EFFECT OF POLYUNSATURATED FATTY ACIDS ON PEPTIC ULCER HEALING AND HELICOBACTER PYLORI

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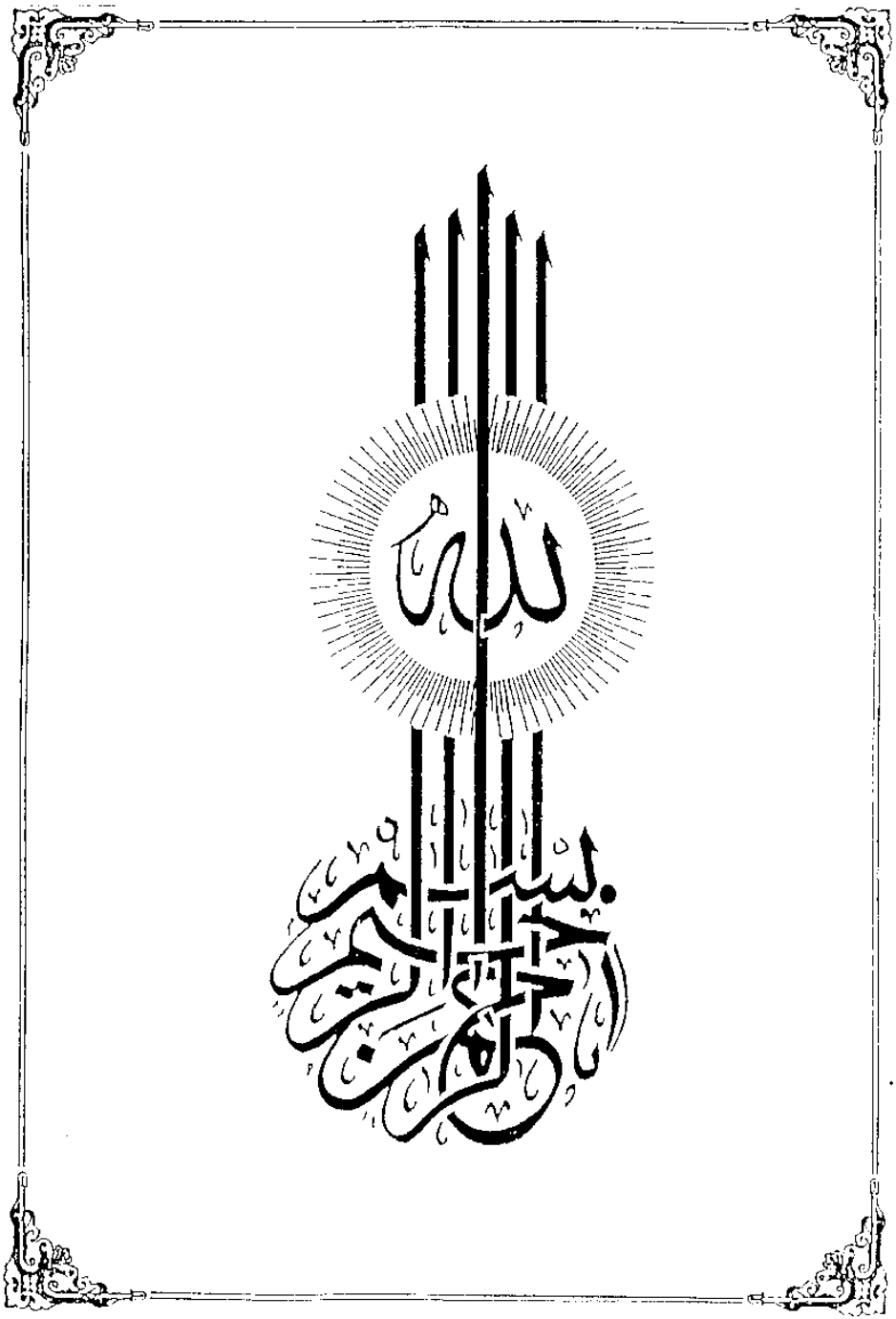

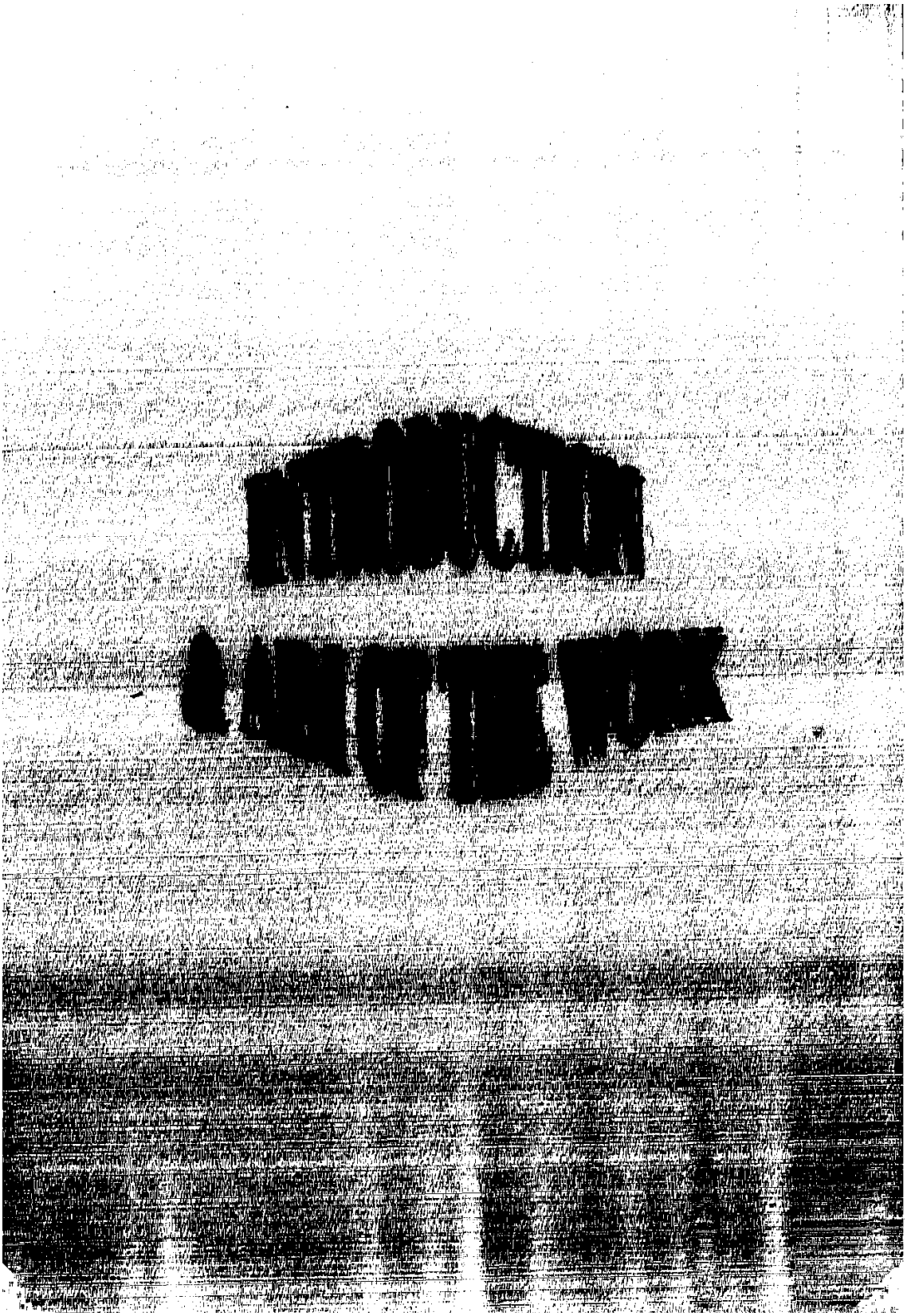

Aim of the work:

The aim of the work is to investigate the possible effect of polyunsaturated fatty acids on the course of healing of peptic ulcer and on the eradication of H. pylori.

PEPTIC ULCER

Ulcers are defects in the gastrointestinal mucosa that penetrate the muscularis mucosa, to distinguish them from superficial erosions which do not extend through the muscularis mucosa *(Richardson, 1992)*.

Peptic ulcers principally involve the most proximal portion of the duodenum and the stomach which have in common participation of acid and pepsin in their pathogenesis, however, acid and pepsin are not the only causes of ulcer, and therefore the term peptic ulcer may be a misnomer *(Richardson, 1992)*.

Normal mucosal defence

Mucosal defence consists of a complex network of components that function in concert with one another. This network includes:

1- Extramucosal components such as mucus, surface active phospholipids, and bicarbonate.

2- Epithelium, microcirculation and sensory afferent neurones beneath the epithelium

3- The mucosal immune system.

4- The ability of mucosa to undergo repair *(Wallace et al., 1996).*

- ***Gastric Mucus:***

It is secreted by gastric mucus cells located on the surface of gastric mucosal epithelium and in gastric glands *(Mc Guigan, 1991).*

Gastric mucus is present in the gastric juice in a soluble phase, and in an insoluble form in the gel layer, which coat the mucosal surface of stomach. Gel thickness is increased by prostaglandin E and decreased by NSAIDs *(Mc Guigan, 1991).*

Mucus functions are:

a- To protect the underlying cells from mechanical forces of digestion.

b- To lubricate mucosa assisting movement of food over mucosal surface.

c- To retain water within mucous gel and therefore providing an aquous environment for underlying cells.

d- To form an unstirred layer impeding, but not blocking, diffusion of H^+ from the lumen to apical membrane of epithelial cells, it is also impermeable to penetration by macromolecules

such as pepsin, so protecting the underlying mucosa from proteolytic injury *(McGuigan, 1991)*.

Under normal conditions mucus is constantly being produced but is also being removed continuously by mechanical forces during mixing and grinding the food, and by pepsin which degrades mucus into soluble glycoprotein subunits *(Richardson, 1992)*.

- ***Bicarbonate:***

This is secreted by the surface epithelium of the stomach and duodenum and also by Brunner's gland of duodenum*(Richardson, 1992)*.

Although some bicarbonate reaches the lumen, much of secreted bicarbonate remains below or within the mucus layer, thus the mucosal surface is in contact with fluid that contains high pH relative to the lumen of stomach *(Richardson, 1992)*.

Under normal conditions H+ ions are neutralized by bicarbonate producing carbon dioxide and water, as they diffuse through the mucus gel layer. A pH gradient is thus established between the lumen and the surface epithelium *(Richardson, 1992)*.

- ***Mucosal Blood Flow:***

The blood supply of the stomach and duodenum is important in maintaning normal mucosal integrity. Gastric and duodenal mucosa are supplied by mucosal capillaries that traverse the glandular area of stomach and duodenum. An extensive system of submucosal arteries and veins regulate blood supply to the surface epithelium *(Richardson, 1992)*.

Blood flow removes acid which may diffuse through the mucosa especially if the mucosa has been damaged, thus decreased mucosal blood flow is accompanied by back diffusion of luminal H+, a factor which is important in producing gastric mucosal damage *(Richardson, 1992)*.

- ***Cell Renewal:***

Normal cell renewal is an important factor in maintaning mucosal integrity. Cells are constantly dying and being replaced by new cells. In order for this system to function normally there must be a balance between cell loss and cell renewal. Disturbance of this steady state may cause mucosal damage *(Richardson, 1992)*.

- ***Endogenous Prostaglandins:***

Prostaglandin E, F and I types are found in gastric and duodenal mucosa. When administered exogenously, prostaglandins stimulate the secretion of mucus and HCO_3, increase mucosal blood flow, and enhance mucus regeneration after injury. Prostaglandins also may have trophic effect on mucosa. Duodenal mucosal PGs appear to stimulate basal duodenal HCO_3 secretion thus, protecting the mucosa against variety of noxious agents including boiling water, ethanol, bile acids and aspirin *(Soll, 1990)*.

Epidemiology and risk factors of peptic ulcer

The life time prevalence of peptic ulcer disease is approximately 10% with about equal prevalence in men and women. Duodenal ulcer is more common than gastric ulcer *(Isenberg et al., 1995)*.

- ***Age:***

The incidence of ulcer disease increases with age which may be explained by increase use of NSAIDs in elderly or by reduction of tissue prostaglandins *(Isenberg et al., 1995)*.

- ***Genetic Factors:***

It seems to be important in some patients with peptic ulcer. There is increased incidence in first degree relatives of patients with duodenal ulcer and a positive association with high level of serum pepsinogen I, which appears to be inherited as a dominant trait and may reflects total chief cell mass *(Isenberg et al., 1995)*.

- ***Emotional Stress:***

The importance of this factor in peptic ulcer remains controversial. Controlled studies suggest a relation between emotional stress and ulcer disease in some patients, the mechanism however, is unclear. Basal acid secretion has been reported to increase during stressful conditions. Emotional stress may alter factors that maintain mucosal integrity, resulting in ulcer because of decrease mucosal defence *(Soll, 1990)*.

However, there is no single characteristic duodenal ulcer personality or differences in frequency of duodenal ulcer among different socioeconomic classes or occupation groups *(McGuigan, 1991)*.

- ***Alcohol or Caffine-Containing Beverages:***

Acute alcoholic intake can result in inflammation of the stomach due to damage of gastric mucosal barrier *(Schuckit, 1991)*.

Although alcohol can stimulate acid secretion there is no evidence that it can cause gastric or duodenal ulcer *(Richardson, 1992)*.

In a study in 1988, Coca Cola was chosen as a physiological exogenous acid load drunk by people every day, to show its relation to peptic ulcer. It produced a marked fall in duodenal mean pH and significantly reduced the period of duodenal alkalinization, thus it could predispose to DU *(Mc Cloy et al., 1988)*.

- ***Hot Drinks:***

The effect of hot drinks was studied and it was concluded that temperature that would normally be injurious to skin and presumbly to mucosa when transmitted down to mucosa of upper GIT may be causally related to peptic ulcer in some patients *(McCloy, 1988)*.

- ***Cigarette Smoking:***

Epidemiological data suggest an association between smoking and peptic ulcer as:

- Smoking is more common among ulcer patients.
- There is a positive relation between the quantity of cigarette smoked and the prevalence of ulcer disease.
- Duodenal ulcers are less likely to heal and recur more frequently in smokers *(Soll, 1990)*.

It was emphasized that cigarette smoking doesn't increase gastric acid secretion *(McGuigan, 1991)*.

An increased reflux of bile salts was found in smokers *(Muller Lissner, 1988)*.

The main ulcerogenic effect of cigarette smoking in DU may be due to inhibition of pancreatic HCO_3 secretion or by accelerating emptying of gastric acid in duodenum *(Isenberg et al., 1995)*.

- ***Corticosteroid Therapy:***

An association between glucocorticoid therapy especially prednisone and peptic ulcer disease has been both supported and denied in several studies, higher incidence of ulcer disease in patients taking large dose of glucocorticoids for long periods of time has been documented *(Soll, 1990)*.

pathogenesis of Peptic Ulcer

The pathogenesis of peptic ulcer disease appear to be a multifactorial, involving an imbalance between aggressive factors such as acid and pepsin, and defensive mechanisms such as prostaglandins, mucus, bicarbonate, and mucosal blood flow *(Peura, 1997)*.

- ***Abnormalities in secretion of acid and pepsin:***

About 30-40% of patients with duodenal ulcers have acid secretion rates above the upper limit of normal range, the same percentage of ulcer patients have increased or normal pepsinogen secretion *(Soll, 1990)*.

In patients with duodenal ulcer the process by which acid is neutralized or removed from the duodenum may be inadequate. In contrast to duodenal ulcer, gastric ulcers have acid secretory rates that are normal or reduced compared with non ulcer subjects, however, true achlorhydra (in response to pentagastrin) never occurs in patients with benign gastric ulcer *(Isenberg et al., 1995)*.

The fact of normal or reduced acid secretory rates in gastric ulcer patients doesn't exclude acid and pepsin as the cause of gastric ulcer disease, but suggests that other factors may be involved, and the

Also it is possible that aspirin may injure small vessels in gastric mucosa by the inhibition of prostacyclin or by inhibition of the synthesis of thromboxane by platelets and therefore can diminish mucosal blood flow *(Richardson, 1992)*.

- ***H.pylori and peptic ulcer:***

Since the initial report by Warren and Marshal, in 1984, H. pylori has assumed an increasingly important role in pathogenesis of peptic ulcer disease, Recent National Institutes of Health Consensus Development conference acknowledged the relationship between H. pylori infection and peptic ulcer disease and recommended that the medical community must treat H. pylori infection in all patients with peptic ulcer and H. pylori infection *(Cleghorn, 1997)*.

Infection with H. pylori is a causal factor in the development of peptic ulcer, there is a strong association between gastritis induced by H. pylori and peptic ulcer. Peptic ulcer disease seldom develops in the absence of infection *(Blum, 1996)*.

There is 100% concordance between H. pylori infection and histological gastritis, indeed the voluntary ingestion of H. pylori by healthy human volunteers with normal gastric histology resulted in development of gastritis *(Morris et al., 1991)*.