

PHYTOCHEMICALS AS BONE REMODELERS. AN IN SILICO /CHEMOINFORMATICS STUDY ON MAP KINASE INHIBITORS

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Bone and Mineral metabolism play a crucial role in preserving bone health while their interruption can cause a decrease in bone density and consequently osteoporosis. The latter is caused when bone resorption by osteoclasts surpasses osteogenesis. Several mechanisms are known to have an impact in bone homeostasis, including Bone Specific Matrix proteins, ER mediated pathways, TGF- β 1/Smad pathways etc. Of major importance are the Mitogen-Activated Protein Kinases, which have been shown to regulate osteoclast differentiation and activation [1]. For this purpose, the inhibition potential of phytochemicals is examined against 5 MAP Kinases related with bone metabolism and osteoporosis focusing on p38a, but also p38b, ERK1, ERK2, JNK1 and JNK2. Collection of several classes of natural compounds was performed from open access chemical libraries. Virtual screening was performed for each protein target. Among several categories, flavonoids, isoflavonoids, saponins and phenolic acids were among the top 10% compounds with best docking scores on bone remodeling targets, while specific flavonoids were predicted to bind on MAPKs. Selected compounds were followed up for further investigation using molecular dynamics simulations.

[1] Lee, Kyunghye, et al. "Roles of mitogen-activated protein kinases in osteoclast biology." *International journal of molecular sciences* 19.10 (2018): 3004.

Acknowledgments: This research has been co-financed by the European Regional Development Fund of the European Union and Greek national funds through the Operational Program Competitiveness, Entrepreneurship and Innovation, under the call RESEARCH – CREATE - INNOVATE (project code: T2EDK-03847)