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The ameliorative effect of dates (*Phoenix dactylifera* L.) on ethanol-induced gastric ulcer in rats

A.A. Al-Qarawi, H. Abdel-Rahman, B.H. Ali *, H.M. Mousa, S.A. El-Mougy

Department of Veterinary Medicine, Faculty of Agriculture and Veterinary Medicine, King Saud University, Al-Gaseem Branch, P.O. 10158, Buraydah, Al-Gaseem 81999, Saudi Arabia

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Abstract

The present work aimed at testing, in a rat model of ethanol-induced gastric ulceration, a local folk medicinal claim that dates are beneficial in gastric ulcers in humans. Aqueous and ethanolic undialyzed and dialyzed extracts from date fruit and pits were given orally to rats at a dose of 4 ml/kg for 14 consecutive days. On the last day of treatment, rats were fasted for 24 h, and were then given ethanol, 80% (1 ml/rat) by gastric intubation to induce gastric ulcer. Rats were killed after 1 h of ethanol exposure, and the incidence and severity of the ulceration were estimated, as well as the concentrations of gastrin in plasma, and histamine and mucus in the gastric mucosa. A single group of rats that were fasted for 24 h, was administered orally with lansoprazole (30 mg/kg), and was given 80% ethanol as above, 8 h thereafter, served as a positive control.

The results indicated that the aqueous and ethanolic extracts of the date fruit and, to a lesser extent, date pits, were effective in ameliorating the severity of gastric ulceration and mitigating the ethanol-induced increase in histamine and gastrin concentrations, and the decrease in mucin gastric levels. The ethanolic undialyzed extract was more effective than the rest of the other extracts used. It is postulated that the basis of the gastroprotective action of date extracts may be multi-factorial, and may include an anti-oxidant action.

Keywords: Dates; Ethanol-induced ulcer; Gastric histamine; Gastrin; Lansoprazole; Mucin; *Phoenix dactylifera* L.; Palmae

1. Introduction

Date palms (*Phoenix dactylifera* L., Palmae) have been cultivated in the Middle East over at least 6000 years ago (Copley et al., 2001). For the natives in this region, dates are considered a staple carbohydrate food (Al-Shahib and Marshall, 2003). Date fruits are also used in the production of local beverages and spirits. In local medicinal practices dates are considered a "tonic" and "aphrodisiac", and in some communities they are thought to be useful against ulcer (Rasheed, personal communication). In fact, Muslims believe that "*He who eats seven dates every morning will not be affected by poison or magic on the day he eats them*" (cited by Miller et al., 2003).

The pollen grains of date palm have been used in Egyptian local practices to improve fertility in women, and in some locations in Arabia date pits are roasted and used in lieu of coffee as a hot beverage.

Relatively few pharmacological studies have been conducted on dates. For example, it has been shown that, depending on the type of extract used, date fruit and pit extracts significantly increase or decrease gastrointestinal transit (GIT) in mice (Al-Qarawi et al., 2003), and that date fruit extract has strong antioxidant and antimutagenic properties (Vayalil, 2002). Date palm kernels have been shown to exhibit antiaging properties and significant reduction in skin wrinkles in women (Bauza, 2002), and natural fats from date palm has been reported to prevent irritant contact dermatitis (Schliemann-Willers et al., 2002). In animals, the pits have been included in the diet of chickens, sheep, fish and rats, and have been shown to enhance

* Corresponding author. Tel.: +966 6 3813372; fax: +966 6 3813372.
E-mail address: alibadreldin@hotmail.com (B.H. Ali).

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growth in these species (see Ali et al., 1999 and references therein).

In view of the wide consumption of dates in our region, the fact that dates are anecdotally reputed to be useful against peptic ulcers, and the fact that Muslims customarily consume more of the dates during the fasting month of Ramadan, possibly to protect the gastric mucosa from the damaging effect of gastric acid, and because of the scarcity of information on the pharmacological properties of date fruits and pits, we considered undertaking this study to assess the influence of date extracts on the incidence and severity of ethanol-induced gastric ulceration. In addition, the effect of date extracts on the gastric concentrations of histamine and mucin, and the plasma concentration of the hormone gastrin has also been investigated.

2. Materials and methods

2.1. Animals

Fifty-four adult male Wistar rats weighing between 200 and 250 g were used in this work. They were obtained for the Animal House of King Saud University in Riyadh, and were divided into eight equal groups. The animals were kept at a controlled temperature of $23 \pm 2\,^{\circ}C$, relative humidity of 65–80% and a light regime of 12 h light:12 h dark (lights on at 6:00). Except otherwise mentioned, pelleted Purina chow and water were provided to the rats ad libitum.

2.2. Plant material

Fresh fruits of Sukari dates (*P. dactylifera* L.) were obtained from a local date manufacturing factory. Samples of these dates were kept frozen for future reference.

2.3. Plant preparation and administration

The date fruits were manually separated from the pits and the latter were washed clear of any fruit, dried at room temperature and ground into powder using a stainless-steel blender. The water extract of the date fruit was made by adding distilled water to coarsely pounded date fruit (3:1), and leaving for 48 h in a refrigerator ($4\,^{\circ}C$) with continuous stirring. The aqueous extract was then used daily for 14 consecutive days. To remove sugars from the extract, the aqueous extract was dialyzed. Dialysis was carried out under running tap water for 24 h. The dialyzed water extract was kept refrigerated and used daily for 14 consecutive days.

A soxhlet apparatus was used to obtain an ethanol extract. The ethanol was then evaporated and the residue diluted with water to give the required concentration. The pounded date fruit or pits were added (1:3) to either ethanol or distilled water. Extraction was carried out at $4\,^{\circ}C$ with continuous stirring. The ethanol extracts were then concentrated to dryness and the residue dissolved in distilled water to the appropriate doses just prior to use.

Dialysis to remove sugars was performed using cellulose tubing (Spectra/Por, width 32 mm, diameter 20.4 mm, volume/length 303 ml, from Spectrum Medical Instruments, Inc., USA).

2.4. Experimental design

Rats were randomly assigned to the following experimental groups:

Group 1: given distilled water (4 ml/kg) orally for 14 consecutive days. On the last day rats were given normal saline (1 ml) 1 h before killing.
Group 2: given distilled water (4 ml/kg (orally for 14 consecutive days. On the last day rats were given 80% ethanol (1 ml) 1 h before killing.
Group 3: Rats were given the aqueous date fruit extract (4 ml/kg) for 14 consecutive days. On the last day rats were given 80% ethanol (1 ml) 1 h before killing.
Group 4: Rats were given the dialyzed aqueous date fruit extract (4 ml/kg) for 14 consecutive days. On the last day rats were given 80% ethanol (1 ml) 1 h before killing.
Group 5: Rats were given the ethanolic date fruit extract (4 ml/kg) for 14 consecutive days. On the last day rats were given 80% ethanol (1 ml) 1 h before killing.
Group 6: Rats were given the aqueous date pit extract (4 ml/kg) for 14 consecutive days. On the last day rats were given 80% ethanol (1 ml) 1 h before killing.
Group 7: Rats were given the dialyzed date pit extract (4 ml/kg) for 14 consecutive days. On the last day rats were given 80% ethanol (1 ml) 1 h before killing.
Group 8: Rats were given the ethanolic date pit extract (4 ml/kg) for 14 consecutive days.
Group 9: Rats were given a single oral dose of lansoprazole (30 mg/kg), and 8 h later was given 80% ethanol as above, 1 h before killing.

2.5. Ethanol-induced gastric lesion

Rats were deprived from food (but not water) on day 14 of the experiment. On the last day of experiment (day 15) rats were given 80% ethanol (1 ml) by gastric intubation 1 h before killing, except for rats in group 1 which was given normal saline (1 ml/rat), and group 9 (positive control) which consisted of six rats that were fasted for 24 h, administered orally with lansoprazole (Sigma, MO, USA) (30 mg/kg), and was given 80% ethanol as above, 8 h thereafter.

The animals were anesthetized with ether, and rapidly decapitated 1 h after ethanol treatment. Blood was collected in heparinized tubes and centrifuged at $900 \times g$ for 15 min at $5\,^{\circ}C$. The plasma obtained was stored at $-20\,^{\circ}C$ pending gastrin assay. The stomach of each animal was excised and opened along the greater curvature. After washing with