Cyclolepis genistoides aqueous extract as source of neuroprotective agents

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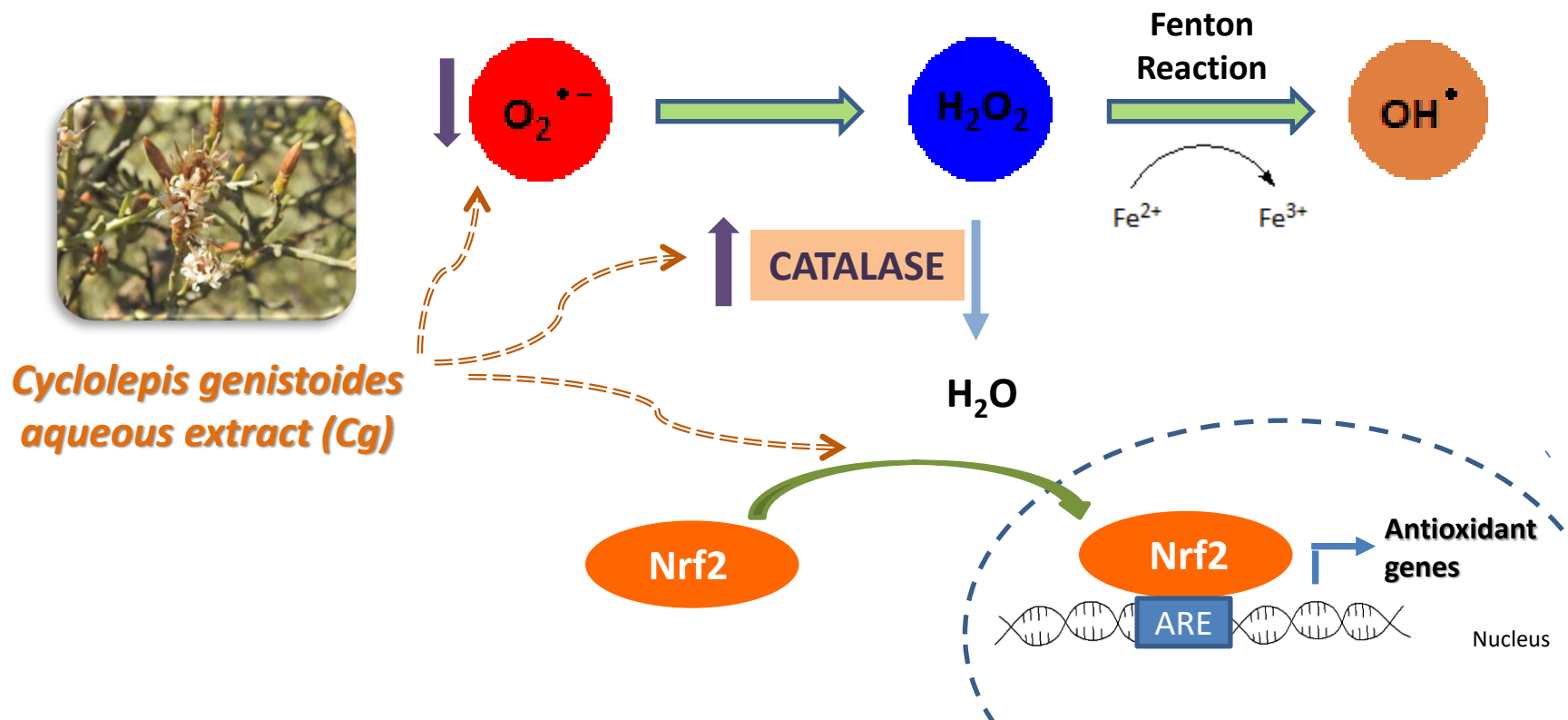
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Cyclolepis genistoides aqueous extract as source of neuroprotective agents

Graphical Abstract

Abstract

Since oxidative stress (OS) is a main component in neurodegenerative diseases, targeting this causative agent constitutes an important approach in drug discovery. In previous studies, we have selected the aqueous extract of *Cyclolepis genistoides* from a set of medicinal plants based on its ability to diminish metal-induced OS cellular markers. The aim of this work was to characterize the mechanism by which *C. genistoides* extract protected cells against OS. For this purpose, human neuroblastoma cells (IMR-32) were exposed to *C. genistoides* extract under conditions favoring OS (ferric ammonium citrate -FAC- exposure). *C. genistoides* extract (20 µg/mL) diminished the generation of superoxide anion in the presence of FAC. Moreover, the extract increased catalase activity when cells were exposed to FAC. Additionally, *C. genistoides* extract triggered the nuclear translocation of Nrf2, a cytoprotective transcription factor involved in antioxidant enzyme expression. The determination of flavonoids in *C. genistoides* extract revealed 16.1 ± 0.1 mg quercetin equivalents/g. To identify the bioactive components, 9 fractions (A-I) were obtained after a bio-guided fractionation. The evaluation of the main fractions F, G and H (20 µg/mL) showed that fractions F and H exposure reduced reactive oxygen species (ROS) production induced by FAC; however, fraction G treatment increased ROS levels. Until now, a sesquiterpene lactone was identified in fraction F. Our findings suggest that *C. genistoides* extract exerts the protective effect via the activation of cellular antioxidant defenses. Further studies are necessary to identify which compounds are responsible for the neuroprotective effect through Nrf2 modulation.

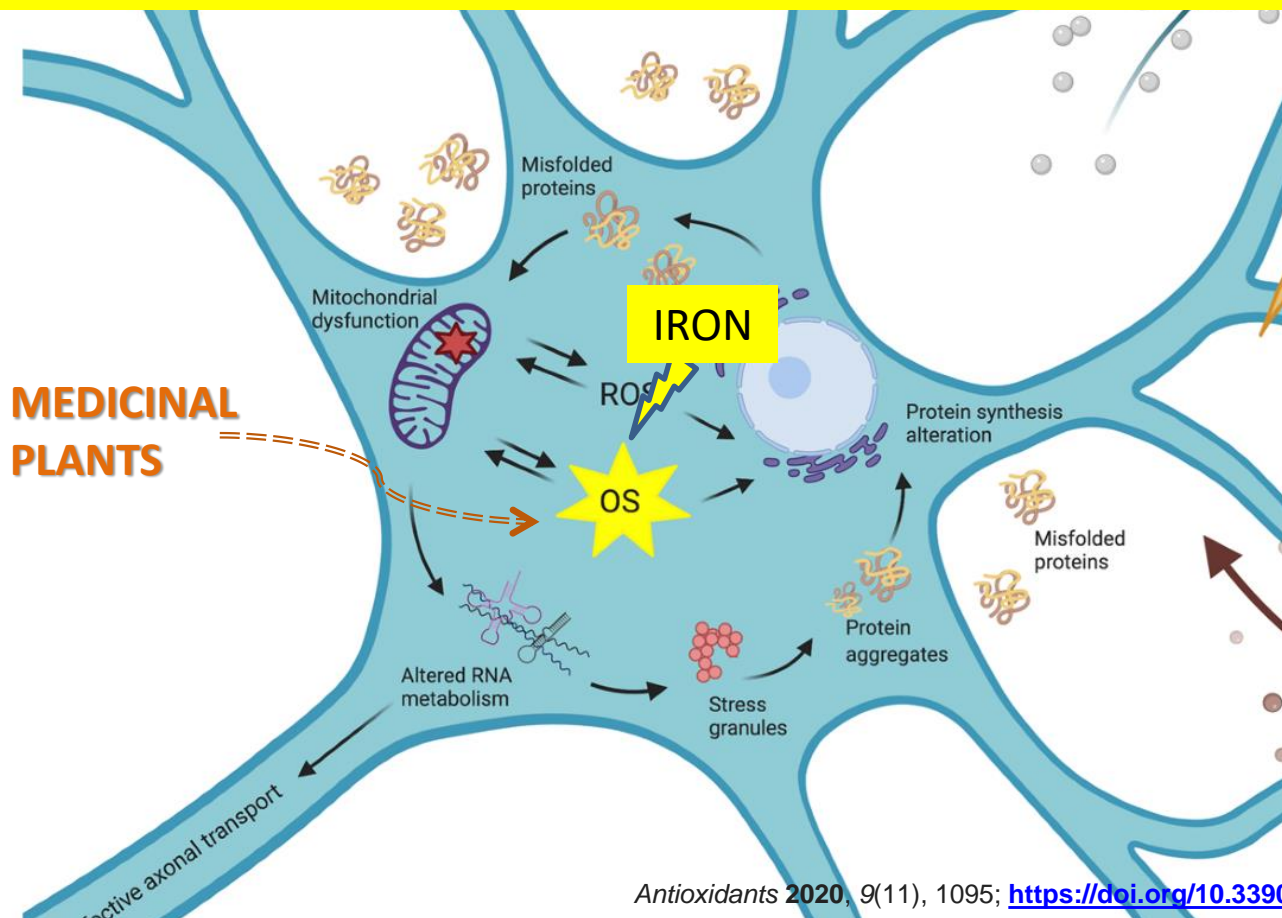**Keywords:** *Cyclolepis genistoides*; cellular oxidative stress, neuroprotective agents

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Introduction

OXIDATIVE STRESS (OS): imbalance between the production of oxidants and antioxidant defenses that may lead to damage of biological systems.
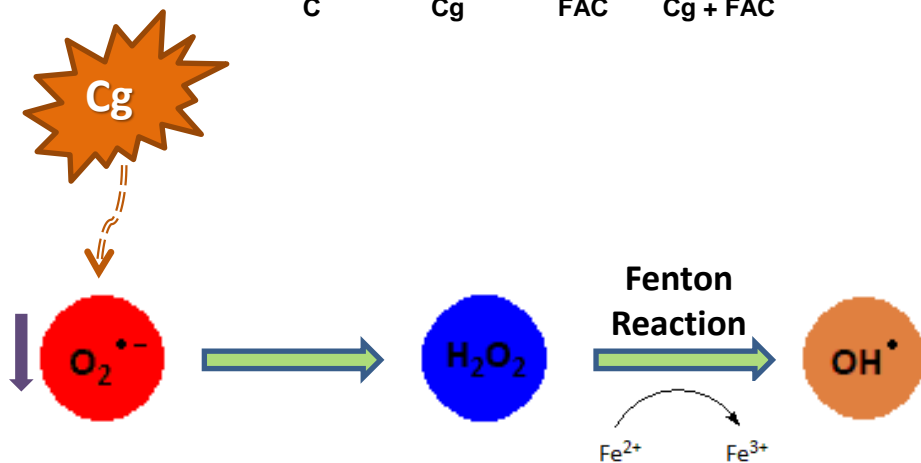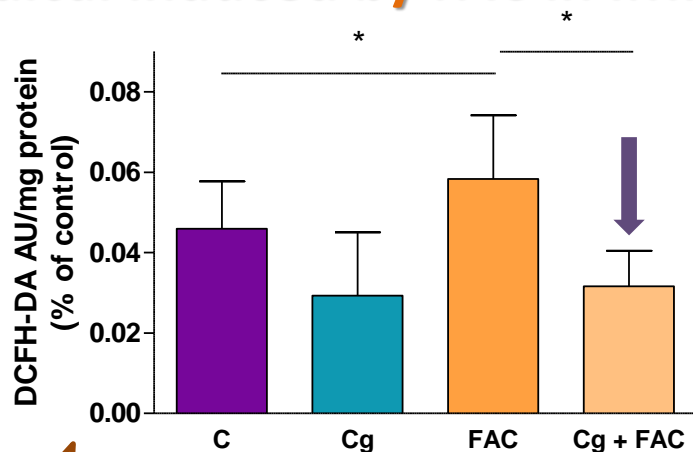

MEDICINAL PLANTS

IRON

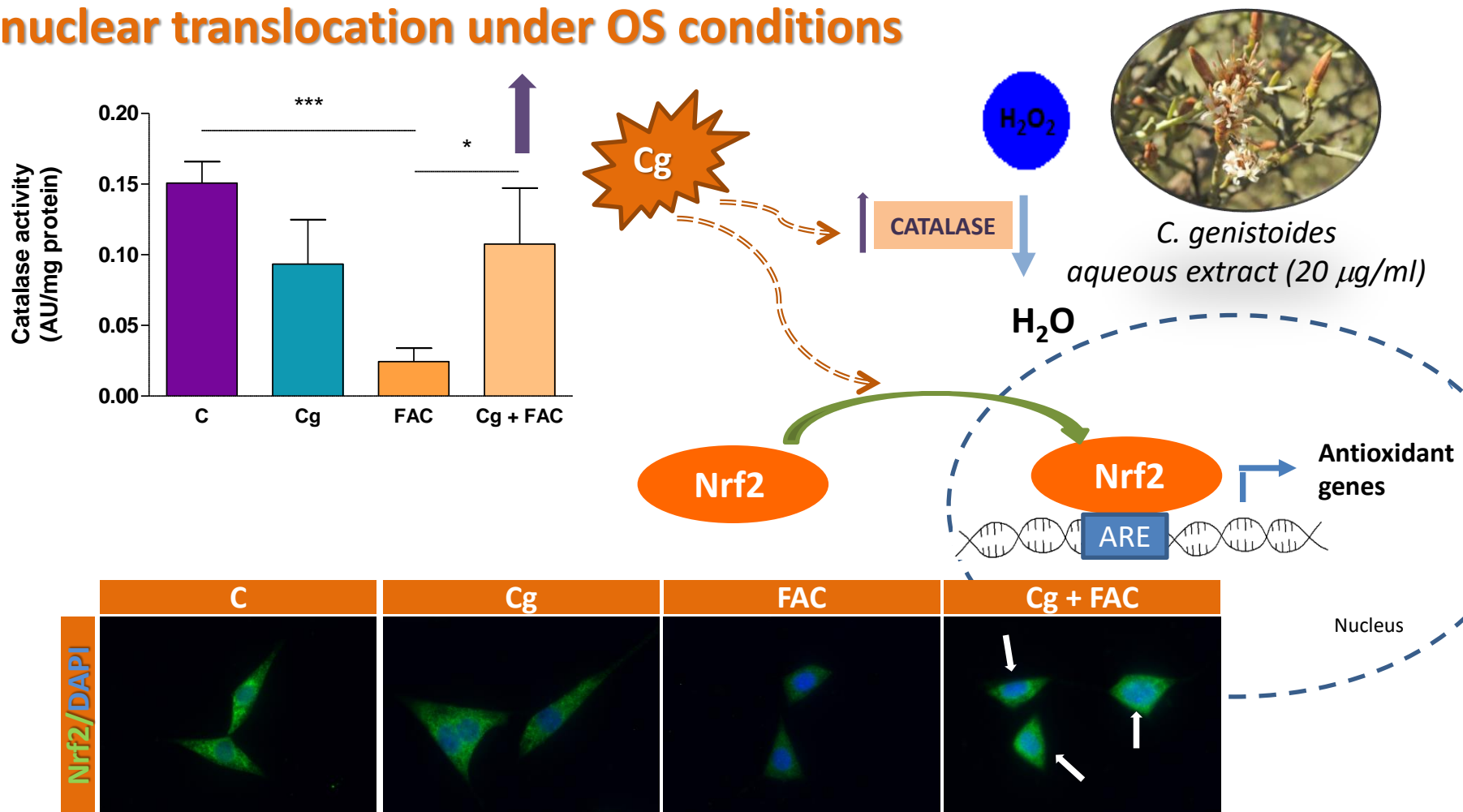*Antioxidants* **2020**, *9*(11), 1095; **https://doi.org/10.3390/antiox9111095**

C. genistoides reduces the production of superoxide anion radical induced by FAC in IMR-32 cells

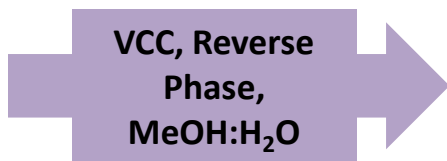*C. genistoides* aqueous extract (20 $\mu g/ml$)
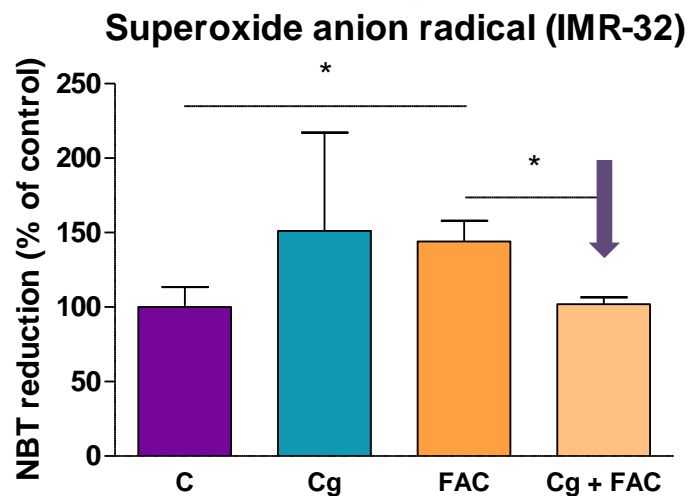
C. genistoides promotes the activation of catalase and Nrf2 nuclear translocation under OS conditions

Catalase activity (AU/mg protein)

0.20 · 0.15 · 0.10 · 0.05 · 0.00

C · Cg · FAC · Cg + FAC

*** · *

Cg

H_2O_2

CATALASE

H_2O

C. genistoides aqueous extract (20 μg/ml)

Nrf2

Nrf2

ARE

Antioxidant genes
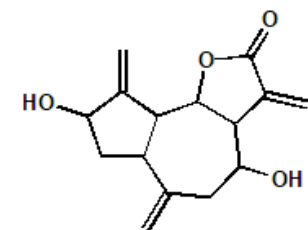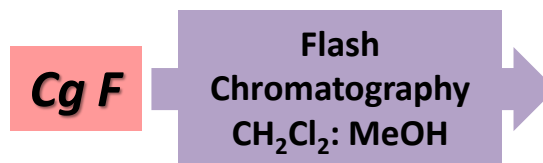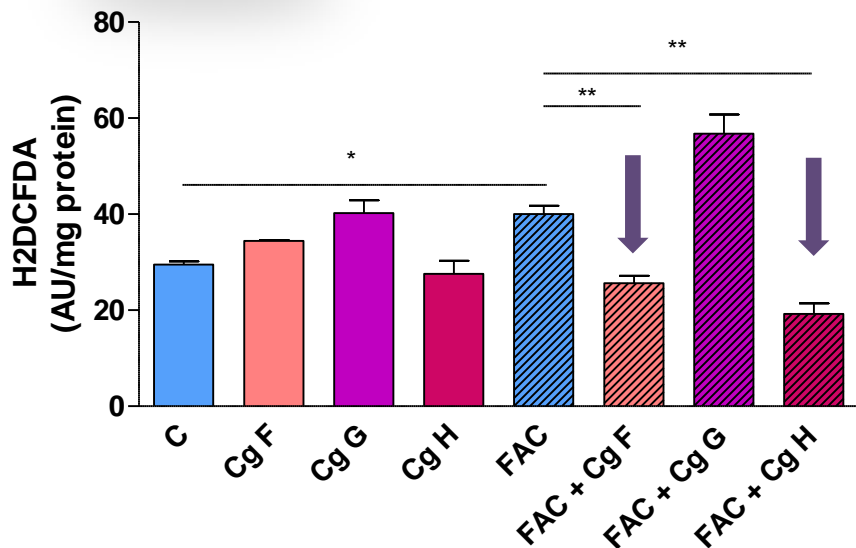
Nucleus

Nrf2/DAPI

| C | Cg | FAC | Cg + FAC |

Bioguided fractionation of *C. genistoides* aqueous extract

C. genistoides

VCC, Reverse Phase, MeOH:H$_2$O

9 fractions (A-I)

MTT Reduction (% of control)

20 µg/ml
10 µg/ml
5 µg/ml

C. genistoides fractions

H2DCFDA (AU/mg protein)

Cg F

Flash Chromatography CH$_2$Cl$_2$: MeOH
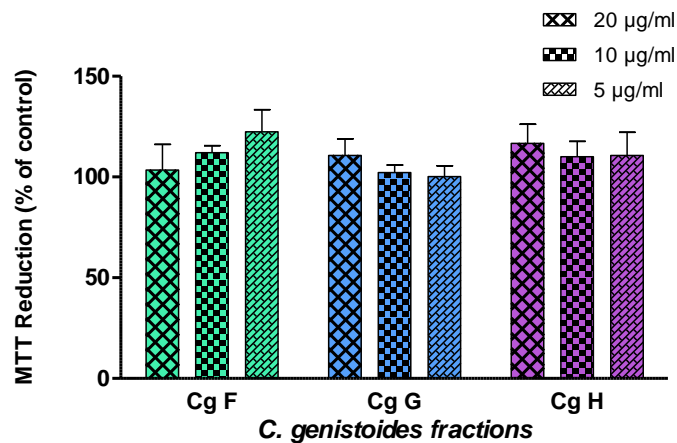
deacylcynaropicrin

Conclusions

C. genistoides

C. genistoides aqueous extract protects cells against OS via the modulation of cellular antioxidant defenses: activation of catalase and Nrf2 nuclear translocation.

C. genistoides is a source of natural products that can target Nrf2 as OS modulator.

Further studies are necessary to identify the active principles responsible for the protective effect of *C. genistoides*.

Acknowledgments