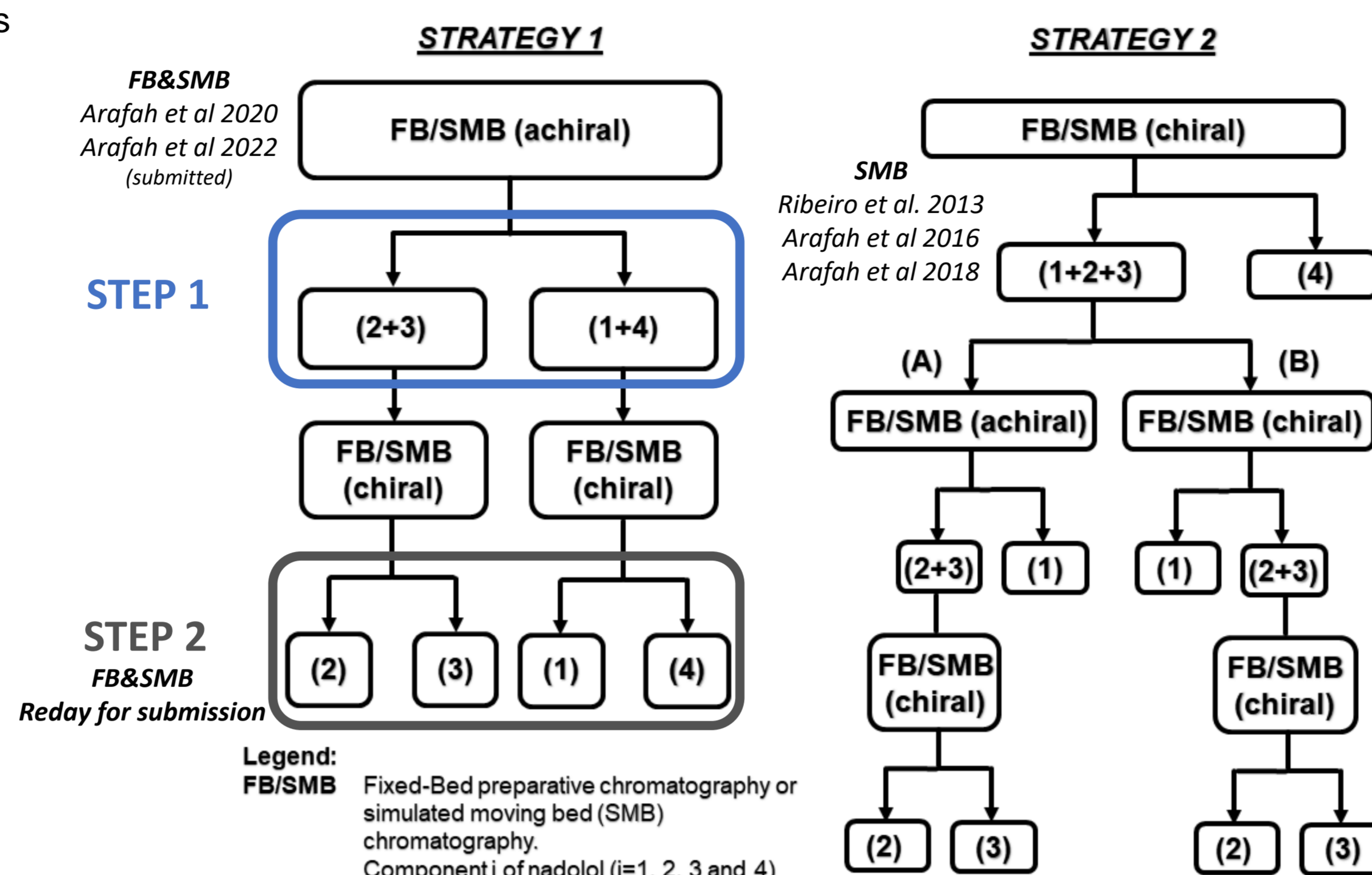
High Blood Pressure
Angina pectoris
Cardiac arrhythmia
Parkinsonian Tremor
Anxiety (...)

SEVERE RISKS

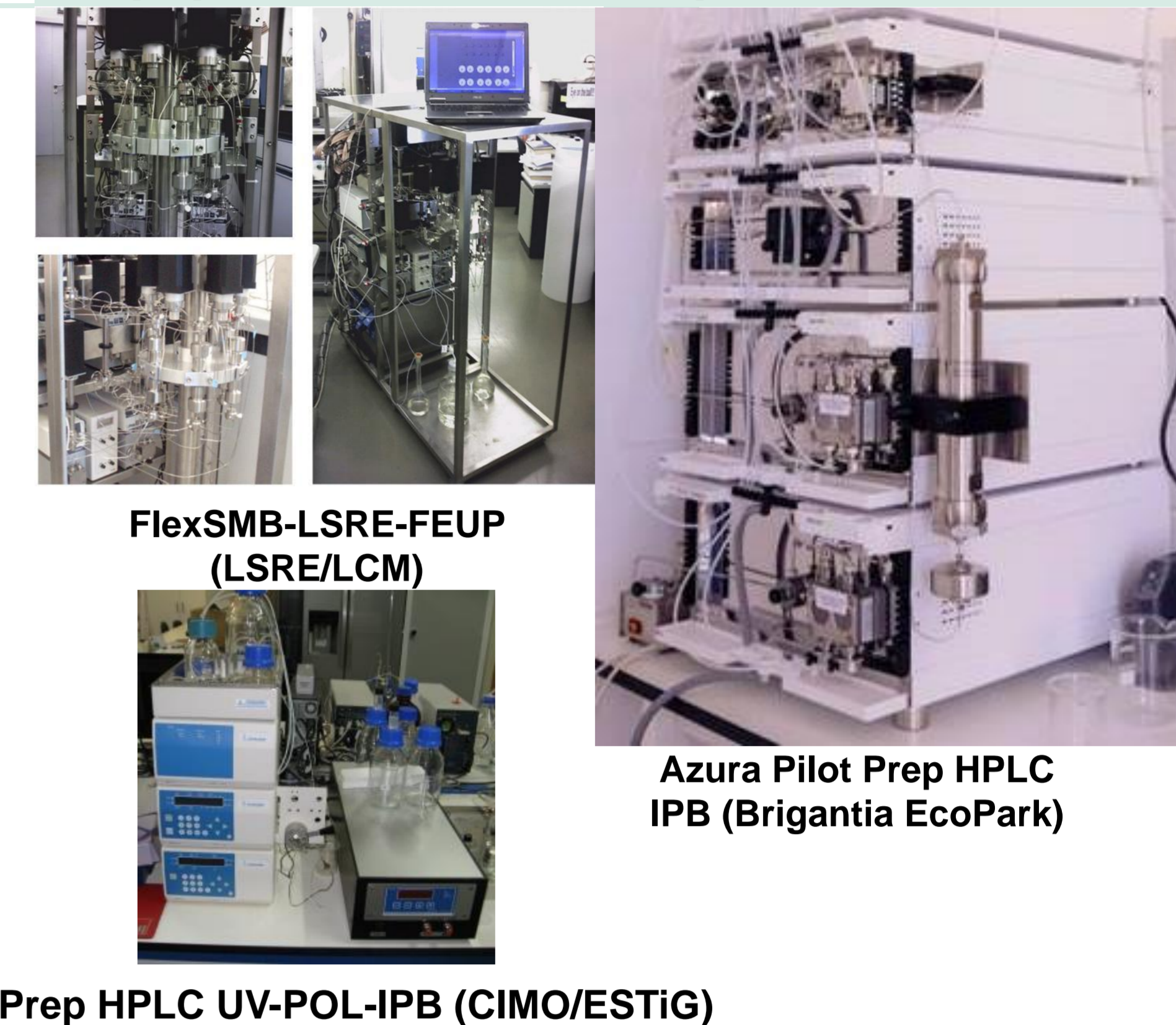
Abdominal pains
Depression / Insomnia
Cardiovascular failure
Dizziness
Hallucinations

OBJECTIVE: Separation of all the four stereoisomers of Nadolol

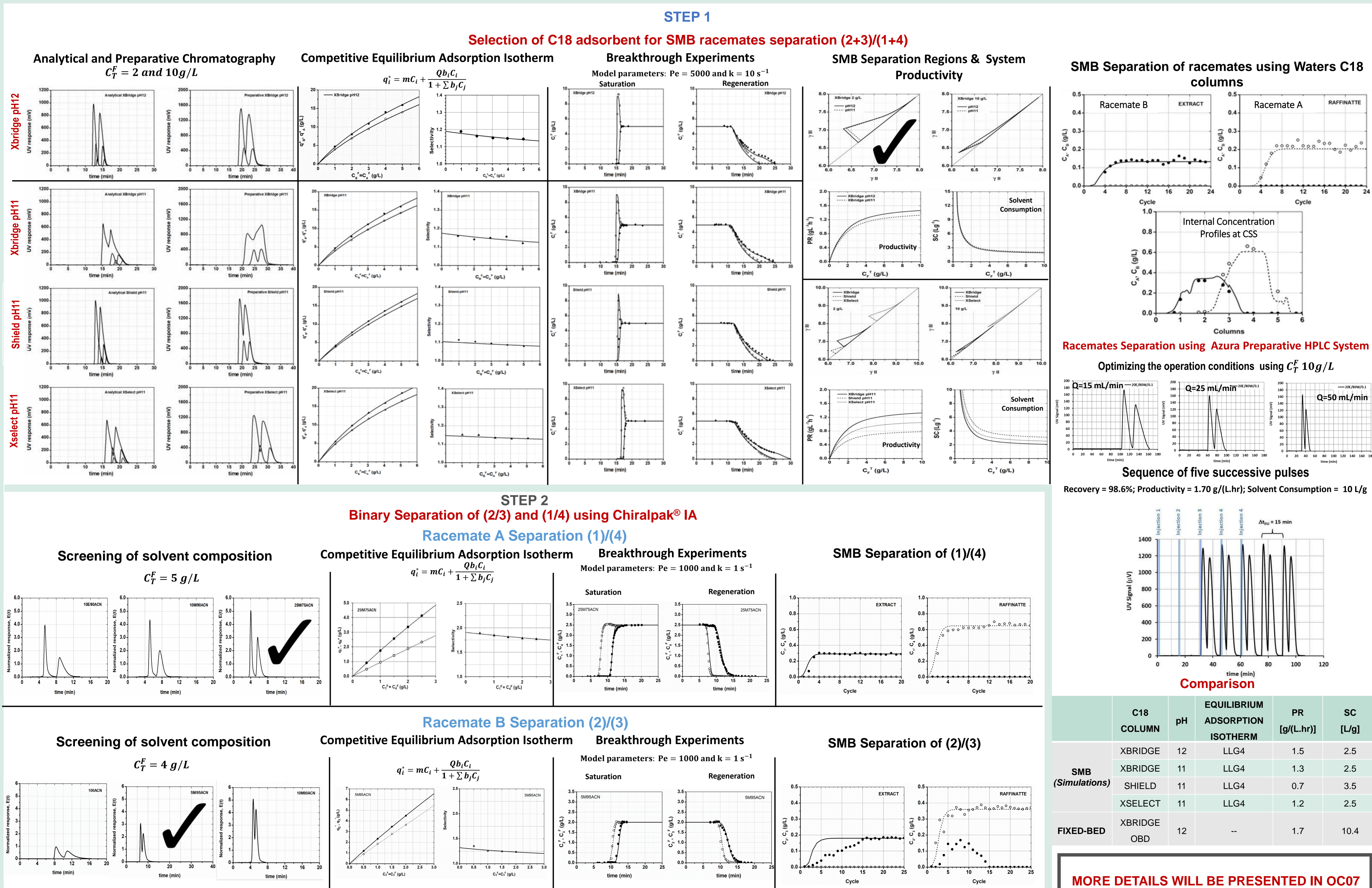
STRATEGIES FOR THE FB/SMB SEPARATION OF ALL THE FOUR STEREOISOMERS



Equipment for P/SMB Separations



Results



Conclusions & Future Work

- Strategies for complete separation of nadolol stereoisomers were well defined and applied.
- Reversed phase mode can be successfully applied for the separation of nadolol racemates.
- Real simulated moving bed separation was carried out using 2 g/L of nadolol, Purities for both extract and raffinate outlet streams was 100%.
- 35E/65E/0.15DEA mobile phase composition was selected to perform (2+3)/(1+4) enantiomer separation of nadolol using fixed bed technic.
- The complete separation of nadolol stereoisomers was achieved by applying different separation techniques, namely, fixed-bed technology and simulated moving bed (SMB) chromatography.

Future Work: Study of pharmacological properties of all the 4 stereoisomers of nadolol.

References:

- [1] A. Ribeiro, A. Rodrigues, L. Pais, Chirality, 25 (2013) 197-205.
- [2] R. Arafah, A. Ribeiro, A. Rodrigues, L. Pais, Chirality, 28 (2016) 399-408.
- [3] R. Arafah, A. Ribeiro, A. Rodrigues, L. Pais, Chirality, 31 (2019) 62-71.
- [4] R. Arafah, A. Ribeiro, A. Rodrigues, L. Pais, Sep. Pur. Technol., 233 (2020) 116018

Acknowledgments

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