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Lipoxins A_4 and B_4 : Comparison of Icosanoids Having Bronchoconstrictor and Vasodilator Actions but Lacking Platelet Aggregatory Activity*

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Lipoxins A_4 (LxA_4) and B_4 (LxB_4), two lipoxygenase-generated icosanoids of arachidonic acid metabolism, were found to have a distinct biological profile. Both strips isolated from guinea pigs, rabits, and rats in a concentration-dependent manner over the range 0.1—1 μM. This bronchoconstrictor effect was not associated with release of peptide leucotrienes or thromboxane A_2, nor was it blocked by lipoxygenase inhibitors or thromboxane receptor antagonists, suggesting it is a direct effect of lipoxins. However, the leucotriene D_4 (LTD_4) receptor antagonist LY-171883 reduced the LxA_4 response, indicating that LTD_4 and LxA_4 may share the same receptor. LxA_4 and LxB_4 also exerted an endothelium-dependent vasorelaxation in guinea pig, rat, and, to a lesser extent, rabbit aortic vascular smooth muscle. In contrast to other vasoactive icosanoids, LxA_4 and LxB_4 failed to aggregate rat, rabbit, or guinea pig platelets or to inhibit ADP-induced aggregation. LxA_4 also enhanced the release of liver lysosomal labilizing action of LxA_4. LxA_4 and LxB_4 share a similar biological profile. It is not clear yet whether the lipoxins could be mediators of circulatory or pulmonary disease states.

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