

Special Article - Food Supplements: Clinical Cases & Short Reports

Food Supplement Development in Russia on the Basis of Cell Culture Experiments

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Letter to the Editor

The large research series has become internationally known after the publications with participation of the former Soviet minister of health [1] and continues until today [2]. In brief, cultures of smooth muscle cells or monocytes/macrophages were used for evaluation of the ability of different substances to enhance or diminish cholesterol deposition in the cells, incubated with sera from atherosclerosis patients, which was interpreted as pro- or anti-atherogenic effects. Among others, the following was reported: during 24 hours of incubation with diluted sera from patients with coronary atherosclerosis, the contents of total intracellular cholesterol in the cultured cells increased 2- to 5-fold. The LDL from coronary atherosclerosis patients caused a 2- to 4-fold elevation of cholesterol level in the cultured cells. Incubation with sera or LDL from healthy subjects did not induce cholesterol accumulation by the cultures [3,4]. According to the personal communication from Dr. Aksenov at the 77th Congress of the European Atherosclerosis Society (2008) the "cultures" did not grow; therefore, it might be more appropriate to name these cells, surviving for about 7 days in serum-containing media [5], not "cell cultures" but "incubated cells". This model was used for evaluation of sex hormones: the estrogens and testosterone were reported to reduce intracellular cholesterol accumulation. Interestingly, dihydrotestosterone had the opposite effect [6]. After the latter remark had been published [7], an analogous communication reported that testosterone "increased intracellular cholesterol content" [5]. Using the same model, various drugs and natural substances were found to have pro- or anti-atherogenic effects [8]. However, as discussed previously [7,9,10], a relationship between the uptake of lipids by cells *in vitro* and hyperlipidemia *in vivo* can be inverse rather than direct. The lipoprotein receptors are expressed both on macrophages and smooth muscle cells. An up-regulation of lipoprotein receptors is one of the action mechanisms of certain lipid-lowering agents [11]. If an agent lowers the uptake of lipids by cells *in vitro*, it should be expected to elevate the blood cholesterol level *in vivo*. Admittedly, modifications of the chemical structure of LDL particles may facilitate LDL ingress into cells through non-receptor-regulated pathways [12]; but it would possibly lower blood

cholesterol level i.e. act against atherogenesis *in vivo*. In any case, the use of cultures or incubated cells for prediction of body responses is limited [9,10]; and drug doses [13] should not be calculated on the basis of cell culture experiments only. Some results obtained *in vitro* or *ex vivo* by the same researchers, such as anti-atherogenic effects of mushroom extracts [14], canned fish [15], or pine needles [16], appear doubtful. Recommendations for practice [17], based on the cell culture experiments discussed above, appear to be unsubstantiated at least in part. This example shows how suboptimal methods are used for official registration of dietary supplements and obtaining permissions for their practical use. Research quality and possible influence by the industry [9] should be taken into account defining inclusion criteria for studies into meta-analyses and reviews.

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