عنوان مقاله:

Structure-Based Virtual Screening of Cinnamic Acid Analogs Against RIPK۳: Implications for Anti-Inflammatory Drug Discovery

محل انتشار:

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خلاصه مقاله:

Background: A common oral inflammatory disease known as apical periodontitis (AP) is caused by the intrusion of microorganisms into the dental pulp, resulting in an inflammatory response and bone degradation in periapical tissues. A growing body of evidence indicates that the receptor-interacting serine-threonine kinase ۳ (RIPK۳) is closely associated with AP. Objectives: This study sought to address the requirement for effective RIPK۳ inhibitors by examining the potential of cinnamic acid natural metabolites capable of inhibiting RIPK۳. Methods: The binding affinity of ۲۰ cinnamic acids to the RIPK۳ active site was evaluated by using AutoDock ۴.۰ software. The most favorable scores were assigned to the highest-ranking cinnamic acids based on their ΔGbinding values to the RIPK۳ catalytic domain. A ۱۰۰-nanosecond (ns) computer simulation was performed using molecular dynamics for the most efficacious inhibitor of RIPK۳, and the findings were contrasted with those obtained for free RIPK۳. The Discovery Studio Visualizer tool was employed to showcase the interactions between the RIPK۳ active site and the highest-ranking metabolites. Results: The binding affinity of cynarin, rosmarinic acid (RosA), and chlorogenic acid (CGA) to the RIPK۳ active site was noteworthy, as the ΔGbinding values were<-۱۰ kcal/mol. Furthermore, cynarin exhibited inhibition constant values at the picomolar range. Upon complexation with cynarin, the RIPK۳ conformation attained stability after approximately ۲۵ ns of simulation. Conclusion: In general, cynarin, RosA, and CGA have the potential to be therapeutically beneficial in treating AP due to their ability to inhibit RIPK۳.

کلمات کلیدی: