

PL1 THE ENDOTHELIN SYSTEM AS A THERAPEUTIC TARGET IN HEART FAILURE

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ABSTRACT

Chronic heart failure (CHF) is common condition in Western countries, often resulting from coronary artery disease and hypertension. Both of these risk factors are increasing in prevalence in developing Eastern countries and it is expected that this will be followed by an increased incidence of CHF. Although there have been many recent developments in the treatment of CHF, including the introduction of angiotensin-converting enzyme inhibitors, beta-adrenoreceptor blocking agents and aldosterone receptor antagonists, this remains a disabling and fatal condition. Several new therapeutic targets are emerging in CHF and among the most promising is the endothelin system. Endothelin-1 (ET-) is a potent vasoconstrictor peptide, primarily produced by the vascular endothelium. ET-1 is also a potent co-mitogenic factor and modulates natriuresis, making it a potentially important player in the progression of CHF. Infact plasma levels of ET-1 and of its precursor peptide big ET-1 are increased in line with the severity of this disease. The effects of ET-1 are mediated by 2 receptor subtypes ET_A and ET_B, and early trials indicate that antagonists of these receptors are beneficial in CHF. This lecture will cover the mechanisms of ET-1 in CHF, and discuss receptor blockade and inhibition of synthesis as potential modes of treatment in CHF.