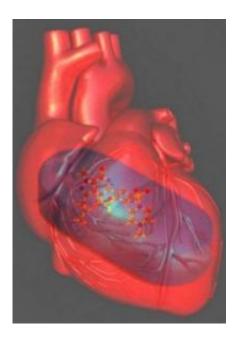


Viagra against heart failure: Researchers throw light on the mechanism

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Sildenafil, the active ingredient of Viagra makes cardiac walls elastic again. Illustration: Prof. Dr. Wolfgang Linke © Prof. Dr. Wolfgang Linke

How sildenafil, the active ingredient in Viagra, can alleviate heart problems is reported by Bochum's researchers in cooperation with colleagues from the Mayo Clinic in Rochester (Minnesota) in the journal Circulation. They studied dogs with diastolic heart failure, a condition in which the heart chamber does not sufficiently fill with blood. The scientists showed that sildenafil makes stiffened cardiac walls more elastic again. The drug activates an enzyme that causes the giant protein



titin in the myocardial cells to relax. "We have developed a therapy in an animal model that, for the first time, also raises hopes for the successful treatment of patients" says Prof. Dr. Wolfgang Linke of the RUB Institute of Physiology.

Sildenafil inhibits a specific enzyme (phosphodiesterase 5 A), which causes the increased formation of a messenger substance (cGMP). The messenger substance activates the <u>enzyme protein</u> kinase G, which attaches phosphate groups to certain proteins. This so-called phosphorylation causes blood vessels to relax, which was why the "potency pill" Viagra originally came onto the market. The Bochum and Rochester researchers found that the cardiac <u>muscle protein</u> titin is also phosphorylated through the same mechanism. "The titin molecules are similar to rubber bands" explains the Bochum physiologist. "They contribute decisively to the stiffness of the cardiac walls." The activity of the protein kinase G causes titin to relax. This makes the cardiac walls more elastic. The effect occurs within minutes of administering the drug.

"Of all the patients aged over 60 who are in hospital because of a weak heart, half suffer from diastolic heart failure" explains Linke. "Although we know that the decreased distensibility of the cardiac walls is the cause, the disease cannot be treated properly with today's medicines." In the so-called "Relax" study of the Heart Failure Network, the efficacy of sildenafil in people is already being tested. "If, for the first time, the drug is found to have a positive effect on <u>heart failure</u>, we would already have a molecular mechanism on hand to explain the effect" says Linke.

More information: K. Bishu, N. Hamdani, S.F. Mohammed, M. Kruger, T. Ohtani, O. Ogut, F.V. Brozovich, J.C. Burnett, W.A. Linke, M.M. Redfield (2011): Sildenafil and B-type natriuretic peptide acutely phosphorylate titin and improve diastolic distensibility in vivo, *Circulation*, doi: 10.1161/CIRCULATIONAHA.111.048520



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