SYSTEMIC PROSTACYCLIN IN CIRRHOTIC PATIENTS

Thesis

Submitted in Partial Fulfilment of M.Sc. Degree in Pediatrics

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By

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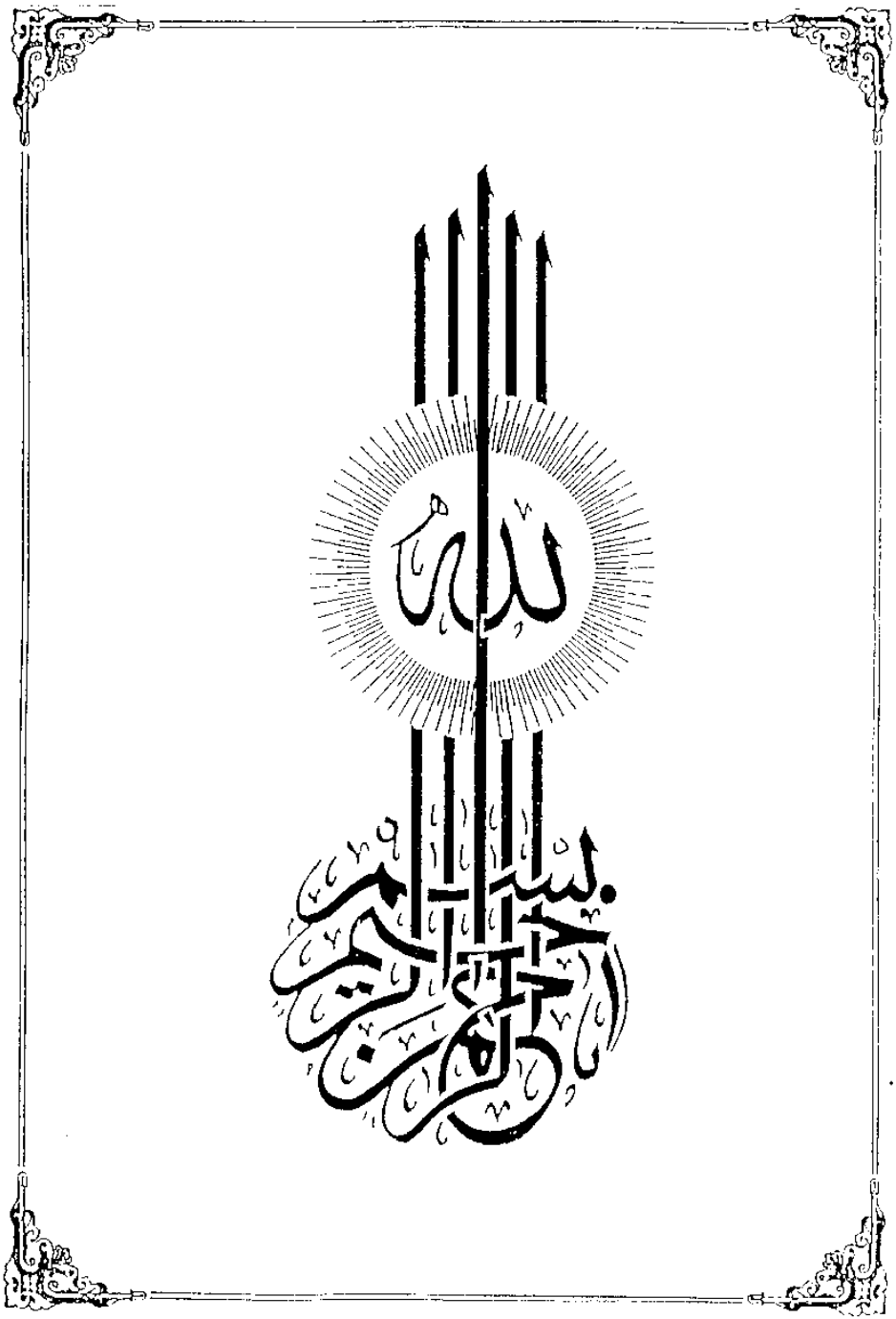
بسم الله الرحمن الرحيم

وما أوتيتم من العلم إلا قليلا

صدق الله العظيم

الآية رقم ٨٥ من سورة الإسراء



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INTRODUCTION

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Prostacyclin is the main cyclooxygenase product generated by blood vessels and acts as a potent vasodilator able to modulate vascular reactivity to pressor hormones. **(Guarner et al, 1986a)** .

Total body production of prostacyclin was shown to be increased in cirrhotic patients suggesting that its synthesis by blood vessels of the systemic circulation is enhanced. However the mechanism by which the synthesis of systemic prostacyclin is stimulated is not known .

Increased renal synthesis of the vasodilator prostaglandin E2 has been reported in cirrhosis with ascites and is currently interpreted as a renal homeostatic response to vasoconstrictor stimuli .

Arachidonic acid metabolism in the human kidney extends to several cyclo-oxygenase products such as prostacyclin, prostaglandins E2 and F2 and thromboxane . In particular, prostacyclin is a powerful vasodilator and it may represent the major cyclo-oxygenase product in human glomeruli **(Guarner et al, 1986 b).**

AIM OF THE WORK

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The aim of the present study is to describe the urinary excretion of 6-keto-prostaglandin F1α in cirrhotic patients with and without ascites and intact renal function, in an attempt to understand the mechanisms responsible for renal vascular homeostasis in cirrhotic patients

REVIEW OF LITERATURE

PROSTAGLANDINS

Prostaglandins are a family of chemically similar fatty acids which were discovered by **von Euler in 1935** . He presumed that these biologically active substances were found in semen as a product of the prostate. **Bergstrom in 1949** confirmed von Euler's finding and added that the biological activity was due to a new group of highly active lipid soluble unsaturated hydroxyl acids . He discovered that prostaglardins were not a single substance but a series of closely related compounds .

Prostaglandins were first isolated in a pure crystalline form by **Bergstrom and Sjovall in 1957** . Two series of prostaglandins were discovered; one was more soluble in ether and was called prostaglandin "E" and the other more soluble in phosphate buffers and was called prostaglandin "F"

Karim in 1967 stated that the distribution of these substances is not restricted to the male accessory genital glands and their secretions. but are widely distributed in mammalian tissues and tissue fluids .

Prostaglandins are identified in menstrual fluid and in amniotic fluid, in placental and maternal blood during pregnancy and labour .

Prostaglandins are also identified in normal blood, in urine, in lungs, in the thymus, thyroid, cervical sympathetic nerves. bronchi. cardiac muscle, and in cerebrospinal fluid .

Vane in 1969 stated that the primary prostaglandins (PGE and PGF) have been shown to be synthesized through the oxidation of arachidonic acid, forming intermediate prostaglandins (PGG and PGH) which in turn are isomerized forming the primary prostaglandins.

Humes et al in 1977 explained the biosynthesis of prostaglandins by inflammatory cells as follows : prostaglandin biosynthesis is catalyzed by an uncharactertized microsomal enzyme called the prostaglandin synthetase which converts the essential fatty acid, arachidonic acid to prostaglandin E and prostaglandin F, both precursors are stored as phospholipids in cell membrane and upon a variety of stimuli prostaglandins are immediately synthesized and released.

Fredrick and Robert, 1980 , discovered two major pathways for the enzymatic oxidation of arachidonic acid.

The first (classic pathway) is called prostaglandin pathway .