

Summary

“Pharmacological study of the possible interactions between pantoprazole and some natural products on experimentally-induced gastric ulcer in rats”

The present study investigated the possible protective effects of three natural products namely vinpocetine, marjoram oil and parsley oil in addition to pantoprazole, a reference standard antiulcerogenic agent, against experimentally-induced gastric ulcer. Gastric ulceration was induced by either pyloric ligation/indomethacin or ethanol.

Five main sets of experiments were carried out. The **first** set was a pilot study carried out to choose suitable doses of indomethacin as well as the test drugs using pyloric ligation/indomethacin model. Indomethacin was administered intraperitoneally in doses of 10, 20, 30 and 40 mg/kg immediately after pyloric ligation to 48 h fasted rats. Test drugs were orally administered one hour before pyloric ligation. The dose levels of both pantoprazole and vinpocetine were 5, 10, 20 and 40 mg/kg, while that of marjoram oil and parsley oil were 25, 50, 75 and 100 mg/kg.

The ulcerogenic effect of indomethacin and the antiulcerogenic potentials of test drugs were evaluated based on number of ulcers and ulcer index. Depending on the obtained results, the selected doses of indomethacin, pantoprazole, vinpocetine, marjoram oil and parsley oil were 30 mg/kg, 20 mg/kg, 20 mg/kg, 75 mg/kg and 75 mg/kg, respectively.

The **second** set of experiments aimed at investigating the possible acute protective effect of the selected single dose of pantoprazole, vinpocetine, marjoram oil or parsley oil on pyloric ligation/indomethacin-induced gastric ulcer.

The **third** set of experiments aimed at studying the possible subchronic antiulcerogenic potential of one week daily treatment with pantoprazole, vinpocetine, marjoram oil or parsley oil on pyloric ligation/indomethacin-induced gastric ulcer.

The **fourth** set of experiments was carried out to evaluate the possible subchronic antiulcerogenic potential of one week daily treatment with pantoprazole (10 mg/kg) in combination with vinpocetine (20 mg/kg), marjoram oil (75 mg/kg) or parsley oil (75 mg/kg) on pyloric ligation/indomethacin-induced gastric ulcer.

The **fifth** set of experiments aimed at investigating the possible acute protective effect of the selected single dose of pantoprazole, vinpocetine, marjoram oil or parsley oil on ethanol-induced ulceration. In this model, test drugs were administered orally one hour before administration of ethanol (70%, p.o.).

The antiulcerogenic potentials of test drugs were evaluated based on number of ulcers, ulcer index, gastric juice volume and titratable acidity. The effects on oxidative stress biomarkers namely malondialdehyde (MDA), glutathione (GSH) and nitric oxide (NO) contents in gastric mucosa were evaluated in addition to superoxide dismutase (SOD) activity in blood. Gastric mucosal contents of histamine and mucus were also estimated.

The findings of the present study can be summarized as follows:-

A) Pyloric ligation/indomethacin model:-

I. Acute treatment:-

All test drugs protected against pyloric ligation/indomethacin-induced gastric ulcer as evidenced by significant reduction in ulcer number, ulcer index and MDA content as well as increased SOD activity in blood. In addition, all test drugs with the exception of parsley reduced gastric acidity and increased gastric mucosal NO content.

II. One week daily treatment:-

Daily administration of the test drugs for 7 days significantly reduced ulcer number, ulcer index, gastric juice volume, titratable acidity and MDA content. All test drugs significantly increased GSH, NO, SOD and mucus except in case of parsley where mucus content was not changed. Furthermore, vinpocetine and marjoram oil decreased gastric mucosal histamine content.

III. Treatment with combination of pantoprazole (10 mg/kg) and individual test drugs daily for one week:-

These combinations showed significant reduction in ulcer number, ulcer index, gastric juice volume, titratable acidity and MDA content as well as increase in gastric mucosal GSH and NO contents. Moreover, the combinations increased the action of pantoprazole.

B) Ethanol model:-

All test drugs protected against ethanol-induced gastric ulcer as evidenced by significant reduction in ulcer number and ulcer index as well as increased superoxide dismutase activity in blood. Marjoram oil only reduced MDA content. Vinpocetine, marjoram oil and parsley oil increased gastric mucosal GSH content. Pantoprazole only increased gastric mucosal NO content.