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**BIOCHEMICAL STUDIES ON THE POTENTIAL ROLE OF
HYPERTHYROIDISM IN THE BIOACTIVATION OF PARACETAMOL TO
INDUCE HEPATIC LESIONS IN EXPERIMENTAL ANIMALS**

Thesis

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as a Requirement for the Degree of Ph.D. in Zoology
"Physiology"

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UP

By

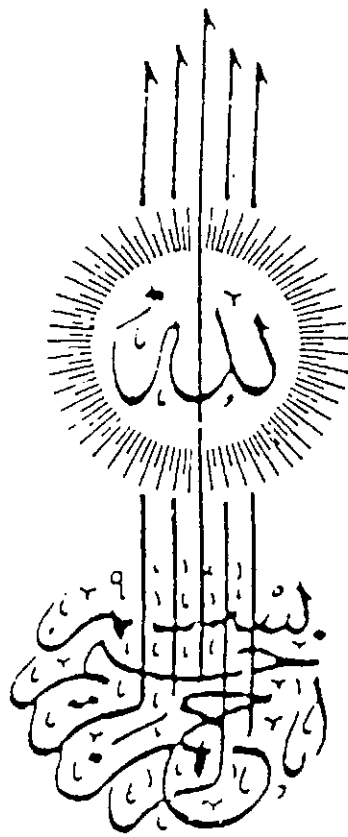
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قَالُوا سُبْحَانَكَ لَا عِلْمَ لَنَا إِلَّا مَا
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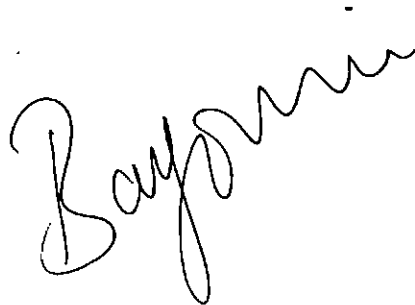
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CHAPTER I

INTRODUCTION

INTRODUCTION

Paracetamol (acetaminophen, N-acetyl-para-aminophenol , APAP; Pandol and many other trade names elsewhere) is a derivative of para-aminophenol (Black, 1980) . It was synthesized at Johns Hopkins University in 1877 (Spooner and Harvey, 1986) and well-described in 1894 (Hinsberg and Treupel , 1894) without side-effect in normal use . Paracetamol is a safe and effective analgesic and anti-pyretic when taken in the usually recommended dose for limited periods of time (Batterman and Grossman, 1955 ; Piperon *et al.*, 1978; Black, 1980; Tee *et al.*, 1987) but when taken in overdose it produces serious, often irreversible and fatal hepatotoxicity, as well as necrosis in other vital organs (Koch-Weser, 1976) in man and experimental animals (Boyd and Bereczky, 1966 ; Davidson and Eastman, 1966 ; Ameer and Greenblatt, 1977; Spooner, 1993). In 1973 there were about 5000 cases of self-poisoning with paracetamol in Britain with 50 deaths. Up to 1976, over 1000 patients with paracetamol overdose were admitted to hospitals in England and Wales every year and about 3% died (Douglas *et al.*, 1976).

Hepatotoxicity of paracetamol is preceded by its metabolic biotransformation by cytochrome P₄₅₀ mixed-function oxidase to reactive intermediate (Jollow *et al.*, 1973; Mitchell *et al.*, 1973 a; Potter *et al.*, 1973; Hinson, 1982). Consequently the severity of the