RESEARCH PAPER

Clinical Evidence of the Efficacy of Agents That Increase Sialic Acid Levels in Low-Density Lipoprotein

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Sialidase plays a key role in altering low-density lipoprotein (LDL) in a way that promotes atherosclerosis [1]. The removal of sialic acid residues from LDL by sialidase leads to lipid accumulation in arterial cells, which in turn initiates the development of atherosclerosis within arterial cells [2]. A recent article titled "Search for agents that increase the level of sialic acid in low-density lipoprotein" used virtual screening, including molecular docking, to identify flavonoids capable of inhibiting sialidase activity [3]. It is predicted that agents with such activity will increase the level of sialic acid in LDL, reducing its atherogenicity. Among the identified flavonoids, epigallocatechin should theoretically exhibit high inhibitory activity; in contrast, avicularin should be a weak inhibitor of sialidase. In vitro experiments, epigallocatechin inhibited sialidase 6.2 times more than avicularin. Thus, the experimental results fully confirmed the virtual screening data. Furthermore, avicularin was found to effectively stimulate sialyltransferase, the enzyme that adds sialic acid to LDL glycoconjugates. Meanwhile, epigallocatechin was found to be only a weak inhibitor of sialyltransferase. Therefore, epigallocatechin is best considered a reliable sialidase inhibitor, and avicularin a sialyltransferase activator.

It was decided to obtain definitive confirmation of the ability of epigallocatechin and avicularin to increase sialic acid levels in LDL. To this end, a pilot clinical trial was designed and conducted.

Tertinat (INAT-Pharma Ltd, Russia), a dietary supplement based on green tea leaf extract and containing 70% epigallocatechin, was used as a source of epigallocatechin. The medicinal product AngioNorm (PharmVILAR Ltd, Russia) was used as an avicularin-containing agent. According to the manufacturer, AngioNorm® dry extract is obtained from a mixture of medicinal plant materials (hawthorn fruit, licorice root, horse chestnut seeds, and rose hips) with a flavonoid content equivalent to 0.50 mg of avicularin.

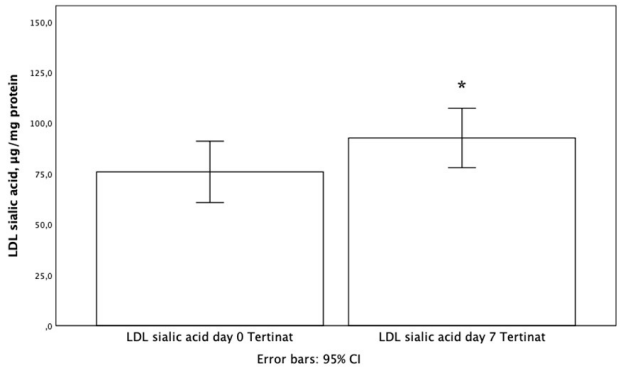
Patients with severe coronary atherosclerosis received Tertinat or AngioNorm for 7 days. LDL samples were obtained from patients' blood sera by two-step ultracentrifugation in KBr density gradient [4]. The LDL sialic acid content was measured by a modified Warren method [5]. Statistical analysis was performed using the IBM SPSS 26.0 software package (IBM Corp., USA).

The results are shown in Figure 1.

Tertinat increased LDL sialic acid levels by 32.0±10.0% (SD=42.6). AngioNorm increased LDL sialic acid levels by 38.5±12.9% (SD=40.6).

Combined administration of Tertinat and AngioNorm increased LDL sialic acid levels by 53.6±23.1%. However, these differences were not statistically significant, likely due to the small sample size in the pilot study.

A



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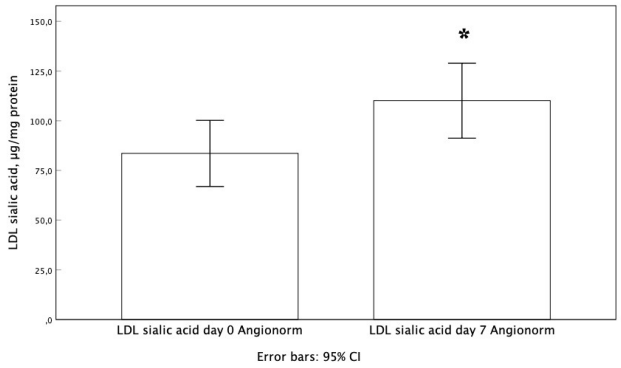

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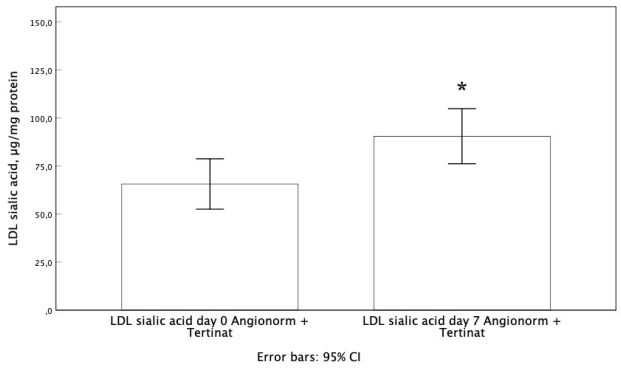

Fig. 1. Effect of agent intake on LDL sialic acid content.
Panel A. 18 male patients with coronary atherosclerosis, Tertinat, 1 capsule once daily for 7 days.
An asterisk indicates a statistically significant difference (p = 0.016 - paired Student's t-test; p = 0.016 - paired Wilcoxon signed-rank test).
Panel B. 10 male patients with coronary atherosclerosis, Angionorm, 1 capsule three times daily for 7 days.
An asterisk indicates a statistically significant difference (p = 0.017 - paired Student's t-test; p = 0.022 - paired Wilcoxon signed-rank test).
Panel C. 10 patients with coronary atherosclerosis, males, Angionorm, 1 capsule 3 times daily + Tertinat, 1 capsule once daily for 7 days.
An asterisk indicates a statistically significant difference (p = 0.028 - paired Student's t-test; p = 0.028 - paired Wilcoxon signed-rank test).

Thus, it was definitively proven that sialidase inhibition and/or sialyltransferase stimulation increase sialic acid levels in LDL in patients. Combined use of a sialidase inhibitor and a sialyltransferase activator clearly tends to enhance the effect.

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