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Letter to the Editor

Letter to Editor on the paper entitled "Curcumin-Celecoxib: a synergistic and rationale combination chemotherapy for breast cancer"

Dear Editor,

We read with interest the paper by Alqahtani et al[1] recently published in Eur Rev Med Pharmacol Sci, presenting a pre-clinical study including the application of a natural compound as adjuvant in cancer treatment.

In the last decades, the combination between natural compounds and standard chemotherapeutic agents has become a useful therapeutic tool allowing a reduction of chemotherapeutic agents' dosage and decreasing their toxicity[2-5]. Moreover, combination therapies enhance the efficiency of standard drugs because of their synergistic effect[6]. This approach is a promising strategy for the clinical treatment of drug-resistant cancers because different compounds target cancer cells exploiting diverse signaling pathways.

Several preclinical studies reported the use of curcumin as adjuvant and chemosensitizing compound and different molecular mechanisms such as the inhibition of nuclear factor-kappa-B (NF-κB) pathway, or the activation of nuclear factor-erythroid 2-related factor 2 (Nrf2)/antioxidant response element (ARE) pathway, underlying its activity, have been described[7].

Dr. Alqahtani et al[1] focused on the synergistic effect of curcumin and celecoxib in breast cancer cells, suggesting that targeting the overexpressed COX-2 increases pro-apoptotic proteins, thus inducing apoptosis. These *in silico* and *in vitro* results need to be validated by *in vivo* studies, which are fundamental for translation to clinical studies. COX-2 plays an important role in metastatic colorectal cancer, which is now treated with standard chemotherapeutic agents, such as oxaliplatin or 5-fluorouracil[8-10]. Indeed, the combination of curcumin and celecoxib was tested in colon cancer, and the synergistic effect was clinically achieved in patients[11].

Despite the already known synergism between plant extracts and standard chemotherapy the clinical translation is supported by very few clinical trials. Notably, several nutraceuticals have poor oral bioavailability therefore tissue concentration will be very low after oral administration in humans[12]. In fact, clinical trials support the administration of nanometric carriers of nutraceuticals in order to optimize their anti-inflammatory and chemo-sensitizing properties[13,14]. We encourage the study of putative cardioprotective effects of nutraceutical-based formulations especially in a cohort of particularly vulnerable patients, where chemotherapy has very frequent cardiotoxic effects such as left ventricular dysfunction, arrhythmias, myocardial infectiousness and venous thromboembolism[15].

Future studies about the combined therapy between natural compounds and standard chemotherapeutic agents could represent promising approaches for cancer treatment also with the final aim to overcome drug resistance. In addition, the combined therapy puts a step forward integrative oncology, which considers the patient as the centre of the care.

Conflict of interest

The authors declare that they have no conflicts of interest.

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