

Thistles from Sardinia: evaluation of the anti-inflammatory activity of different species in a cell model of gastric inflammation

1)M. Fumagalli 2)A. Marengo 3)E. Sangiovanni 4)C. Sanna 5)S. Piazza 6)A. Maxia 7)P. Rubiolo 8)M. Dell'Agli

University of Milan

Gastritis is an inflammatory disease involving millions of people in the world; about 90% of cases of gastritis are caused by the presence of the bacterium *Helicobacter pylori* (*H. pylori*) while only 10% is due to other risk factors including autoimmune reactions, drugs and alcohol. During *H. pylori* infection, gastric epithelial cells release high levels of IL-8, a chemokine that plays a key role in inflammation by promoting the recruitment of immune cells (for example macrophages and neutrophils) at the site of inflammation (Shimada et al., 1998). IL-8 expression is regulated, at transcriptional level, by different transcription factors, including NF- κ B; this nuclear factor is strictly involved in the expression of several inflammatory genes during gastric inflammatory process (Yasumoto et al., 1992).

Thistles species belong to the Asteraceae family. They are widely distributed in the Mediterranean area and are mostly used in Sardinia for both nutritional and therapeutic purposes. The well-known edible plant *Silybum marianum* (L.) Gaertn., is traditionally used to prevent or treat gastrointestinal or liver diseases. However, no studies regarding the anti-inflammatory activity, at the gastric level, of other thistles species, have been reported so far.

The aim of the present study was to compare the anti-inflammatory activity of eight wild edible thistles species from Sardinia in an in vitro model of gastric inflammation.

Eight thistles species belonging to different genus (4 to the *Carduus* genus, 2 to the *Onopordum* genus, 1 to the *Ptilostemon* genus and 1 to the *Silybum* genus) were collected in different areas of Sardinia region. The extracts were prepared from eight thistles species using a mixture methanol/water 70:30. TNF α -induced IL-8 release and NF- κ B nuclear translocation were assayed by ELISA assays. NF- κ B driven transcription and IL-8 promoter activity were assayed transfecting cells with reporter plasmids containing luciferase gene.

Among the selected thistle hydroalcoholic extracts, only those belonging to the *Onopordum* genus (*Onopordum horridum* Viv. and *Onopordum illyricum* L.) were able to reduce the IL-8 release in a concentration-dependent manner (IC₅₀ 4.31 μ g/mL and 12.3 μ g/mL, respectively). *Onopordum* extracts were also able to inhibit IL-8 promoter activity, with an IC₅₀ of 17.1 μ g/mL and 14.8 μ g/mL respectively. The effect observed was due, at least in part, to the inhibition of NF- κ B pathway, particularly the NF- κ B driven transcription (IC₅₀ 6.2 μ g/mL for *Onopordum horridum* and 7.31 μ g/mL for *Onopordum illyricum*) and nuclear translocation (IC₅₀ 18.21 μ g/mL for *Onopordum horridum* and 10.04 μ g/mL for *Onopordum illyricum*). The phytochemical investigation of the two extracts revealed that the most abundant compounds contained in both thistle extracts were chlorogenic acid, 1,5 dicaffeoylquinic acid, and 3,5 dicaffeoylquinic acid. Only 3,5 dicaffeoylquinic acid reduced TNF α -induced IL-8 secretion in a statistically significant way, with an IC₅₀ of 0.65 μ M.

Taken together, our results support the traditional use of *Onopordum* species for food and medicinal purposes, and make these edible plants exploitable as preventive or co-adjuvant agents in gastric diseases. Since caffeoylquinic acid derivatives are commonly present in botanical supplements on the market, these extracts could be considered as new sources of compounds active against gastric inflammation.

Shimada T. et al. (1998). *Journal of gastroenterology*. 33, 613-61.

Yasumoto K. et al. (1992). *The Journal of biological chemistry*. 267, 22506-22511.