Multi-Target anticancer activity of *Moringa oleifera*: Targeting EGFR, COX-2 and Caspase-3

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ABSTRACT

Introduction: Abnormal cellular signaling associated with cancer discovery and development is also common in many cases. Whereas, the epidermal growth factor receptor (EGFR), cyclooxygenase-2 (COX-2) and Caspase-3 demonstrate prevalent, defective forms during solid tumor initiation, allowing uncontrolled proliferation and chronic inflammation followed by altered apoptosis. Directed therapies directed to select targeted pathways show promise, but compensatory signaling responses and initiation of other pathways have hampered their effects. Therefore, multi-target therapies have become more and more popular now. In this respect, also interest has increased in the modulation of natural compounds by the multisystem target-based therapeutic action. The medicinal plant, *Moringa oleifera* is known to have bioactive phytochemicals that have been found to be anticancer. Three compounds from *M. oleifera* were molecular docking studied against EGFR, COX-2 and Caspase-3 in the present work. **Materials and Methods:** Quercetin, kaempferol and niazimicin were chosen due to high anticancer activity and high content in *M. oleifera*. To extract three-dimensional structures of EGFR, COX-2 and Caspase-3 from the Protein Data Bank, they were analyzed using standard approach followed with the removal of water and reduction of energy input cost. The binding affinity and active sites at target protein sites having satisfactory interaction were then calculated by molecular docking. Binding strength docking scores were calculated, with smaller numbers yielding tighter binding. **Results:** COX-2 had maximum binding with niazimicin (-221.86) of target candidate and stable co-site interaction were proved that COX-2 could function as an immunofunctional regulator of inflammation-related processes involved in cancer cell fate. Strongly binding quercetin is also supportive of inhibition of proliferation signalling and promotion of apoptotic signaling pathways and EGFR (-140.01) and Caspase-3 (-182.09) were determined as the most active targets. Kaempferol presented a mild binding to the three targets (docking scores -134.78 to -172.28) and thus presented a diversified interaction profile. So, these compounds exhibit their relative target preference, indicating that compounds can have an impact synergistically. **Conclusion:** This conclusion indicates that in *M. oleifera* phytochemical extracts that have been extracted have a multi-target activity against cancer-progressive protein. Niazimicin is very sensitive to COX-2 and quercetin is highly bound to EGFR and Caspase-3 as well. Based on the results of the tests, Kaempferol works consistently on all targets examined. Accordingly, these compounds appear to have exertive effects via various tumorigenesis, inflammation, tumor growth and apoptosis resistance mechanisms. These results further confirm the promise of *M. oleifera* derived candidates for multistage anticancer therapies. However, additional cellular assays, molecular dynamics methodologies and animal studies could be undertaken to validate them and to characterize the therapeutic ability.

Keywords: *Moringa oleifera*, EGFR, COX-2, Caspase-3, cancer signaling, phytochemicals, multi-target therapy