

Insights into aspirin side effects: In silico analysis of relationship between population polymorphisms and cyclooxygenase-1 inhibition

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Background and Aims: Aspirin a widely used non steroidal anti-inflammatory drug (NSAID) exerts its therapeutic effects through inhibition of cyclooxygenase isoform 2 (COX-2), while inhibition of cyclooxygenase isoform 1 (COX-1) leads to appearing side effects. The aim of this study was to simulate Aspirin mechanism of action and scoring the potency of drug inhibition based on population polymorphisms and consequently, eliminating the related side effects by introducing new theoretical model in prescribing Aspirin.

Methods: Molecular DOCKing of Aspirin into cyclooxygenase-1 was performed and functional impacts of 24 missense single nucleotide polymorphisms (SNPs) by scoring based on DOCK Amber scores were computationally analyzed.

Results: The data indicated that among 37 SNPs which were analyzed, 22 could reduce COX-1 inhibition by aspirin, while 15 showed increasing inhibition level in comparison to the regular COX-1 protein. Moreover, three amino acids located at the active site of COX-1 were site-directed mutagenised and their effects were analyzed. Among the investigated amino acids, R120A and R120Q were inhibited following interaction of Aspirin with the enzyme. Interestingly, R120A showed less negative score compare to other amino acids.

Conclusions: It is presumable that different people show altered aspirin inhibition potency of COX-1. In the way of personalized medicine, we represent a sub-population prescribing pattern to eliminate the related side effects of aspirin.

Keywords: Aspirin; Cyclooxygenase; SNPs; Personalized medicine