Available online at www.sciencedirect.com
SCIENCE DIRECT
Journal of Ethnopharmacology 104 (2006) 156–163
Journal of ETHNO-PHARMACOLOGY
www.elsevier.com/locate/jethpharm

Antiulcerogenic and ulcer healing effects of *Solanum nigrum* (L.) on experimental ulcer models: Possible mechanism for the inhibition of acid formation

Mallika Jainu *, Chennam Srinivasulu Shyamala Devi

Department of Biochemistry, University of Madras, Guindy Campus, Chennai 600025, Tamil Nadu, India

Received 17 April 2005; received in revised form 10 July 2005; accepted 27 August 2005
Available online 30 September 2005

Abstract

Solanum nigrum, an herbal plant which is recommended in ayurveda for the management of gastric ulcers. Therefore, the purpose of the study was to investigate the antiulcer effect of *Solanum nigrum* fruits extract (SNE) on cold restraint stress (CRU), indomethacin (IND), pyloric ligation (PL) and ethanol (EtOH) induced gastric ulcer models and ulcer healing activity on acetic acid induced ulcer model in rats. The treatment with SNE at higher dose significantly inhibited the gastric lesions induced by CRU (76.6%), IND (73.8%), PL (80.1%) and EtOH (70.6%), respectively, with equal or higher potency than omeprazole. SNE showed concomitant attenuation of gastric secretory volume, acidity and pepsin secretion in ulcerated rats. In addition, SNE (200 and 400 mg/kg b.w.) accelerated the healing of acetic acid induced ulcers after the treatment for 7 days. Further, to ascertain the antisecretory action, the effects of SNE on H^+K^+ATPase activity and plasma concentration of gastrin hormone in ulcerated rats were determined. SNE significantly inhibits H^+K^+ATPase activity and decreases the gastrin secretion in EtOH-induced ulcer model. The severity of the reaction of ulcerogen and the reduction of ulcer size by SNE was evident by histological findings. Toxicity studies of SNE have also been carried out for its safety evaluation. SNE, thus, offers antiulcer activity by blocking acid secretion through inhibition of H^+K^+ATPase and decrease of gastrin secretion. These results further suggest that SNE was found to possess antiulcerogenic as well as ulcer healing properties, which might also be due to its antisecretory activity.

Keywords: *Solanum nigrum*; Gastric acid; Antisecretory; H^+K^+ATPase; Gastrin

1. Introduction

Gastric hyperacidity and gastroduodenal ulcer is a very common global problem today. It is now generally agreed that gastric lesions develop when the delicate balance between some gastroprotective and aggressive factors is lost. Major aggressive factors are acid, pepsin, *Helicobacter pylori* and bile salts. Defensive factors mainly involve mucus-bicarbonate secretion and prostaglandins (Hoogerwerf and Pasricha, 2001). Hypersecretion of gastric acid is a pathological condition, which occurs due to uncontrolled secretion of hydrochloric acid from the parietal cells of the gastric mucosa through the proton pumping H^+K^+ATPase (Sachs et al., 1995). Even the normal rate of acid secretion may cause ulceration in the breached mucosa when some gastroprotective factors are lost.

The modern approach to control gastric ulceration is to inhibit gastric acid secretion, to promote gastroprotection, to block apoptosis and to stimulate epithelial cell proliferation for effective healing (Bandhopadhyay et al., 2002). Most of the antisecretory drugs such as proton pump inhibitors (omeprazole, lansoprazole, etc.) and histamine H_2-receptor blocker (ranitidine, famotidine, etc.) are extensively used to control increased acid secretion and acid related disorders caused by stress, NSAID's and *H. pylori*, but there are reports of adverse effects and relapse in the long run (Martelli et al., 1998; Wolfe and Sachs, 2000). On the contrary most of the herbal drugs reduces the offensive factors and proved to be safe, clinically effective, better patient tolerance, relatively less expensive and globally competitive (Goel and Sairam, 2002). Plant extracts, however, are some of the most attractive sources of new drugs and have been shown to produce promising results in the treatment of gastric ulcers.

* Corresponding author at: Old No. 285, New No. 32, Royapettah High Road, Chennai 600014, Tamilnadu, India. Tel.: +91 44 28132902; fax: +91 44 2352494.
E-mail address: malsleo80@yahoo.co.in (M. Jainu).

0378-8741/$ – see front matter © 2005 Elsevier Ireland Ltd. All rights reserved.
doi:10.1016/j.jep.2005.08.064

Solanum nigrum Linn. (Solanaceae) commonly known as 'Black nightshade' that have been extensively used in traditional medicine in India and other parts of world to cure liver disorders, chronic skin ailments (psoriasis and ringworm), inflammatory conditions, painful periods, fevers, diarrhoea, eye diseases, hydrophobia, etc. (Kritikar and Basu, 1935). Our research interest in this plant arose because of its potential medicinal value against peptic ulcer, as used in folk medicine. The plant contains glycoalkaloids (solanine, solamargine, solanigrine and solasodine (0.09–0.65%)), steroidal glycosides (β-solamargine, solasonine and α,β-solansodamine), steroidal saponins (diosgenin (0.4–1.2%)), steroidal genin (gitogenin), tannin (7–10%) and polyphenolic compounds. Mature fruits are low in alkaloid (solanine) content (Saijo et al., 1982; Duke, 1985; Son et al., 2003).

Previous reports indicated that *Solanum nigrum* fruits possess beneficial activity as antiulcer, antioxidant and antitumor promoting agent in rats (Prashanth Kumar et al., 2001; Son et al., 2003; Jainu and Devi, 2004). *Solanum nigrum* fruits are very commonly used as hepatoprotective agents (Raju et al., 2003), which also afford protection against free radical mediated damage (Bardhan et al., 1985). More recent reports revealed that the plant exerted cytoprotection against gentamycin-induced toxicity on vero cells (Prashanth Kumar et al., 2001). It has been reported earlier that aerial parts of *Solanum nigrum* is believed to offer its antiulcer action through acid and peptic suppression in aspirin induced ulcerogenesis in rats (Akthar and Munir, 1989).

Any potent antiulcer drug should possess both antiulcer as well as ulcer healing property. Experimental studies to determine both of these properties of *Solanum nigrum* are very limited, so it was worthwhile to undertake such investigation using the extract of mature fruits of *Solanum nigrum* (SNE). The present study incorporates the evaluation of antiulcer effect of SNE in cold restraint stress (CRU), indomethacin (IND), pyloric ligation (PL) and ethanol (EtOH) induced ulcer models. In addition, the healing effect of SNE in acetic acid induced ulcer model was also analyzed. Using EtOH-induced gastric ulcer model, evidence has been presented in this paper to show that gastroprotective effect of SNE is mediated through acid inhibitory effect, by inactivating H^+K^+ATPase and suppression of gastrin release. This study thus provides an insight on the mechanism of the antiulcer effect of SNE.

2. Materials and methods

2.1. Drugs and chemicals

Methanol (MeOH), dichloromethane (DCM), indomethacin, lansoprazole (LNZ) and omeprazole (OMP) (Sigma Chemical Co., St. Louis, MO, USA) were used in this study. A commercial gastrin hormone assay kit was obtained from Diagnostic Products Corporation (Los Angeles, CA). All substances were prepared immediately before use and the reagents used were of analytical grade.

2.2. Plant material

The mature fruits of *Solanum nigrum* used in this study were purchased from Native Care and Cure Center, India and identified with the standard sample by Dr. P. Brindha, Department of Pharmacognosy, Captain Srinivasa Murthy Drug Research Institute for Ayurveda, Chennai. A voucher specimen has been deposited at the herbarium of the same institute.

2.3. Extract preparation

Solanum nigrum mature fruits were shade dried and coarsely powdered. One kilogram of this powdered plant material was soaked in 2 l of methanol for 5 days and then extracted in Soxhlet apparatus with methanol for 10 h. The last traces of the solvent were removed and concentrated to dryness under vacuo by using a rotary evaporator. The dried extract was weighed and then kept at −4 °C until ready for use. The yield of the extract was 16.7% (w/w) of powdered methanolic extract. In each experiment, the extract was diluted with water to desired concentration.

2.4. Phytochemical screening

A preliminary phytochemical screening of SNE was conducted to determine the presence or absence of alkaloids, tannins, phenols, anthraquinones, saponins, volatile oil, carbohydrates, steroids, xanthones and glycosides according to the methods described by Kokate et al. (1996).

2.5. Animals

Adult male albino rats of Wistar strain weighing about 120–150 g were used for the study. The animals were obtained from Tamil Nadu University of Veterinary and Animal Sciences [TANUVAS], Madhavaram, Chennai. The animal room was well ventilated with a 12 h light/dark cycle throughout the experimental period. They were maintained in clean, sterile, polypropylene cages and fed with commercial pelleted rat chow (M/S Hindustan Lever Limited, Bangalore, India) and water ad libitum. All animals were deprived of food for 18 h before subjecting to ulcerogens and were allocated to different experimental groups. Six rats were used for each group in antiulcer and ulcer healing study. The study was approved by the institutional ethical committee, which follows the guidelines of CPSCEA (Committee for the Purpose of Control and Supervision of Experimental on Animals), which complies with international norms of INSA.

2.6. Toxicity studies

For acute oral toxicity studies, rats were divided into four groups of six animals each. Group I served as control rats that received only distilled water while groups II, III and IV orally fed with SNE at a dose level of 1.0, 2.0 and 4.0 g/kg body weight (b.w.) for 14 days. On 14th day the animals were sacrificed, blood was collected by sinus puncture and analyzed for red blood cell count (RBC), white blood cell count (WBC), hemoglobin (Hb), hematocrit (HCT), mean corpuscular volume (MCV) and blood