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Quercetin inhibits hepatocellular carcinoma progression via modulation of HOTAIR/miR-526b-3p/DHX33 axis

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Hepatocellular carcinoma (HCC) remains a highly aggressive malignancy with limited therapeutic options. The long non-coding RNA (lncRNA) HOTAIR contributes to HCC progression through the regulation of the miR-526b-3p/DHX33 axis. This study investigated the antitumor effects of quercetin (Que) on HCC using both Hep3B and HepG2 cell lines, focusing on the modulation of this molecular pathway. In this regard, the study evaluated Que's effects on HOTAIR, miR-526b-3p, and DHX33 expression using qRT-PCR and ELISA. Cell viability was assessed by MTT assay, while apoptosis was measured through Annexin V-FITC/PI staining and analysis of BCL-2/CASP-3 expression. Additional investigations included cell cycle analysis (cyclin A2 and D1), invasion assays (p53 and PTEN), and assessment of oxidative stress markers (SOD, CAT, MDA). Results demonstrated that Que significantly suppressed HOTAIR and DHX33 while upregulating miR-526b-3p in both cell lines (P-value<0.001). Treatment with Que caused dose-dependent apoptosis (54.3% in Hep3B and 48.9% in HepG2 at 100μM) and cell cycle arrest while reducing invasion through TP53 downregulation and PTEN upregulation. Que also ameliorated oxidative stress by enhancing antioxidant enzyme activity (P-value<0.01). These findings suggest Que may exert potent antitumor effects in HCC through modulation of the HOTAIR/miR-526b-3p/DHX33 axis, though further *in vivo* and clinical investigations are warranted.

Keywords: lncRNA, MicroRNA, Cancer, Phytotherapy, Cell cycle arrest