Ginkgo Biloba Flavonoid Extracts as a Carbonic Anhydrase II Inhibitors for Acute Mountain Sickness Prevention: A Molecular Docking Study

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Introduction

Based on research regarding phytomedicine as a prophylactic agent for acute mountain sickness (AMS), Ginkgo biloba extracts are among promising candidates. However, a mechanism of action of these extracts remains unknown. Previous studies have shown that some flavonoids, a phenolic metabolite found in various plants, have capability to inhibit carbonic anhydrase II (CAII), a zinc metalloenzyme that regulates acid-base homeostasis. This inhibition could potentially ameliorate an increase in systolic pressure and respiratory alkalosis found in AMS.

Objective

We aim to investigate effectiveness of flavonoid extracts from Ginkgo biloba as CAII inhibitor for opening up more possibilities of new AMS drug development based on natural extracts.

Method

Molecular docking technique was applied to screen candidate substances in order to shorten a period of the pre-clinical phase of drug development. Applying AutoDockVina docking and LigPlot+ interaction plotting, the results predict a binding affinity and interaction diagram of the coherence between the selected ligands and the CAII zinc binding site.

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Result
All flavonoid extracts demonstrated higher binding affinity score compared to CAII original substrates: carbon dioxide and bicarbonate. Moreover, quercetin, the highest affinity flavonoid, has zinc interaction and H-bond on the enzyme active site, similar to natural ligands with the greater cohesion stability from higher hydrophobic contact.

Conclusion
From the affinity results, G Biloba flavonoids competitively inhibit CAII and consequently mitigate the AMS. They are, therefore, highly likely to be tested as substitute drugs for acetazolamide, which is currently commercially used, in order to reduce the potential side effects of synthetic drug and increase bioavailability. Since this study is a pre-screening in silico, further studies including molecular dynamic, preclinical and clinical testing are essential for further development of a drug for AMS.

Keywords:
Ginkgo biloba; flavonoid; carbonic anhydrase isozyme II (CAII) inhibitor; acute mountain sickness (AMS); acetazolamide (AZM)