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Letter to Editor

Promising tumor inhibiting potentials of Fisetin through PI3K/AKT/mTOR pathway

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Recently, Zhuo et al. reported an interesting data in their article. Fisetin, a dietary bioflavonoid, reverses acquired Cisplatin-resistance of lung adenocarcinoma cells through MAPK/Survivin/Caspase pathway [1].

Tumor inhibiting potentials of Fisetin was reported earlier by different research groups. Initiation of BRAF/MEK/ERK (MAPK) pathway by activating PI3K/AKT/mTOR signaling induces epithelial to mesenchymal transition (EMT) in cancer cells, leading to cell invasion and metastasis. Targeting these signaling mechanisms is crucial to develop an effective drug in cancer treatment. Fisetin inhibits ADAM9 expressions, activates ERK1/2 in glioma cancer cells [2] and attenuates colon tumor growth by inhibiting heat shock factor 1 (HSF1) in HCT-116 colon carcinoma cells [3]. Pal et al. showed inhibition of EMT in melanoma cells with reduction in MMP-2 and MMP-9 levels [4]. Fisetin in combination with sorafenib (chemotherapeutic drug) also inhibits Snail1, Twist1, Slug and ZEB1 protein expressions. It was reported to inhibit tumor growth by down-regulating PI3K/AKT and mTOR signaling and expressing PTEN protein levels in A549 lung carcinoma [5] and inmultiple myeloma U266 cells [6]. Furthermore, it also decreases phosphorylation of AKT, mTOR, mitf & p70S6K proteins in human melanoma 451Lu cells [7].

In Swiss albino mice, Fisetin showed protection against benzo(a)pyrene-induced lung carcinogenesis by restoring PCNA expression levels [8]. It exhibits protection against UV-B induced inflammation by inhibiting NF-κB/PI3K/AKT pathway in SKH-1 hairless mice. It also reduced DNA damage by activating markers such as p53 and p21 proteins [4] and inhibits phosphorylation of H2AX protein- a key element in DNA damage detection.

Novel inhibitors of PI3K, AKT, and mTOR are now under early clinical phase trials [9]. Since Fisetin acts through PI3K/AKT/mTOR pathway in many cancer cells, as evident from above examples, it might bring attention to use as a novel chemopreventive drug in cancer treatment.

Disclosure of conflict of interest

None.

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