Can CAPE be used as ideal antitumor agent "safely"?

Dears Editors,

Ozturk et al have recently published a paper in the journal European Review for Medical and Pharmacological Sciences, entitled "The anticancer mechanism of caffeic acid. Phenethyl ester (CAPE): review of melanomas, lung and prostate cancers"[1]. According to the literature, the Authors mentioned that, caffeic acid phenethyl ester (CAPE) might have a beneficial effect owing to antiinflammatory, antiproliferative, antioxidant, cytostatic, antiviral, antibacterial, antifungal and antineoplastic effects. They suggested that the CAPE can normalize disrupted metabolic functions by these stated mechanisms. The interactions between cytotoxicity and malignancies were well described. However, possible perfusion-oxidation related mechanisms were not reported.

I read the article by Ozturk et al with great interest. The Authors presented the possible reasons and recent therapeutical effects of CAPE in various malignancies. They reviewed the significant reports of CAPE in common cancer types that claimed the beneficial effects of CAPE. However, they did not mention the other supporting studies that designed in different patient population without cancer. But, there are a substantial number of studies that have demonstrated the antioxidation ability and cytoprotective behaviors of CAPE on ischemia reperfusion conditions, both in vitro and *in vivo*[2,3]. Wang et al[4] claimed that the purpose of their study was to determine if CAPE has similar effects in human umbilical vein endothelial cells (HUVEC). CAPE up-regulate the release of heme oxygenase-1 (HO-1) in a dose-dependent manner in HUVEC line. They suggested an important role of HO-1 induction in CAPE cytoprotection against oxidant stress, which may not relate to CAPE structural antioxidant activity nor to its traditional enzymatic activity. As Saavedra-Lopes et al[5] reported, "CAPE was able to protect the liver against normothermic I/R injury in rats by the inhibition of the NF-kappaB signaling pathway and decrease of the acute inflammatory response". Also, another study concluded that CAPE prevents higher myeloperoxidase and lipid peroxidation-mediated myocardial injury via inhibition of neutrophil's MPO activity presented by Oktar et al[3].

CAPE is active component of honeybee propolis that bodied like flavonoids. It is inhibiting the oxidation that produced from the interactions between 5'-lipoxygenase and linolenic acid-arachidonic acid[6]. The tissue protective effects of CAPE against the ischemia-reperfusion conditions were demonstrated in the recent studies[7]. Therefore, Basini et al claimed that CAPE had inhibitory effects to the angiogenesis[8]. Song et al similarly suggested that angiogenesis might have been inhibited by propolis[9].

To sum up, the main purpose of all anti-tumor therapies is regression tumoral tissue by inhibiting the tumor angiogenesis with minimal harm to the organism. CAPE is seems to be an ideal anti-tumor agent that has cytoprotective effect with antiangiogenic behaviors. However, the impacts of CAPE to the normal vascular structures are still unknown. So, it should be carefully used in cancer patients with vascular disorders such as diabetic vasculopathies, etc.

References

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