Ain Shams University
Faculty of Medicine
Anatomy Department

A study of the protective role of olive oil versus licorice on indomethacin-induced gastric insult in albino rat

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By

Noha Mohamed Gaber Abd El-Aziz

M.B.B.Ch., M.Sc.
Assistant lecturer of Anatomy and Embryology
Faculty of Medicine - Ain Shams University

Under supervision of

Prof. Dr. Elerian Youssef Ekladiuos
Professor of Anatomy and Embryology
Faculty of Medicine - Ain Shams University

Prof. Dr. Shahira Samir Zaki
Professor of Anatomy and Embryology
Faculty of Medicine - Ain Shams University

Ass. Prof. Dr. Marwa Mohamed Ahmed Elsawy
Assistant Professor of Anatomy and Embryology
Faculty of Medicine - Ain Shams University

Dr. Shereen Adel Saad
Lecturer of Anatomy and Embryology
Faculty of Medicine - Ain Shams University

Dr. Gamal Taha El-Sayed
Lecturer of Anatomy and Embryology
Faculty of Medicine - Ain Shams University

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LIST OF ABBREVIATIONS

- COX: Cyclooxygenase enzyme.
- EVOO: Extra virgin olive oil.
- GI: Gastrointestinal.
- GOT: Glutamic Oxaloacetic Transaminase.
- GPT: Glutamic pyruvic transaminase.
- H. pylori: Helicobacter pylori.
- IBD: Inflammatory bowel disease.
- INDO: Indomethacin.
- LDH: Lactic acid dehydrogenase.
- LDL: Low Density Lipoprotein.
- NSAIDs: Non-steroidal anti-inflammatory drugs.
- PG: Prostaglandins.
- ROS: Reactive oxygen species.

A study of the protective role of olive oil versus licorice on indomethacin-induced gastric insult in albino rat

ABSTRACT

Introduction: Gastric ulcer is one of the common disorders of gastrointestinal tract that affects a considerable number of people worldwide. Licorice is one of the most widely used herbal drugs around the world; it exhibits many biological activities and possibly even has protective effects against chronic diseases.

Aim of the work: This study was conducted to investigate the gastroprotective effect of licorice in the rats induced gastric ulcer by Indomethacin.

Material and methods: thirty-five albino rats were used in the current study. They were divided into control (group I) and experimental groups. The experimental group was group II (rats were given indomethacin and were sacrificed six hours after drug intake) and group III(rats were given licorice administered orally by gastric gavage for 3 weeks, then they received indomethacin a single dose and were sacrificed six hours after drug intake.

Results: The general cellular morphology of the gastric mucosa after indomethacin administration was greatly affected. Ulceration with sloughing of the mucosal surface epithelium and widening of glandular pits were revealed, together with loss of the regular parallel pattern of the gastric glands. The histopathological findings of group III revealed preservation of the normal tubular arrangement of gastric glands. Minor changes in the structure of gastric glands were observed in form of widening of the pits with no visible ulceration. In the licorice receiving group, the parietal cells with eosinophilic cytoplasm were observed in the middle part of the gland.

Conclusions: Indomethacin is capable of producing injury to gastrointestinal mucosa. There is marked improvement of gastric mucosa in association with the use of licorice. The present study suggests that licorice should be used together with indomethacin for better gastroprotective effect.

Key words: Indomethacin, licorice, gastric ulcer, protection

INTRODUCTION

The stomach, in its capacity as a food reservoir whose role is to gradually deliver ingested food to the small intestine, is constantly exposed to toxins. The gastric barrier contains several lines of defense. When offensive agents, whether infectious or chemical in nature, overcome mucosal defense systems, the result is epithelial damage and ulceration ***(Boltin and Niv, 2014).***

Incidence of gastric ulcer increased due to stress, frequent and indiscriminate use of non-steroidal anti-inflammatory drugs (NSAIDs), smoking, infection and nutritional deficiencies ***(Khazaei and Salehi, 2006)***. Moreover, environmental and host factors might also affect the distribution of Helicobacter pylori in the stomach, consequently, the pattern of gastritis ***(Chan and Leung, 2002).***

One of the most important drugs that contribute to gastric insult is nonsteroidal anti-inflammatory drugs. A major limitation of long term use of NSAIDs such as indomethacin and aspirin is the damage caused to the small

intestine and stomach, as revealed by studies in experimental animal models and human trials ***(Wang, et al., 2011).*** Recent studies have shown that more than 50% of patients taking indomethacin have adverse reactions include discomfort, ulcers, and bleeding ***(Dupeyrón, et al., 2013)***.

Licorice has been used as a medicinal plant for thousands of years. The active component of licorice, glycyrrhizic acid, is hydrolyzed in vivo to glycyrrhetinic acid, which is responsible for most of its pharmacological properties. Licorice has held claim for therapeutic use for dyspepsia, gastric ulcers, sore throat, asthma, bronchitis, Addison's disease and rheumatoid arthritis and also has been used as a laxative, antitussive and expectorant ***(Huo, et al., 2011).***

Besides all its benefits, Licorice has shown many side effects, it is responsible for sodium retention, hypokalemia and hypertension, which is the most common side-effects especially in patients treated with higher doses and long-term administration ***(Morgan, et al., 2011).*** Moreover, Licorice could potentially contribute to development of coronary artery spasm, vasospasm-mediated transient visual loss and migraine ***(Konik, et al., 2012).***

Olive oil is a vegetable oil obtained from olive trees (oleaeuropaea); a traditional tree crop of the Mediterranean Basin. It is the major source of dietary fat in the Mediterranean diet, and its regular consumption is thought to have various beneficial effects on human health ***(Waterman and Lockwood, 2007)***. It has many applications including cooking, cosmetics, pharmaceutical preparations and soaps. Olive oil is considered to be a healthy product because of its constituents, which include oleic acid, palmitic acid and other fatty acids ***(El-Kholy, et al., 2014)***.

There is considerable data showing that the consumption of olive oil has been directly associated with protection of cardiovascular health protection and prevention of cancer and neurodegenerative disorders ***(Rincon-Cervera, et al., 2016).***

AIM OF THE WORK

The aim of the present work was to investigate the possible role of olive oil on the structure of gastric mucosa when consumed prior to indomethacin induced gastric insult in albino rats. Moreover, the current study aimed to compare the protective effect of olive oil versus licorice on the structure of gastric mucosa.

REVIEW OF LITERATURE

Anatomy and Histology of the stomach

The stomach is the most distensible part of the gastrointestinal tract, located in the upper left abdominal quadrant, immediately below the diaphragm. The stomach is continuous with the esophagus superiorly and empties into the duodenal portion of the small intestine inferiorly. Food passes from the esophagus into the stomach where it may be retained for 2 hours or more ***(Shruti, et al., 2011).***

In the stomach, the food undergoes mechanical and chemical breakdown to form chyme. Solid foods are broken up by a strong muscular churning action while chemical breakdown is produced by gastric juices secreted by the glands of the stomach mucosa. Once chyme formation is completed, the pyloric sphincter relaxes and allows the liquid chyme to be gushed into the duodenum ***(Karan and Patel, 2013).***

Anatomically, the stomach is divided into four regions:

- The cardia, which surrounds the opening of the esophagus into the stomach.
- The fundus of stomach, which is the area above the level of the Cardiac orifice ***(Shruti, et al., 2011).***
- The body of stomach, which is the largest region of the stomach.
- The pyloric part, which is divided into the pyloric antrum and pyloric canal ***(Karan and Patel, 2013).***

The outlet of the stomach (pyloric orifice) is marked by the pyloric constriction and surrounded by a thickened ring of gastric circular muscle (the pyloric sphincter). The pyloric orifice is just to the right of midline in a plane that passes through the lower border of vertebra L1 (the transpyloric plane) ***(Standring, 2008).***

The wall of the human stomach has four basic layers: mucosa, submucosa, muscularis externa, and serous layer ***(Byanet, et al., 2011)***:

I. The Mucosa:

In the non-distended state, the stomach mucosa is thrown into prominent longitudinal folds called rugae that disappear when the stomach is distended ***(Ghosh and Chakrabarti, 2015)***.

- Mucosal Epithelium:

The lining epithelium is columnar and mucous secreting. Apical parts of the lining cells are filled by mucin that is usually removed during processing of tissues so that the cells look empty (or vacuolated). Mucous secreted by cells of the lining epithelium protects the gastric mucosa against acid and enzymes produced by the mucosa itself.

At numerous places the lining epithelium dips into the lamina propria to form the walls of depressions called gastric pits. These pits extend for a variable distance into the thickness of the mucosa. Deep to the gastric pits the mucous membrane is packed with numerous gastric glands. These glands are of three types: main gastric, cardiac and pyloric glands ***(Călămar, et al., 2014)***.

- The Lamina Propria

The connective tissue of the lamina propria is scanty. Few aggregations of lymphoid tissue are present in it occasionally.

- The Muscularis Mucosa

The muscularis mucosa of the stomach is well developed. It consists of two layers, the circular (inner) and

longitudinal (outer) layers and an additional circular layer may be present outside the longitudinal layer ***(Singh, 2014).***

II. The submucosa is composed of dense connective tissue containing blood and lymph vessels; it is infiltrated by lymphoid cells, macrophages, and mast cells ***(Yu, et al., 2015).***

III. The Muscularis Externa

The muscularis externa of the stomach is well developed. Three layers, oblique, circular and longitudinal (from inside out) are described. The circular fibers are greatly thickened at the pylorus where they form the pyloric sphincter. There is no corresponding thickening at the cardiac end.

IV. The serosa:

Covering the muscle coat, there is the serous layer. This layer is merely the visceral peritoneum that covers most parts of the gastro-intestinal tract ***(Singh, 2014)***.

Gastric glands:

Histologically, the cardia is a narrow circular band, 1.5–3 cm in width; its mucosa contains simple or branched