http://dx.doi.org/10.7124/bc.000AD3

The effect of plant alkaloid Chelidonin with fullerene C_{60} carbon nanoparticles on the permeability of hERG potassium channels

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Background. In recent years, many drugs approved by Food and Drug Administration have been withdrawn from the pharmaceutical industry due to their off-target effects, which often lead to cardio cytotoxicity. As a result, there is an increasing interest in the identification of drugs with potential impact on the cardiac rhythm at early stages of the drug development process, as well as the way to reduce their cardiotoxic effects. Nowadays, several cell-based assays identify inhibitors and modulators of cardiac functions. FluxOR assay is one of the important cell models for investigating cardio cytotoxicity *in vitro*. It is based on the usage of HEK293-hERG cell line expressing the hERG (Human Ether-à-go-go Related Gene) potassium channel, which has a key role in regulation of the heart rhythm. Chelidonin is a secondary metabolite of *Chelidonium majus* L. It was shown that Chelidonin inhibits cell proliferation and induces mitotic arrest, which in turn is accompanied by an increase in the number of cells with apoptosis. Currently, Chelidonin is considered a potential anti-tumor drug, so the investigation of its potential off-target effects and the way to reduce them is important. Due to the antioxidant properties of fullerene C_{60} and its ability to protect cells from oxidative stress, it is a promising candidate for reducing the cardiotoxic effects of certain drugs. **Aim.** Our study aimed at investigating the effect of plant alkaloid Chelidonin as a monotherapy and in the co-treatment with carbon nanoparticles fullerene C_{60} on the K^+ ion permeability through hERG potassium channel using FluxOR assay. **Methods.** The stably transfected HEK293-hERG cells were treated with Chelidonin alone, C_{60} fullerene alone, or with a mixture of Chelidonin and C_{60} fullerene. The activity of the hERG channels was measured using FluxOR assay kit. Real-time changes in the activity of potassium channels were measured using FLIPR Tetra High Throughput Screening System. The data were analyzed with ScreenWorks v.3.2 software. **Results.** Dose-dependent inhibition of K+ channels permeability in the HEK293-hERG cells was found after 30-min treatment with Chelidonin in the concentration range of 0.1–200 μM. The IC_{50} value in HEK293-hERG cells for alkaloid was 24.9 μM. C_{60} fullerene in the concentration range of 0.02–40 μM did not affect the inhibition of potassium channels. The IC_{50} value under the combined action of Chelidonin and C_{60} fullerene was increased by 3.9-fold compared to the IC_{50} value for Chelidonin alone and amounted to 97.8 μM. The obtained results indicated a positive effect of C_{60} fullerene nanoparticles, as evidenced by an increase in K^+ permeability through ion channels under the action of the alkaloid. **Conclusions.** Thus, studies on potassium channels permeability are extremely important due to their wide-ranging effects on various physiological processes. The use of the FluxOR screening assay is an effective tool for identifying molecules that inhibit the cellular hERG potassium channels. The inhibitory effect of Chelidonin on the hERG potassium channels can be reduced by C_{60} fullerene nanoparticles.

Keywords: fullerene C_{60}, chelidonine, hERG channels.