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Recent developments in the kallikrein-kinin system with hypertension and diabetes

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Diabetes has been implicated as a major risk factor in the development of cardiovascular and renal complications. Previous studies have indicated altered activities of the bradykinin-forming components in diabetic patients as well as diabetic experimental animals. Type2 diabetes can lead to hypertension, renal and cardiac complications resulting in high rates of mortality worldwide and in Kuwait as well. Bradykinin (BK), a pharmacologically active polypeptide, is one of kinins which is released in the tissues and body fluids as a result of enzymatic action of kallikreins on kininogens. The two types of kallikreins are tissue kallikrein and plasma kallikrein. Tissue kallikrein is mainly expressed in the kidney (urine), glandular tissue, vasculature, heart and brain. It preferentially acts on low molecular weight kininogen substrate to release lysyl-BK. Tissue kallikrein has also been reported to be present in plasma . Plasma kallikrein acts on high molecular weight kininogen substrate to release BK. BK promotes both cardiovascular and renal functions, for example, vasodilation, naturesis and diuresis (7,8). BK is rapidly (< 15 sec) inactivated by circulating kinases (9). BK acts on B1receptors and B2 receptors to elicit physiological and pharmacological actions. It has been shown previously that type 1 diabetic patients are at a risk of developing nephropathy.

In addition, BK has been implicated in the pathophysiology of hypertension. In this regard, it is suggested that the role of renal BK is to excrete the excess of sodium. Therefore, a reduction in the generation of renal BK may be the cause in the development of hypertension as a result of the accumulation of sodium in the body. Thus, the development of a compound having renal kallikrein-like activity may serve the purpose of excreting excessive sodium from the kidney in the treatment of hypertension. Transgenic mice over-expressing renal tissue kallikrein were hypotensive and that administration of aprotinin, a tissue kallikrein inhibitor, restored the BP of the transgenic mice. Recently, it has been proposed that tissue kallikrein gene delivery into various hypertensive models exhibits protection, such as reduction in high blood pressure, attenuation of cardiac hypertrophy, inhibition of renal damage and stenosis. This may indicate the future therapeutics aspect of tissue kallikrein gene therapy for hypertension, cardiovascular and renal pathology. Abnormal BK and nitric oxide levels have been demonstrated in diabetic patients in our study.

Speaker Biography

Jagdish N. Sharma is currently a Professor in the Department of Pharmacology and Therapeutics of which he is the Founding Chairman, Faculty of Pharmacy, Kuwait University, Kuwait. He has also served as a Professor of Pharmacology at the Universiti Sains Malaysia, Penang, Malaysia, prior to joining Kuwait University in 1999. Prof. Sharma received his B.V.Sc. & A.H. (D.V.M.) in 1970 from Jawaharlal Nehru Agricultural University, Jabalpur, India; his M.Sc. in Medical Pharmacology in 1973 from the All-India Institute of Medical Sciences, New Delhi, India; and his Ph.D. in Pharmacology in1976 from the University of Strathclyde, Glasgow, Scotland, UK. The Calamus International University, London in 2011, awarded D.Sc. degree in Health Sciences to Professor Sharma in recognition of his outstanding highly accomplished professional achievements in research and academic contributions. In 1995, he was elected to an F.C.P. (Fellow) from the American College of Clinical Pharmacology, New York, USA and an F.I.Biol. (Fellow) in 1997 from the Royal Institute of Biology, London, UK. This is a highly prestigious award considered to be at the level of British DSc. Prof. Sharma is an author of a book entitled "Topics in Mediators Pharmacology", which has been published by the Nova Science Publishers Inc., N.Y., USA. Prof. Sharma is the Editor of a book Progress in Drug Research" series entitled "Recent Developments in the Regulation of Kinins" 2014 which is published by Springer Basel AG, Switzerland. He has been to numerous International conferences as invited speaker. Prof. Sharma has been holding several research grants for the support of his clinical and basic research activities and supervised PhD and MSc theses. He has been PhD external examiner and evaluator for promotions to the ranks of Associate Professor and Professor externally. In Malaysia, his research investigations were funded by the Ministry of Science and Technology, Malaysia. Currently his clinical priority research grant is funded by the Kuwait University research sector. He is the editorial board member of Pharmacy Times (USA) of Middle East from 2007 to date, Inflammopharmacology (UK) from 1997 to date, International Journal of Immunopathology and Pharmacology (Italy) from 2006 to date, European Journal of Inflammation (Italy) from 2006 to date, Archives of Medical Research (Mexico City) from 2006 to date, Clinical Medicine: Endocrinology and Diabetes (New Zealand) from 2008 to date, Clinical Medicine: Therapeutics (New Zealand) from 2009 to date, American Journal of Biomedical Sciences (USA) from 2009 to date and Journal of Pharmaceutical Technology and Drug Research (UK) from 2011 to date. He has 110 publications in reputed international biomedical journals, and 65 abstracts of national and international conferences. His work is supported by the Kuwait University Grant RP01/09.

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