## *PREFACE*

This research thesis is prepared as a completion for the degree of Doctor of Philosophy at the Vidyasagar University, Midnapore, West Bengal, India. The whole research work which has been depicted herein was led under the supervision of Dr. Smarajit Maiti (Associate Professor and Head of the Department, Department of Biochemistry, Oriental Institute of Science & Technology, Vidyasagar University, Midnapore) and Prof. Subrata Kumar De (Department of Zoology, Vidyasagar University, Midnapore).

Acute Myocardial Infarction (AMI) is the leading cause of death worldwide. Many factors are responsible for the development of AMI – some are modifiable factors (hypertension, diabetes mellitus, increased level of total cholesterol, excessive intake of saturated fat, smoking, sedentary lifestyles, stress etc.) and some are nonmodifiable factors (family history of AMI, post-menopausal women, aging, etc.). From our laboratory, it has been reported that dermcidin is an 11kDa small protein that is found in the circulation of acute myocardial infarction patients and it was also reported that the protein triggers platelet aggregation. There is no discovery on dermcidin protein-mediated cardiovascular disease. It is well known that aspirin is the cornerstone therapy in acute coronary syndromes (ACS) but its effect is resistant in AMI and recently there is no specific use of aspirin in AMI. And a high dose of aspirin may be not only ineffective but also harmful. But the mechanistic explanation was not clear how dermcidin works and inhibits the effect of aspirin.

I herein demonstrated in my research thesis about the role of dermcidin in the case of aspirin resistance and have also analyzed the specific and unique way of the use of aspirin. It has been reported that stress is the prime reason for the generation of diabetes and many works have been published but it remains a discordant issue. And one of the important matters: there is no such direct evidence of such a protein which actually may tell about the correlation of production dermcidin in AMI with the development of diabetes. From the previously reported

results of our laboratory, it was found that dermcidin is stress-induced protein, so it could be involved in the formation of diabetes.

A total of seven chapters was prepared, including references for this thesis.

***chapter 1*** describes literature studies to find out about AMI and the role of aspirin and its uses. The pathophysiology of AMI has been described. The resistance of aspirin effect and its dose. Description of different types of strokes – hemorrhagic stroke, ischemic stroke, and transient ischemic attack. Neutrophil and endothelial cell interaction in stroke, Platelet biology, Atherosclerosis, Nitric oxide chemistry, different types of nitric oxide synthases, the structure of dermcidin protein, dermcidin in hypertension, the role of dermcidin on nitric oxide, GLUT-4 translocation in glucose homoeostasis. ***Chapter 2*** describes the whole Methodology related to this thesis work done. ***Chapter 3*** demonstrates the effect of dermcidin protein in acute myocardial infarction (AMI). Dermcidin can increase the aggregation of platelets through its binding on the platelet surface. It was found that dermcidin antibody can inhibit platelet aggregation. In this chapter we have shown that the specific and unique dose of aspirin can inhibit dermcidin induced aggregation of platelets in AMI patients, where first dose was unable to stop platelet aggregation but can induce nitric oxide which removed dermcidin then followed by dose can inhibit platelet aggregation and it was noticed that the high dose of aspirin was actually failed to do that. ***Chapter 4*** explains that insulin plays an important role in the maintenance of platelet aggregation with the low dose of aspirin in stroke patients and it was found that the use of insulin in stroke patients removes diabetes-like condition in them and sensitized the platelets, so that next low dose of aspirin will act promptly on aggregation. ***Chapter 5*** delineates the chest pain in acute heart patients and the involvement of nitric oxide in pain regulation. Different anti-anginal compounds can reduce pain in such cases, here we demonstrated that these compounds even glucose and insulin also express protein di-sulfide isomerase which can regulate pain through nitric oxide synthase. ***Chapter 6*** demonstrates that

different kinds of stresses like aqueous extract of tobacco leaves and hypoxia can trigger the expression of dermcidin gene. Here, it was also found that the protein can increase the level of glucose in the circulation of mice when it was injected to the tail vein of mice and simultaneously reduced the nitric oxide level. And it was revealed that stress induced expression of dermcidin protein mediated all these incidents happened through the impediment of GLUT4 translocation and nitric oxide production.

**Chapter 7** discuss the preparation of oral insulin was depicted. It is explained about the making of oral insulin by using the milk-insulin protein complex which extended the degradation action of trypsin. This research work was investigated in mice model.

This thesis work is ultimately based on many experiments and data which were achieved by experimental research works. The results of the thesis are not taken from anywhere or any published articles. With the help of existing data of our laboratory and from the literature review we performed so many experiments for the successful completion of the thesis work where many persons provided support to complete the thesis and the author is deeply beholden to all of them.

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