MICROENCAPSULAR UREASE FOR ARTIFICIAL RENAL FAILURE

THESIS

Submitted For Partial Fulfillment Of Master Degree

In Biochemistry

BY

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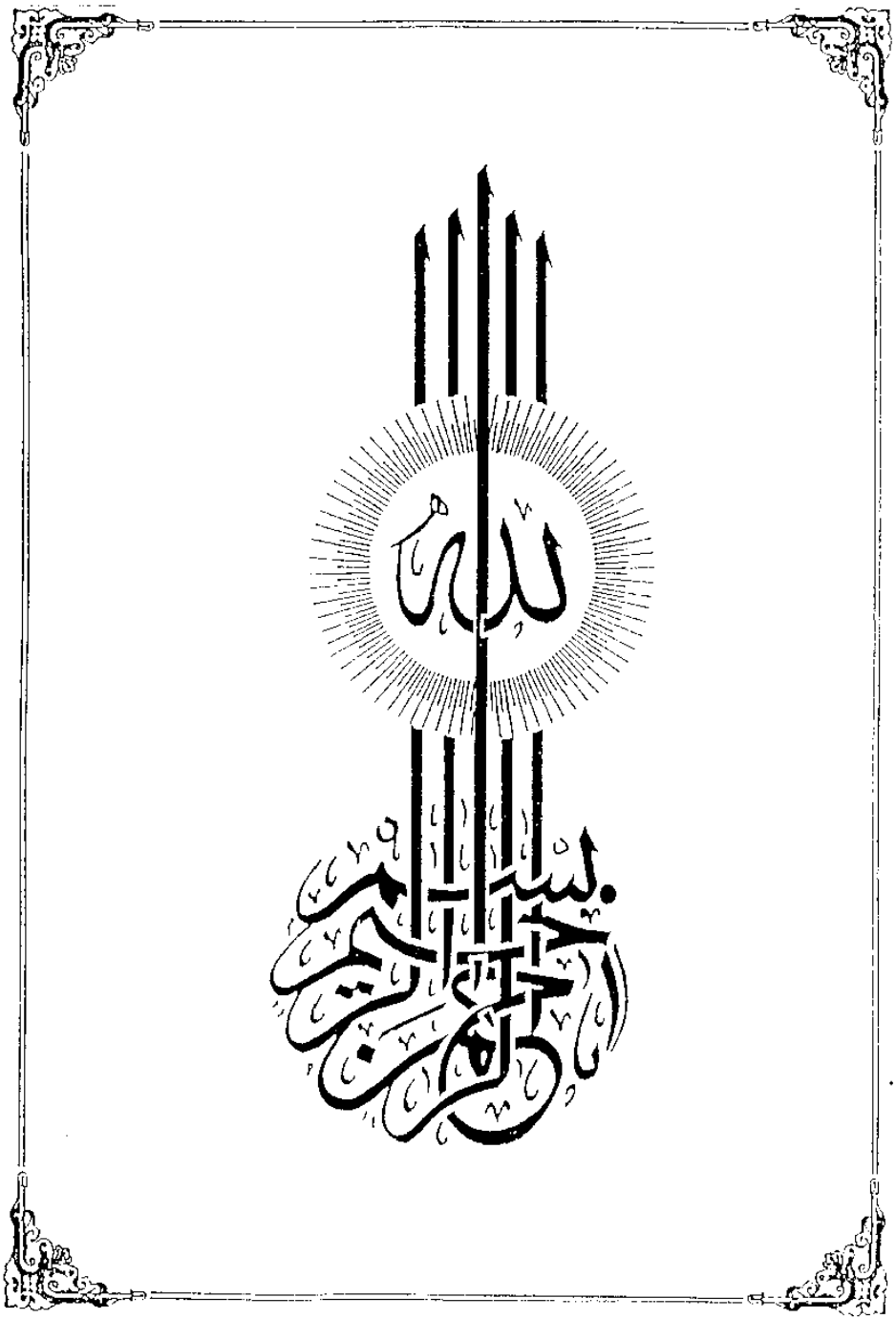
1989

بسم الله الرحمن الرحيم

وقل ربي زدني علما

صدق الله العظيم



TO MY FAMILY

THIS THESIS HAS NOT BEEN SUBMITTED
FOR A DEGREE AT THIS OR ANY OTHER
UNIVERSITIES

Mona A.M. Abo Zahra

ACKNOWLEDGMENT

I wish to express my deep thanks to Prof. Dr. **ABDEL HALIM, A.H., MUSTAFA**, Prof. of Biochemistry, Faculty of Science, Ain Shams University for his interest and cooperation.

I would like to take the opportunity to thank **Assist. Prof. Dr. TAHANY, M. MAHAREM**, Assistant Professor of Biochemistry, Faculty of Science, Ain Shams University for her tutorial guidance and active supervision.

I would like to thank **Dr. EL-SAYED, M.E., MAHDY**, Lecturer of Biochemistry, Faculty of Science, Helwan University, for his sincere continued support and encouragement.

LIST OF ABBREVIATIONS

ALT	: Alanine transaminase.
ALP	: Alkaline phosphatase.
ARF	: Acute renal failure.
AST	: Aspartate transaminase.
BUN	: Blood urea nitrogen.
C_{In}	: Inulin clearance.
CPK	: Creatine phosphokinase.
E&H	: Eosin & Haematoxylin.
γ.GT	: Gama glutamyltransferase.
GFR	: Glomerular filtration rate.
K-Dichromate	: Potassium dichromate.
i.m.	: Intramuscular
I.U.	: International units.
LDH	: Lactate dehydrogenase.
LMC	: Liquid membrane capsules
N.S.	: Non significant.
P-value	: Probability.
r.p.m.	: Revolutions per minute.
S.C.	: Subcutaneous.
S.D.	: Standard deviation.
S.E.	: Standard error.
SUN	: Serum urea nitrogen
vs	: Versus.

CONTENTS

AIM OF THE WORK

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Acute renal failure is the abrupt decline in renal functions sufficient to result in the retention of nitrogenous wastes.

The ability to induce a standardized stable uremia, uncomplicated by the administration of nephrotoxic material, represents an advance on existing methods for producing experimental renal failure.

Uses of adsorbent systems of the removal of toxins could be a valuable adjunct to dialysis in the treatment of uremia. Low toxin levels might be maintained and/or the frequency of dialysis might be reduced.

Liquid membranes capsules (LMC) can function as toxin traps which could be used as adsorbents.

In the present work ARF was induced in normal rats by subcutaneous injection of K-dichromate and the appropriate urease level needed to convert blood urea nitrogen (BUN) to ammonia and the time course of glomerular filtration rate were determined.

The study aims to investigate the efficiency of liquid membrane capsule encapsulating urease + citric acid in the treatment of the ARF in rats via the measurements of a different nitrogenous compounds and assays of some enzymes activities.

REVIEW OF LITERATURES

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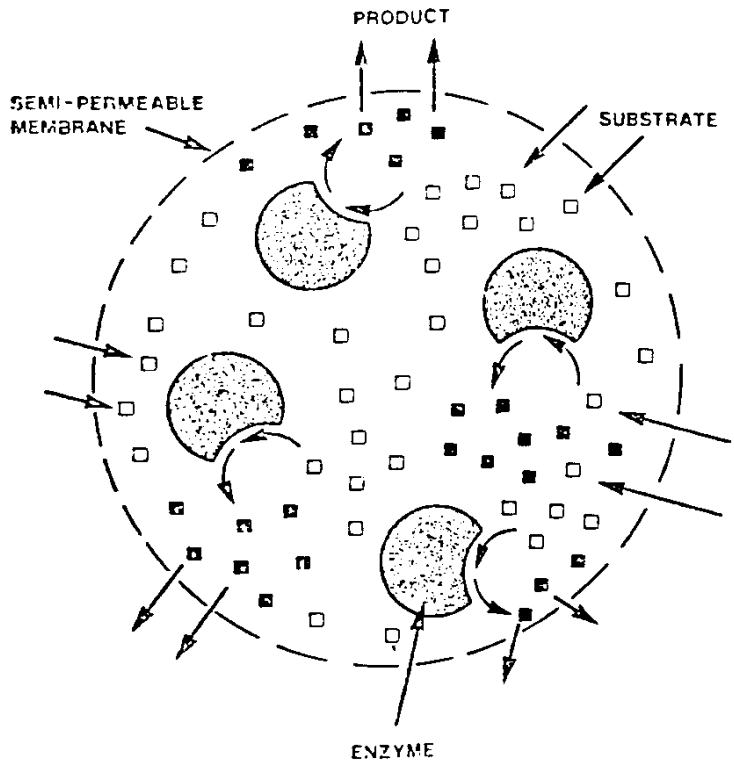
Gilboe & Javid (1963), stated that the course of uremic syndrome can be accelerated in bilaterally nephrectomized dogs treated with peritoneal lavage solution containing either 1% urea or 0.015% potassium isocyanate. They suggested that ammonium isocyanate formed from urea in aqueous solutions may contribute to the uremic syndrome via carbamylation reactions with free amino acids and proteins. Blood ammonia levels were not significantly elevated in any of the animals tested.

Chang (1964), developed a simple method for encapsulating aqueous solutions of protein within polymer membranes. Stable microcapsules 1 to 100 μ in diameter, with semipermeable membranes, can be made by depositing polymer around emulsified aqueous droplets, either by interfacial coacervation or by interfacial polycondensation. Aqueous suspensions of enzyme-loaded microcapsules act well on samll molecular substrates both in vitro and in vivo.

Schultz et al. (1969), found an increase in Na excretion per nephron in dogs after contralateral nephrectomy and persisted despite experimentally induced acute reduction in the glomerular filtration rate to below prenephrectomy levels.

Chang (1969), studied the removal of endogenous and exogenous toxins by three types of microencapsulated absorbent, activated charcoal in the free form, Heparin - complexed and albumin coated collodion activated charcoal.



Enzyme immobilized within a semi-permeable membrane.

(Chang, 1964).

He found that activated charcoal was effective in lowering arterial creatinine, but it caused a serious fall in the arterial platelet level. Albumin-coated collodion microencapsulated activated charcoal was more efficient than the heparin - complexed form in lowering the blood creatinine level.

According to **Chang (1971)**, most enzymes in nature are presented in an intracellular environment either in solution with a high concentration of cytoplasmic protein, or in an insolubilized form associated with intracellular organelles. Semipermeable mcirocapsules containing native or insolubilized enzymes have been used for the study of enzymes in a synthetic intracellular environment.

The same auther showed that semipermeable microcapsules are spherical ultrathin polymer membranes of cellular dimensions enveloping biologically active materials like enzymes or detoxicants. The semipermeable membranes prevent the enclosed enzymes from leaking out to cause hypersensitivity or immunological reactions, but at the same time allow permeant substrates to equilibrate rapidly across the ultrathin membranes to be acted on by the enclosed enzymes. High concentrations of enzymes can be microencapsulated to give effective in vivo activity. Thus microencapsulated urease acted efficiently to lower blood urea in vivo. Semipermeable microcapsules have already been used clinically for the treatment of patients with chronic renal failure.