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ANTIULCER ACTIVITY OF SHARK LIVER OIL ON ASPIRIN INDUCED GASTRIC ULCER IN RATS

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ABSTRACT:

Shark liver oil is one of the sources of cellular energy and provides repair and restoration of damaged cells, and supports in protection of the body from the emergence of tumorous conditions. The Shark liver oil was tested orally at the dose of 1gm/kg/oral body weight, on gastric ulceration experimentally induced by Aspirin. The parameters considered to assess the Antiulcer activity were percentage of ulcer, ulcer index, percentage of inhibition, pH, free acidity and total acidity. Pretreatment with the Shark liver oil resulted in significant decrease of the ulcerated area and reduced pH, free acidity and total acidity.

Keywords: Shark liver oil, Antiulcer activity, Percentage of ulcer, Percentage of inhibition.

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INTRODUCTION

Ulcer is a break in the continuity of epithelial layer or mucus membrane due to various causes like physical/chemical injuries or trauma etc. Common causes for ulcer is imbalance between the offensive factor like gastric acid, pepsin and defensive factor like mucin secretion etc. Other causes for gastric ulcer includes *Helicobacter pylori* infection, local trauma, ischemia reflux of bile, drugs like non steroidal anti-inflammatory agents, alcohol etc[1,2]. Presently multimodel treatment for gastric acid includes the use of antisecretory drugs like H_2 blockers (ranitidine, famotidine etc), M_1 blockers (pirenzepine, telenzepine etc), proton pump inhibitors (omeprazole, lansoprazole etc), and antibacterial agents like metronidazole, amoxicillin etc. Gastric acid suppressant having prohealing effect would be an ideal agent for the treatment of gastric ulcer. Use of carbanoxolone sodium derived from plant with an attempt to promote the healing of gastric acid was not satisfactory. Search continued to find a gastroprotective agent with healing promoting property. Hence, it was necessary to find out a suitable agent for treatment of peptic ulcer in natural marine oil of Shark[3].

Shark liver oil is one of the source of cellular energy. It provides repair and restoration of damaged cells, contributes in cholesterol reduction, helps in the treatment of skin diseases, promotes skin regeneration and supports in protection of the body from the emergence of tumorous conditions and the negative effects of radiotherapy or chemotherapy. It also enhances oxygen transport and is a powerful antioxidant that can scavenge free radicals from the body before they start their debilitating effects. Shark squalene is an amazing immune enhancer that helps the body protect against all three types of common offenders: bacterial, viral, and fungal infections[4]. Squalene ($C_{30}H_{50}$) is a polyunsaturated aliphatic hydrocarbon of low density found in large quantities in the liver oils of deep-sea sharks (Centrophorus Granulosus). Squalene and its constituent Squalane are used in the pharmaceutical, cosmetic, lubrication, electronic, textile, aromatic and rubber industries.

Interest in their medical and dermatological significance intensified when squalene was found to be a precursor of cholesterol and possessed a possible anticarcinogenic effect. Shark liver oil is used in natural medicine as immunity stimulant, cardiovascular protector and anti aging agent. These properties were related with the high amounts of alkylglycerols which are known to possess healing properties. Shark squalene also possesses excellent anti-inflammatory and peripheral antinociceptive effects that may contribute to its use in the treatment of arthritis and other inflammatory disorders[5]. Shark liver oil is promoted as dietary supplement used to boost the immune system, fight off infections, heal wounds and to treat cancer. It also possess cell protecting abilities. Compare to other fish oils, Shark liver oils contains high amount of alkoxyglycerols and squalaminne which promotes healing properties[6]. Because of their immune boosting effects they are also claimed to help against colds, flu, chronic infections, asthma, psoriasis, arthritis and AIDS. Most of the scientific studies with shark liver oil have focused on its possible benefits against cancer and infections. Therefore Shark liver oil has been used for over 40 years as both a therapeutic and preventive agent.

Various plant extracts has been tested for finding a suitable gastroprotectives, other fish oils are found to produce significant anti-ulcer properties[7]. Here in our study we pay our attention to find out a suitable agent for treatment of peptic ulcer in natural marine Shark liver oil[8].

MATERIAL AND METHOD

Chemicals and drugs

Aspirin powder (gift sample) used as reference standard was obtained from Cipla Pharmaceuticals Ltd., Bangalore India. All other chemicals and reagents used in this study were of analytical grade. Shark liver oil used as the test drug at a dose (1gm/kg p.o) was procured from Blueline Foods (India) Pvt. Ltd. Mangalore, Karnataka, India.

Experimental animals

Male Wistar rats, weighing 150-200 g were used for antiulcer activity. The rats were housed in polyacrylic cages and maintained at 27 ± 2°C, 45-60% RH and 12 h photo period. They were provided with a standard pellet diet (Gold Mohur food and feeds Ltd., Vikhroli (East), Mumbai) India and water *ad libitum*. The experiment was carried out according to Committee for the Purpose of Control and Supervision of Experiments on Animals (CPCSEA) (112/1999/CPCSEA) and the study was approved by Institutional Animal Ethical Committee. Wistar rats of weighing between 150-200g body weights were divided into 4 groups and each group comprised of 6 animals (n=6).

Group 1: Normal
Group 2: Control
Group 3: Ranitidine-30 mg /kg, p.o.
Group 4: Shark liver oil 1gm/kg p.o[9]

Test animals were treated for 7 days with the Shark lever oil[9]. After 7 days treatment animals were fasted for 24 h with free access to water. The normal group animals were given normal feed and free access to water. The control and the standard animals were also fasted for 24 h with free access to water. Vehicle, standard drug and Shark liver oil were administered by oral route, 30 min prior to the administration of oral Aspirin in a dose of 200 mg/kg p. o. to 24 h fasted animals. Four hour after Aspirin administration, the animal were sacrificed**.** The stomach was removed and the gastric contents were collected. The gastric juice was centrifuged at 3000 rpm for min and gastric volume, pH, free acidity and total acidity were estimated. Subsequently, the stomachs were incised along the greater curvature and ulcer scoring was done using the dissecting microscope with a square grid eye piece[10]. Percentage of ulcer, ulcer index and percentage of inhibition were calculated by using the following formula[11].

0=no ulcer, 1=superficial ulcer, 2=deep ulcer, 3=perforation.

$UI = UN + US + UP \times 10\text{-}1$

UN -Average No. of ulcers per animal, US-Average of severity score, UP- % of ulcers with ulcer.

Inhibition %=[(UI control–UI treated)/UI control]x 100

The isolated stomachs were kept in formalin solution (15%) and then histopathological examination was done. Statistical analysis is expressed as Mean ± SEM, followed by using one-way analysis of variance (ANOVA) followed by Dunnett's test. $p<0.0001$ was considered statistically significant.

RESULTS

Present study reports the Anti ulcer activity of the Shark liver oil against Aspirin induced ulcer model. Exposure to Aspirin induced mucosal damage resulted in the formation of significant number of ulcers compared to control, wherein no ulcers were found. It is evident from Table 1, the ulcer index in Control, Ranitidine and Shark liver oil is 5.25±0.21408, 1.5±0.28807, 2.333±0.33477 respectively. The % protection of Shark liver oil was 55.61%and for Ranitidine it was 71.42%. (Table 1).

Oral administration of Shark liver oil reduced significantly decreased pH, free acidity and total acidity (Table 2). The results was found to be statistically

significant (p value<0.0001). From the above result, when compared with Ranitidine, Shark liver oil showed good effect on Aspirin induced ulcer model (Fig 1 & 2). Although, the etiology of ulcer is unknown, Aspirin induced mucosal damage plays an important role in ulcerogenesis. The pathophysiologies of Chemical induced gastric ulcers are complex. Nonsteroidal anti-inflammatory drugs (NSAIDs), like aspirin and indomethacin, are known to induce ulcers during the course of anti-inflammatory therapy, by inhibiting prostaglandin synthesis through the cyclooxygenase pathway.

Table 1. Antiulcer activity of Shark liver oil in Aspirin induced ulcer model.

Sl. No.	Treatment	Ulcer index (mean ± SEM)	% Ulcer protection
1	Control	5.25±0.21408	0.00%
2	Ranitidine	1.5±0.28807***	71.42%
3	Shark liver oil	2.333±0.33477***	55.61%

***P<0.001 Data were expressed as the mean ± S.E.M., n = 6 in each group.
Dunnett's t test: *** P<0.0001, * P<0.05

In the stomach, prostaglandins play a vital protective role, stimulating the secretion of bicarbonate and mucus, maintaining mucosal blood flow and maintaining the mucosal cell turnover and repair. Thus, the suppression of prostaglandin synthesis by NSAIDs results in increased susceptibility to mucosal injury and gastric ulceration. It was observed that Shark liver oil displayed significant reduction in mucosal damage of aspirin induced ulcer rat model.

Sl. No	Treatment	Vol of gastric juice in ml	pH	Free acidity meq/l/100g	Total acidity meq/l/100g
1	Control	1.4 ± 0.10801	2.565 ± 0.08712	69.50 ± 2.1408	146.1 ± 3.8938
2	Ranitidine	0.8 ± 0.1238***	3.62 ± 0.1594***	54.3 ± 1.3814***	116.83 ± 2.9159***
3	Shark liver oil	1.13 ± 0.0494***	3.146 ± 0.02932***	62.6 ± 1.2852***	129 ± 3.5023***

Data were expressed as the mean ± S.E.M., n = 6 in each group.
Dunnett's t test: *** P<0.0001, * P<0.05

Shark liver oil is rich in alkylglycerols, which are naturally found in mother's milk and in bone marrow. It also contains pristane, squalene, vitamins A, D, omega-3 fatty acids, triglycerides, glycerol ethers, and fatty alcohols[12]. The present section summarizes the Antiulcer property of Shark liver oil on Aspirin induced ulcer model in rats. In Aspirin induced ulcer model it significantly inhibits the ulcer index as compared to control. However in Aspirin induced ulcer model for Shark liver oil showed good ulcer protection. The cytoprotective activity was supported by histopathological studies.

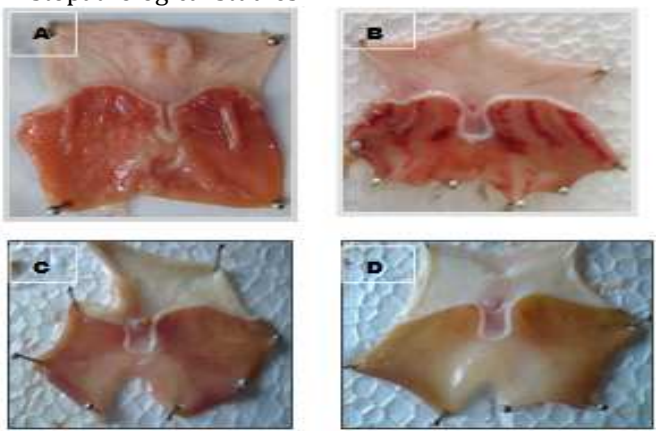

Figure 1. (A) Gastric mucosa of normal rats (B) Gastric mucosa of untreated rats showing severe ulceration. (C) Gastric mucosa of Ranitidine group showing less intense ulceration. (D) Gastric mucosa of Shark liver oil treated group showing mild ulceration.

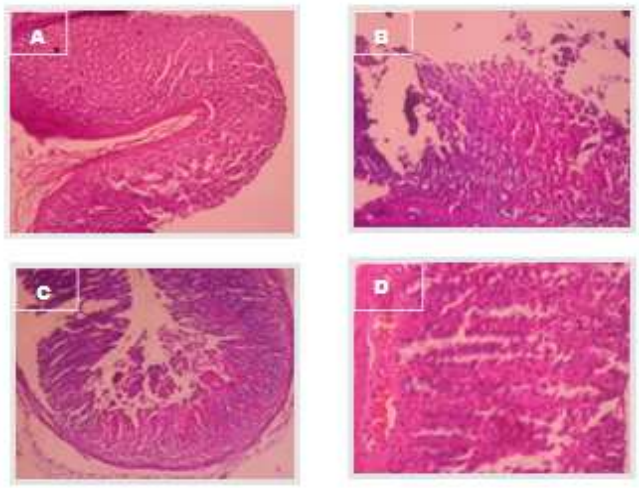

Figure 2. (A) Gastric section of normal rats showing normal mucosa and sub-mucosa. (B) Gastric section of untreated rats showing ulceration of the mucosal cells associated with mixed inflammatory changes and necrosis intervening these epithelial cells are seen aggregates of macrophages and neutrophil infiltration in the gastric mucosa and submucosa shows severe edema. (C) Gastric section of Ranitidine group showing gastric mucosa with intact epithelium, lamina propria and muscularis mucosa intervening the epithelial cells are seen scattered mononuclear inflammatory cells and few congested vascular spaces and submucosa shows moderate edema. (D) Gastric section of Shark liver oil treated group showing scattered neutrophils, lymphocytes and mild submucosal edema. Also seen are some regenerated epithelial cells.

DISCUSSION

There are several factors that may induce ulcer in human beings, such as; stress, chronic use of anti-inflammatory drugs and continuous alcohol ingestion.

Although in most cases the etiology of ulcer is unknown, it is accepted that it is result of an imbalance between aggressive factors and maintenance of the mucosal integrity through the endogenous defence mechanism. The candidate for an effective drug against peptic ulcer should basically act either by reducing the aggressive factors on gastrointestinal mucosa or by increasing mucosal resistance against them[13]. Result of the present study indicates that Shark liver oil has significant beneficial effects in Aspirin induced mucosal damage model. Therefore, the presence of alkoxyglycerols content and other bioactive compounds in Shark liver oil may be associated with the gastroprotective effect. Also the antioxidant and antimicrobial property as reported of Shark liver oil could be one of the possible mechanisms for antiulcer action[14]. However other mechanisms of action might be involved in gastroprotective action. Further studies are required to explore the gastroprotective action.

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