

Inhibitory Action of a Novel Phytherapeutic Compound Against Human Hepatoma Cells

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The search for effective chemotherapeutic agents remains an important goal aimed to improve the survival rate of patients with advanced or recurrent HCC after surgical treatment. This prompts the need for the evaluation of new active drugs against HCC.

In recent years we have performed experimental and clinical tests suggesting the potent hepatoprotective properties of a natural compound, i.e. YHK (panax pseudo-ginseng, *Eucommia Ulmoides*, polygonati rhizome, glycyrrhiza licorice, panax ginseng, Kyotsu Jigyo, Tokyo, Japan) besides its safety profile. HepG2 human hepatoma cells were incubated for 24 or 48 h. with various concentrations of YHK solution. After 24 h incubation, cell proliferation and cytotoxicity were determined by 3-(4,5-dimethylthiazol-2-yl)-5-(3-carboxymethoxyphenyl)-2-(4-sulphophenyl)-2Htetrazolium (MTT) assay.

Cytotoxicity or necrosis was expressed as lactate dehydrogenase (LDH) release. After exponential growth phase HepG2 cells were treated with different doses of YHK and apoptosis was assessed by using an Annexin V-FITC kit. Further, oxidative stress was measured by dichlorofluorescein-diacetate (DCFH-DA) assay. As compared to control, YHK-treated cultures showed a significant time-course decrease of the proliferation rate of HepG2 cell growth ($p<0.01$). This is likely to be due to an enhanced cytotoxicity (MTT and LDH tests) ($p<0.001$). On the other hand, YHK showed in vitro to significantly enhance the oxidative stress of HepG2 cell ($p<0.01$) while also markedly increasing apoptosis at 72hr with cells G2/M phase arrest ($p<0.01$).

These data suggest that YHK seem to modulate the extrinsic and intrinsic regulators of apoptosis and sensitize tumour cells to apoptosis. These preliminary data are worth interest when considering that this nutraceutical has been shown in vitro and in vivo to exert protective anti-tumour effect by redox status-modulating and immuno-regulatory actions. Given its lack of toxicity so far reported, such natural product might represent a potential nutritional supplement in a number of pathological conditions where a chemo-preventive strategy is planned.