EFFECT OF LOCAL APPLICATION OF ROYAL JELLY ON FIBROBLASTIC ACTIVITY IN DIABETIC ULCERS

THESIS

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بسم الله الرحمن الرحيم

"وأوحى ربك إلى النحل أن اتخذي من الجبال بيوتا ومن الشجر
ومما يعرشون. ثم كلي من كل الثمرات فاسلكي سبل ربك ذللا
يخرج من بطونها شراب مختلف ألوانه فيه شفاء للناس إن في
ذلك لآية لقوم يتفكرون"

صدق الله العظيم

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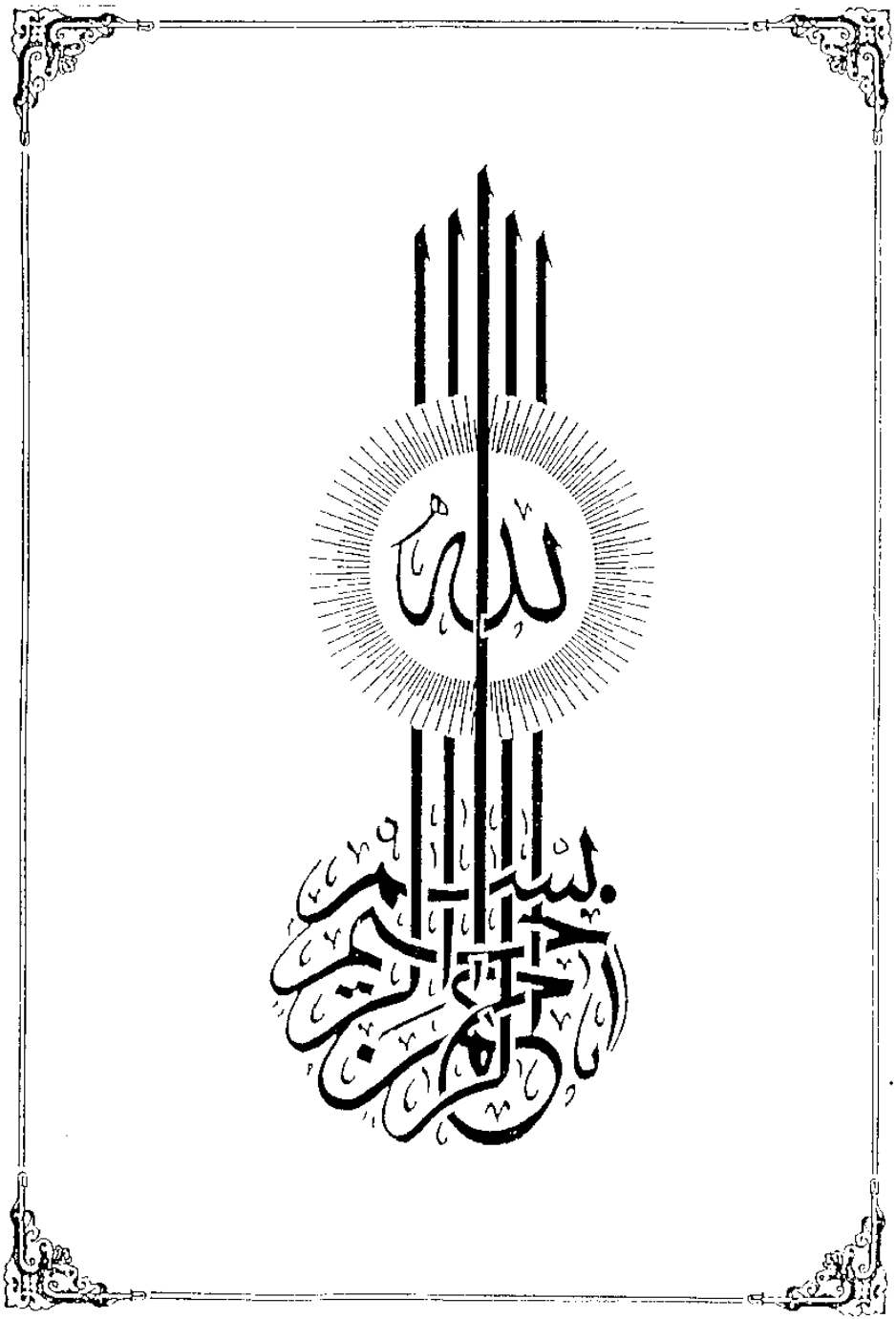

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ABBREVIATIONS

ADP : Adenosine diphosphate.

AF : Atrial Fibrillation

ATP : Adenosine triphosphate

A.V. : Arterio-Venous

C.H.F. : Congestive Heart Failur

C.N.S. : Central Nervous System

C.V.S. : Cardiovascular System

F.B.S. : Fasting blood Sugar

IDDM : Insulin -Dependant Daibetes Mellitus

IHD : Ischaemic Heart Disease

L.L. : Lower Limb

NIDDM : Non-Insulin Dependant Diabetes Mellitus

P : Level of significarce

PP : Post prandial

SD : Standard Deviation

t : Student "t" test

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C O N T E N T S

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INTRODUCTION

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INTRODUCTION

Fibroblasts are the major cellular component of the unspecialized connective tissue. Their structure related to the functions performed. Fibroblasts are concerned with important functions, of which is biosynthesis of collagen and mucoproteins of the ground substance. [Walter and Isreal, 1979] .

Fibroblasts play an important role in wound healing. The restoration of tissue continuity after injury and stregnthening of repair tissue depend primarily on the function of the fibroblast. [Smith , 1985] .

Diabetic ulcer is a chalenging clinical problem that is complicated by multifactorial pathogenesis such as angiopathy, neuropathy, and infection in various combinations. [Jackson and Louw, 1979] .

Diabetic wound healing is impaired, and the poor collagen formation and tensile stregnth of diabetic wound delay its healing. [James and MaCurry, 1984] .

Studies on Skin fibroblasts derived from diabetic patients have demonestrated that these cells were abnormal in a variety of ways e.g decreased plating effeciency

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and growth, faulty protein synthesis, increase of acetate utilization, abnormal cross-linking of collagen, defects in glycogen synthase and many other aspects. Not in every case have these abnormalities been confirmed. [Podskalny and Kahn, 1982].

God says :

BY THE NAME OF GOD .

" And thy Lord inspired the bee, Saying : Choose thou habitations in the hills and in the trees and that which they thatch ; Then eat of all fruits, and follow the ways of the Lord, made smooth [for thee]. There cometh forth from their bellies a drink divers of hues, wherein is healing for man-kind. Lo! herein is indeed a portent for people who reflect."
[SURAH XVI ; THE BEE , V V. 68-69] .

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REVIEW OF LITERATURE

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DIABETIC ULCERS

INTRODUCTION

Diabetic ulcer is a chalenging clinical problem that is complicated by multifactorial pathogenesis such as angiopathy, neuropathy , and infection in various combinations. [Jackson and Louw, 1979] .

A cause of illness and disability in diabetics are the complications affecting the lower limbs : more hospital beds are occupied by diabetic patients with such complications than for all other causes associated with the disease . That diabetics are prone to ulceration and gangrene of the feet, often leading to amputation, has been recognized for many years, but a proper understanding of the aetiology of such ulceration dates from the paper of Oakley et al., 1956 who drew attention to the importance of peripheral neuropathy as a cause of planter ulceration and described these factors-arterial disease, neuropathy and sepsis-as being the essential causes of foot lesions in diabetics. [Delbridge et al., 1985] .

The foot is the primary target of neuropathic, vascular , and infective complications of diabetes. [Charles,1983].

Apart from ulceration, all diabetics have potential pathological changes in their feet which may lead to serious

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consequences such as corns, callosities, clow toes, deformities, and disarticulations [Charcot's Joints], cellulitis, suppuration, and above all gangrene. [Jackson and Louw,1979]

The combination of vascular disease, neuropathy, and connective tissue abnormalities produce unstable foot that is susceptible for such lesions. The occurance of these lesions depends upon other factors such as the patient's psychologic attitude, level of education and their subsequent ability to care for their feet. [Delbridge et al., 1983] .

Gangrene in the diabetic foot usually follows the addition of sepsis to the foot already desensitized by neuropathy and devitalized by ischaemia. [Catterall, 1983] .

CLINICAL FEATURES OF DIABETIC ULCERS

A. Neuropathic diabetic ulcer

Though sometimes multiple, characteristically these ulcers are single, and develop on the sole of the foot. The commonest site is beneath the head of the first metatarsal bone, but they may develop at any site. The ulcer consists of a central cavity , usually much larger than the opening into it which is surrounded by a hard, thick plaque of hyperkeratotic tissue. Characteristically the ulcer is painless, all modalities of sensation

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in the foot being diminished, the foot itself being warm pink and dry, with palpable ankle pulses and full veins. Owing to impaired sensation the patient is often unaware of the presence of the lesion until his attention is drawn to it by the discharge of pus and blood, or the development of spreading infection in the tissues of the foot. [Delbridge et al., 1985] .

B. Diabetic vascular ulcers

They usually occur on the distal aspects of the toes and on the heel. Peripheral pulses are diminished or absent. The extremity is pale and cool and demonestrates a loss of dermal appendages with atrophic shiny skin. The ulcers are usually painful, begining with dusky erythema, and evolving into necrosis and gangrene in some cases. They are potentially susceptible to secondary infection and underlying osteomyelitis. [Ronald and Ricky, 1984] .

MECHANISM OF ULCER FORMATION

Diabetic ulceration commences with tissue breakdown and the formation of a cavity deep to the epithelial surface, followed by subsequent ulceration of the overlying skin . The intial event is the formation of a plaque of unusually hard keratin. Tissue breakdown occurs deep to

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this plauqe, and subsequently a cavity, filled with plasma and blood develops. This cavity progressively enlarges and eventually ruptures out of the skin surface forming an ulcer with intially a small opening and a larger cavity underneath. This ulcer becomes contaminated with organisms from the skin and footwear but the infection remains superficial with little reaction in the surrounding tissues for a variable, often prolonged period provided there is adequate drainage through the opening . However, if this becomes blocked by keratin and inspissated discharge, overt infection may occur in the closed space and this may rapidly spread to involve underlying tendons, and bone, with the development of cellulitis, a planter abscess, and often osteomyelitis or septic arthritis. [Delbridge et al., 1985].

A. ANGIOPATHY [Ischaemia]

Roughly one half of all lower extremity amputations performed are related to diabetes. [Bendick et al., 1983].

Peripheral ischaemia in diabetes is caused by atherosclerosis affecting large and medium sized vessels and partly by a microangiopathy of the skin and muscle capillaries. [Jackson and Louw, 1979] .However there is increasing evidence that ischaemia in extremities is strongly related to major vessel atherosclerotic occlusive disease. [Bendick et al., 1983] .

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