

Inhibitory effect of garlic (*Allium sativum*) juice on nitroglycerin-induced vasorelaxation tolerance in rat isolated thoracic aorta

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Background and Aims: Nitroglycerin is a drug used against angina pectoris. Nitroglycerin is converted in the vasculature to nitric oxide (NO) or a closely related molecule. However, long-term administration of nitroglycerin can cause the development of tolerance. The mechanisms responsible for tolerance to nitroglycerin are not clearly understood. Main proposed mechanisms include oxidative stress, inhibition of nitroglycerin-metabolizing enzyme. Oxidative stress may contribute directly to nitroglycerin tolerance, either by oxidative inhibition of ALDH-2 or perhaps by oxidizing key enzyme cofactors. Present study was based on a theory which antioxidant effect of garlic juice may attenuate the tolerance induced by prolonged exposure to nitroglycerin in rat isolated aorta rings.

Results: This study revealed that, garlic juice has dose dependent vasodilatory effect on rat isolated aorta pre-contracted with phenylephrine or KCl. The relaxation was not affected by indomethacin, an inhibitor of cyclooxygenase or tetra ethyl ammonium (an inhibitor of K channels), but was affected by endothelium removal or absence of calcium, concluding probable mechanisms related to endothelium and calcium channels mediated vasorelaxation. Also garlic juice has been examined whether it could affect vasorelaxation tolerance induced by nitroglycerin. Data revealed that garlic juice has a contradictive effect depending on the concentration used. At low concentration (0.5 µl/ml) attenuated nitroglycerin-induced tolerance but in higher concentrations (1 and 2 µl/ml) enhanced the tolerance. N-acetyl cystein which has shown a protective effect on vasculature dysfunction by decreasing the level of reactive oxygen species in laboratory animals and human hypertension, decreased nitroglycerin tolerance and also reduced tolerance increment by garlic juice at the dose of 1 and 2 µl/ml. Similar results was obtained by grape seed extract a powerful antioxidant substance.

Conclusions: These results suggest that antioxidant effect of garlic juice may be (at least) one of the main mechanisms in reducing tolerance to nitroglycerin in rat thoracic aorta.

Keywords: Garlic juice; Nitroglycerin; Rat aorta; Vasorelaxant effect