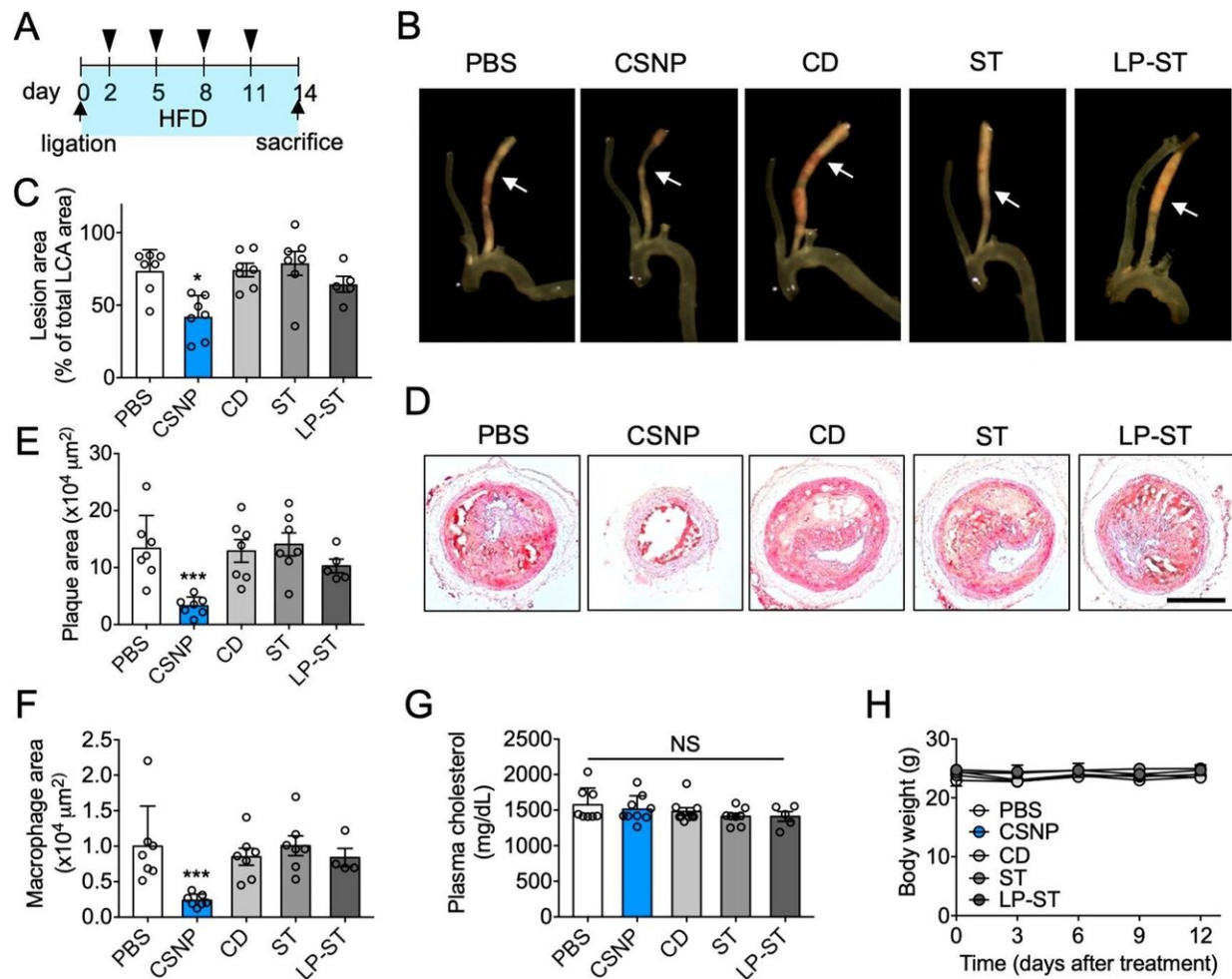


# New nanoparticle drug combination for atherosclerosis developed

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Antiatherogenic effect of CSNP. Credit: The Korea Advanced Institute of Science and Technology (KAIST)

Physicochemical cargo-switching nanoparticles (CSNP) designed by KAIST can help significantly reduce cholesterol and macrophage foam cells in arteries, which are the two main triggers for atherosclerotic plaque and inflammation.

The CSNP-based combination drug delivery therapy was proved to exert cholesterol-lowering, anti-inflammatory, and anti-proliferative functions of two common medications for treating and preventing atherosclerosis that are [cyclodextrin](#) and statin. Professor Ji-Ho Park and Dr. Heegon Kim from KAIST's Department of Bio and Brain Engineering said their study has shown great potential for future applications with reduced side effects.

Atherosclerosis is a chronic inflammatory vascular disease that is characterized by the accumulation of cholesterol and cholesterol-loaded macrophage foam cells in the intima. When this [atherosclerotic plaque](#) clogs and narrows the artery walls, they restrict [blood flow](#) and cause various cardiovascular conditions such as heart attacks and strokes. Heart attacks and strokes are the world's first and fifth causes of death respectively.

Oral statin administration has been used in clinics as a standard care for atherosclerosis, which is prescribed to lower blood cholesterol and inhibit its accumulation within the plaque. Although statins can effectively prevent the progression of plaque growth, they have only shown modest efficacy in eliminating the already-established plaque. Therefore, patients are required to take statin drugs for the rest of their lives and will always carry the risk of plaque ruptures that can trigger a blood clot.

To address these issues, Professor Park and Dr. Kim exploited another antiatherogenic agent called cyclodextrin. In their paper published in the *Journal of Controlled Release* on March 10, Professor Park and Dr. Kim

reported that the polymeric formulation of cyclodextrin with a diameter of approximately 10 nanometers(nm) can accumulate within the atherosclerotic plaque 14 times more and effectively reduce the plaque even at lower doses, compared to cyclodextrin in a non-polymer structure.

Moreover, although cyclodextrin is known to have a cytotoxic effect on [hair cells](#) in the cochlea, which can lead to [hearing loss](#), cyclodextrin polymers developed by Professor Park's research group exhibited a varying biodistribution profile and did not have this side effect.

In the follow-up study reported in *ACS Nano* on April 28, the researchers exploited both cyclodextrin and statin and form the cyclodextrin-statin self-assembly drug complex, based on previous findings that each drug can exert local anti-atherosclerosis effect within the plaque. The complex formation processes were optimized to obtain homogeneous and stable nanoparticles with a diameter of about 100 nm for systematic injection.

The therapeutic synergy of cyclodextrin and [statin](#) could reportedly enhance plaque-targeted drug delivery and anti-inflammation. Cyclodextrin led to the regression of cholesterol in the established plaque, and the statins were shown to inhibit the proliferation of macrophage foam cells. The study suggested that [combination therapy](#) is required to resolve the complex inflammatory cholesterol-rich microenvironment within the [plaque](#).

Professor Park said, "While nanomedicine has been mainly developed for the treatment of cancers, our studies show that nanomedicine can also play a significant role in treating and preventing atherosclerosis, which causes various cardiovascular diseases that are the leading causes of death worldwide."

**More information:** Heegon Kim et al. Cyclodextrin polymer improves atherosclerosis therapy and reduces ototoxicity, *Journal of Controlled Release* (2019). [DOI: 10.1016/j.jconrel.2019.12.021](https://doi.org/10.1016/j.jconrel.2019.12.021)

Heegon Kim et al. Affinity-Driven Design of Cargo-Switching Nanoparticles to Leverage a Cholesterol-Rich Microenvironment for Atherosclerosis Therapy, *ACS Nano* (2020). [DOI: 10.1021/acsnano.9b08216](https://doi.org/10.1021/acsnano.9b08216)

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