NON STEROIDAL ANTIINFLAMMATORY DRUGS AND LOWER GASTROINTESTINAL TRACT

THESIS

Submitted for partial fulfillment of the
Master Degree in
Internal Medicine

Presented by
Ali Saad Ali
M. B., B.Ch.(1990)

616.33
A.S

Supervised by:
Prof. Dr. Mohammed Abdel-Fattah Taha
Professor of Internal Medicine
Faculty of Medicine
Ain Shams University

Dr. Ahmed Shawky El-Sawaby
Ass. Professor of Internal Medicine
Faculty of Medicine
Ain Shams University

Dr. Salwa Ibrahim El-Haddad
Ass. Professor of Pathology
Faculty of Medicine
Ain Shams University

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AIN SHAMS UNIVERSITY
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بسم الله الرحمن الرحيم

الحمد لله الذى هدانا لهذا وماكنا

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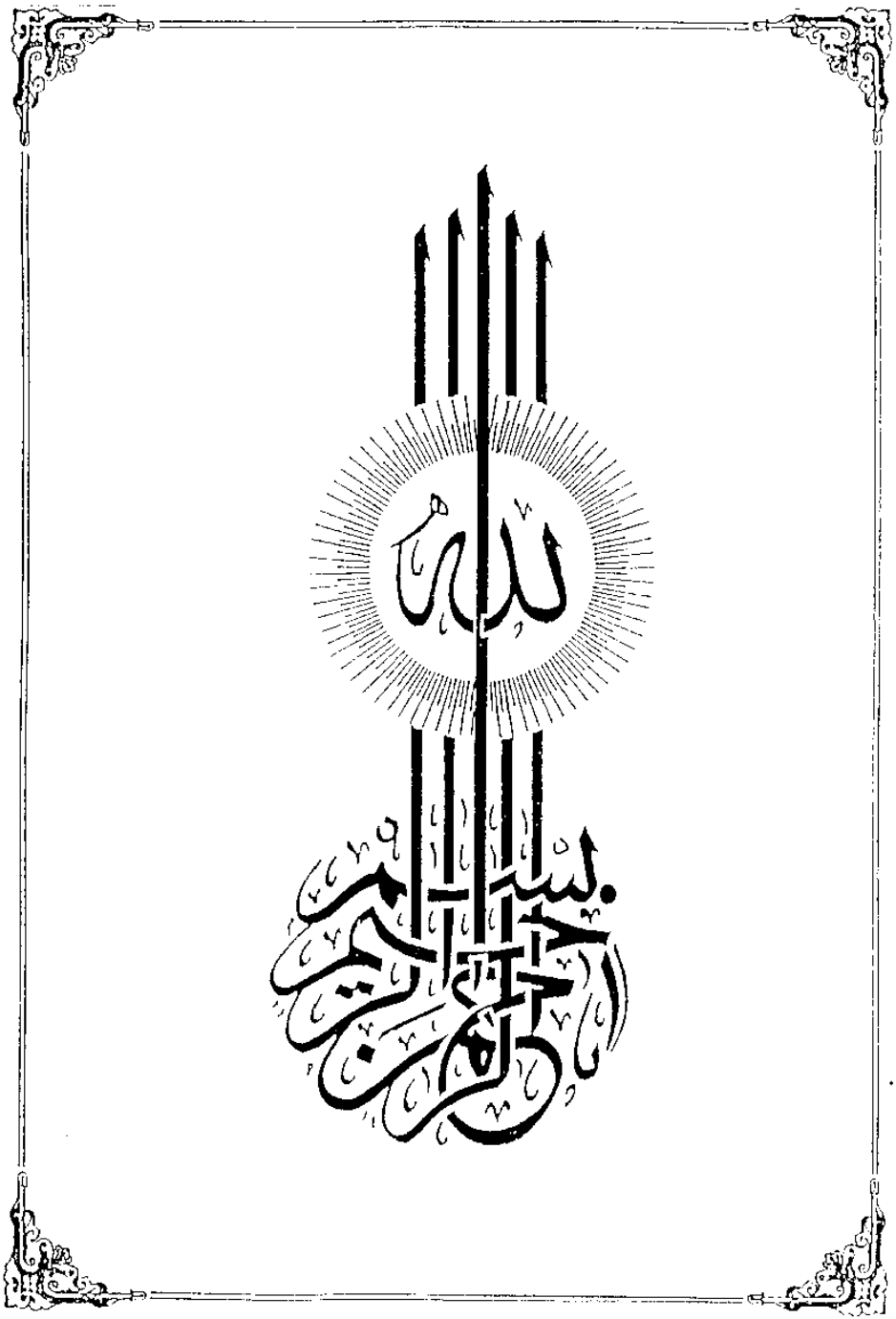

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TO MY PARENTS..

Who offered too much

and took nothing.

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Acknowledgment

First and foremost , thanks are all to GOD for blessing this study until it has reached its end as a little part of his generous help throughout my life.

I find no words by which I can express my extreme thankfulness , appreciation and profound gratitude to my professor Dr. Mohammed Abdel-Fattah Taha, professor of internal medicine, Ain Shams Faculty of Medicine, for his valuable instructions and remarks, fatherly guidance and support and supply of recent literature.

My deepest appreciation goes to Dr. Ahmed Shawky El-Sawaby, assistant professor of internal medicine, Ain Shams Faculty of Medicine, for his meticulous revision, great support and guidance, without which this work would not have been completed.

My sincere thanks go to Dr. Salwa Ibrahiem El-haddad, assistant professor of pathology, Ain Shams Faculty of Medicine, for her guidance and cooperation as regards the histopathological studies in this work.

Last but not least, my love and appreciation go to my wife and children for thier continuous support throughout this work.

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List of Abbreviations

ANA	**= Antinuclear antibody.**
ATP	**= Adenosine triphosphate.**
Ca^{2+}	**= Calcium**
cm	**= Centimeter.**
GD	**= Gastro duodenal.**
GI	**= Gastrointestinal.**
GIT	**= Gastrointestinal tract.**
gm	**= Gram.**
H^{+}	**= Hydrogen ions.**
H_2O_2	**= Hydrogen peroxide.**
Hx & E	**= Haematoxylin and eosin.**
H-pylori	**= Hilocobacter pylori**
J. R. A.	**= Juvenile rheumatoid arthritis.**
mg	**= Milligram.**
mm	**= Millimeter.**
No.	**= Number.**
N. S.	**= Non significant relationship.**
NSAIDs	**= Non steroidal antiinflammatory drugs.**
P.	**= Probability.**
P Gs	**= Prostaglandins.**
PGI_2	**= Prostacyclin.**
Pt.	**= Patient.**
S L E	**= Systemic lupus erythematosus.**
S. D.	**= Standard deviation.**
TxA_2	**= Thromboxanes.**

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Introduction and Aim of the Work

It is not widely appreciated that Non-steroidal Anti-inflammatory drugs (NSAIDs) may cause damage distal to the duodenum and most of studies concentrate on the complications of (NSAIDs) on the upper Gastrointestinal tract (GIT) and hazards of peptic ulceration and haematemesis on chronic use of these drugs *(Lanas et al., 1992).*

The adverse effects of (NSAIDs) on the lower GIT were not thoroughly studied. **The aim of this work** is to study the possible complications of (NSAIDs) on the lower GIT and how can the adverse effects of these drugs represent a range of pathologies that may be asymptomatic but some of them are life threatening *(Bjarnason et al., 1993).* These pathologies include:

.. Ano-rectal lesions in patients taking suppositories containing (NSAIDs) in the form of erosions or ulcer in the rectum and stenosis of the anal verge *(Gizzi et al., 1993).* Also ano-rectal stenosis could occur in patients with prolonged use of suppositories containing paracetamol and acetylsalicylic acid *(Gossum et al., 1993).*

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.. Stercoral perforation of the colon in patients taking (NSAIDs) for long duration especially in constipated patients as constipation is thought to be the most significant contributing factor in the development of sterocoral perforation *(**Hollingworth and Willimas, 1991**)*.

.. Increased risk of lower gastrointestinal bleeding. *(**Holt et al., 1993**)*.

.. NSAID-induced colonic and small bowel diaphragm disease. *(**Pucius et al., 1993**)*

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REVIEW OF LITERATURE

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"Non Steroidal Anti-inflammatory Drugs " "Aspirin-Like Drugs"

These drugs are antipyretic, analgesic and anti-inflammatory, however there are differences in their individual activity as well as in the individual response to these drugs. Their prototype is Aspirin, hence these compounds are reffered to as aspirin-like drugs. Aspirin is almost certainly the most widely used drug in the world. It is used both theraputically (to reduce pain, inflammation, and fever) and prophylactically (to prevent thrombotic events). *(Lee et al.,1994)*. These non steroidal antiinflammatory drugs (NSAIDs) reduce the signs and symptoms of established inflammation but do not in themselves eliminate the underlying causes of the inflammation. They have no effect on the course of the basic disease process and do not protect against tissue or joint injury; thus damage to joints continues to occur during the administration of such a drug to patients with chronic inflammatory arthritis. *(Clements and Paulus,1993)*.

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General Mechanism of Action :

Currently favored mechanism of action of NSAIDs include inhibition of cyclo-oxygenase. Essentially all cells in the body have the capacity to synthesize prostaglandins (Figure 1). In response to inflammatory stimuli arachidonic acid is cleaved from membrane phospholipids by specific phospholipases. Arachidonic acid is oxidized and cyclized by the enzyme cyclo-oxygenase to form cyclic endoperoxide prostaglandin G_2 (PG G_2), which is converted to PG H_2 by peroxidation with concomitant production of unstable toxic oxygen radicals. PG H_2 is then converted to the stable prostaglandins E_2 and $F_{2\alpha}$, thromboxane , or prostacyclin by appropriate enzymes as indicated in (Figure 1). Elevated levels of prostaglandins have been demonestrated in synovial effusions from untreated patients with inflammatory arthritis. ***(Clements and Paulus,1993)***.

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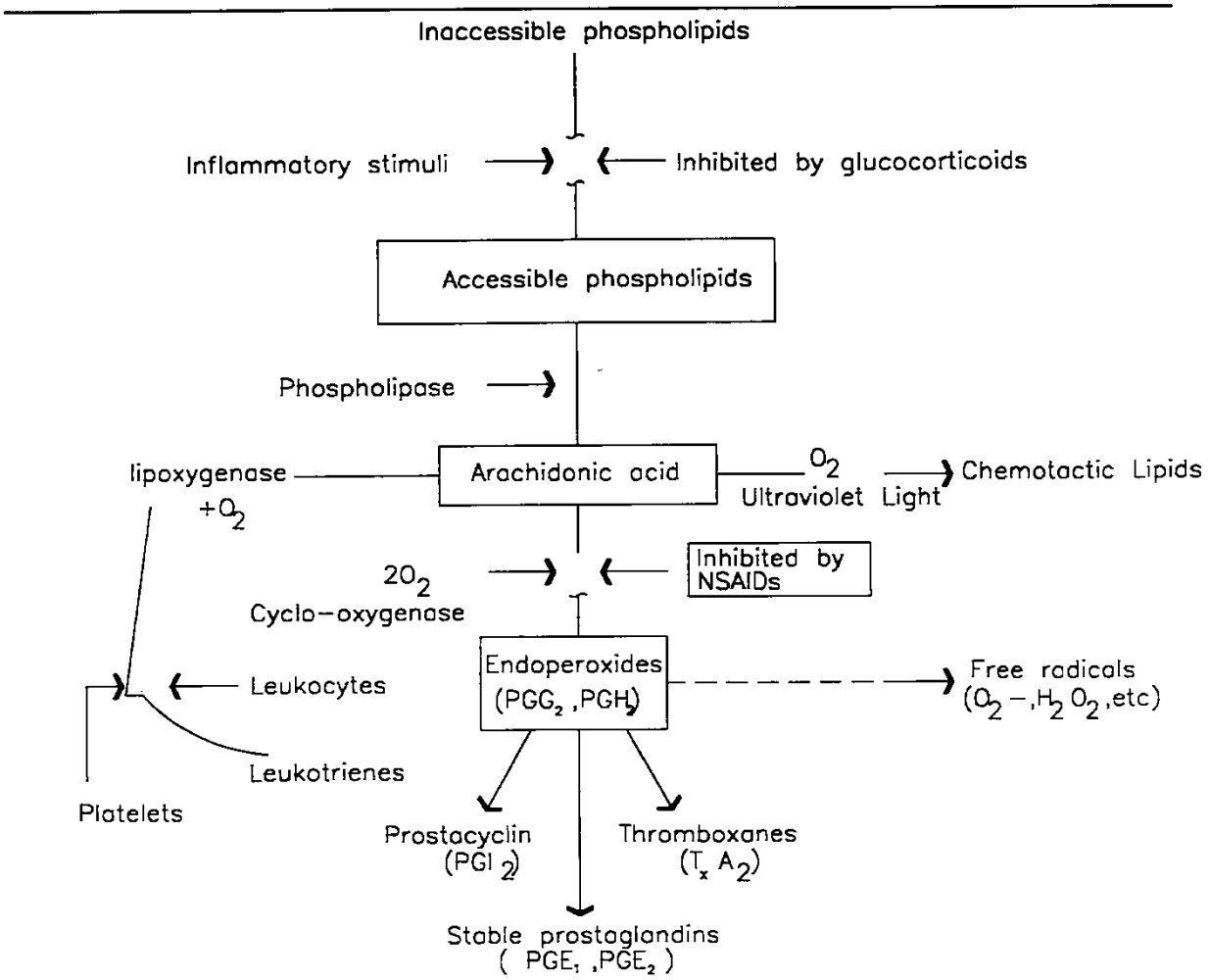

FIGURE (1), Arachidonic acid metabolism

(Furst and paulus ,1993)

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