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Gut Microbiota-derived Metabolite, Shikimic Acid, is a Novel Regulator of Vascular Tone

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Introduction: Gut dysbiosis is linked to vascular wall disease, yet the mechanisms through which gut microbiota interact with host cells remain largely unexplored. Shikimic acid is a biochemical intermediate synthesized in plants and microorganisms, but not mammals. We have recently identified shikimic acid as a novel gut microbiota-derived metabolite that is readily detectable in human and murine blood. Since vascular cells are the first to encounter circulating metabolites, in this study, we examined, for the first time, the potential effects of shikimic acid on vascular tone utilizing isolated conduit and resistance arteries from WT C57BL/6 mice.

Methods: Vascular reactivity was assessed ex vivo using wire myography utilizing dorsal aortic rings and mesenteric resistance arteries isolated from male and female adult WT C57BL/6 mice. Results: Our results demonstrate that while shikimic acid alone does not alter basal vascular tone, it triggers substantial, concentration-dependent vasorelaxation in dorsal aortic rings preconstricted with Gq-coupled pathway agonists, such as phenylephrine (PE) or serotonin (5-HT). Time course assays demonstrated that treatment with a single concentration of shikimic acid (10 mM) induces reversible relaxation that persists for at least 20 minutes after treatment. Consistently, we found that pretreatment of vessels with shikimic acid attenuates sensitivity (EC50) to both PE and 5-HT but does not alter maximum response (Emax). Notably, these observations were reproducible in mesenteric arteries and did not exhibit differences between male versus female mice. Ongoing experiments aim to elucidate the potential underlying mechanisms mediating the effects of shikimic acid on vascular reactivity.

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Conclusion: This study provides the first evidence of substantial vasorelaxant effects of the microbiota-derived metabolite, shikimic acid, establishing a foundation for future research into its potential therapeutic role as a postbiotic in mitigating arterial hypertension.

Keywords: SA - Shikimic acid, Gut microbiota, Blood Pressure, Cardiovascular disease

