

Abstract

# Ins and Outs of Flavonoids in Cancer Prevention vs. Cancer Therapy: A Lesson from Quercetin in Leukemia <sup>†</sup>

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**Abstract:** We recently critically reviewed clinical and pre-clinical studies on the concept that polyphenols, being antioxidant compounds, can fight cancer. We suggest that a clear distinction must be done between the use of polyphenols, such as flavonoids, in cancer treatment versus cancer prevention, starting from adequate and specifically selected cellular models. As an example, we will present data on the potential application of quercetin against chronic lymphocytic leukemia (CLL). Previous studies from our group indicated that quercetin synergistically sensitizes to apoptosis several leukemic cell lines and B-cells isolated from CLL patients, when associated with other pro-apoptotic agents. Using HG3 cells, derived from primary B-cells immortalized with Epstein-Barr virus, we demonstrated that the association between ABT-737, a BH3-mimetics, and quercetin synergistically induces apoptosis through the inhibition of PI3K/Akt signaling pathway. More importantly, we identified the protein kinase CK2 as a new, direct and primary target of quercetin, since CK2 activity was inhibited by the flavonoid within one minute from the treatment. Considering the rapid uptake of quercetin and its low toxicity against normal peripheral blood cells, we recommend the design of clinical studies aimed to demonstrate the potential use of the molecule in the adjuvant chemotherapy against CLL.

**Keywords:** quercetin; chemoprevention; chronic lymphocytic leukemia; antioxidants



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