Abstract

Computational Drug Repositioning of Mast Cell Stabilizers against Human Protease-Activated Receptor 2 (PAR2) Involved in Rheumatoid Arthritis †

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1. Introduction

Protease-activated receptor 2 (PAR2) plays a pivotal role in activating pain and inflammation pathways in rheumatoid arthritis (RA), contributing to cartilage destruction, synovial inflammation, and heightened joint pain. This study aims at identifying mast cell stabilizers with potential functionality in inhibiting PAR2 activation, focusing on FDA-approved candidates for their safety and efficacy.

2. Methods

Twelve mast cell stabilizers were selected based on toxicity screening and clearance time from PubChem. Molecular docking simulations were performed, assessing their interactions with the PAR2 molecule. Docking scores were meticulously analyzed to identify potential candidates with superior functionality compared to existing RA treatments, namely, Bicalutamide and Methotrexate. Lipinski’s rules of drug validity were applied to ensure drug-like properties.

3. Results

Among the mast cell stabilizers, S-Azelastine and Cromoglicic acid exhibited superior functionality, surpassing Bicalutamide and Methotrexate. The evaluation considered patient safety aspects and the efficacy of inhibiting PAR2 activation. Notably, the selected mast cell stabilizers demonstrated compliance with Lipinski’s rules, indicating their potential suitability for drug development.

4. Conclusions

This study highlights PAR2 as a promising target for drug repurposing in RA treatment. Mast cell stabilizers, particularly S-Azelastine and Cromoglicic acid, show potential for safer pain management in RA patients. Their superior functionality, especially in PAR2 inhibition and patient safety, suggests a viable avenue for drug repurposing strategies. Further exploration and development of these mast cell stabilizers could lead to novel therapeutic options for RA, addressing the critical need for more effective and safe pain management strategies in this patient population.
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