Chalcones *versus* 2-styrylchromones: which are the best oxygen and nitrogen reactive species scavengers?

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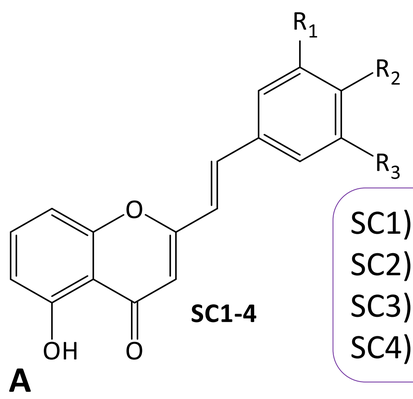
Introduction

During the inflammatory process a state of oxidative stress can arise, characterized by an imbalance between the production of prooxidant reactive species [*e.g.* hydrogen peroxide (H_2O_2), superoxide anion radical ($O_2^{\bullet -}$) and nitric oxide radical ($^{\bullet}NO$)], by inflammatory cells, and an incapacity of the body's antioxidant defence systems to counteract these reactive species' products. This condition often results in increased tissue damage and development of chronic diseases (*e.g.* rheumatoid arthritis and atherosclerosis) [1]. 2-Styrylchromones (2-SC) and chalcones are two classes of naturally occurring chromones, showing several biological activities (*e.g.* antiviral and anti-inflammatory) with potential therapeutic application, and with interesting scaffolds for drug design [2,3]. However, as far as we know, their antioxidant potential has never been compared using the same *in vitro* methodologies.

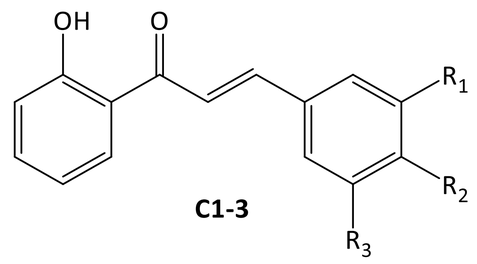
Aim

The aim of this study was to evaluate the potential antioxidant activity of seven structurally related hydroxylated 2-SC (**Fig. 1A**) and chalcones (**Fig. 1B**) through the scavenging of physiological relevant reactive oxygen (H_2O_2 and $O_2^{\bullet -}$) and nitrogen ($^{\bullet}NO$) species, using non-cellular *in vitro* systems, and to establish a structure-activity relationship.



A

SC1) R_1 = H; R_2, R_3 = OH
SC2) R_1, R_3 = H; R_2 = OH
SC3) R_1, R_2 = H; R_3 = OH
SC4) R_1, R_2, R_3 = OH



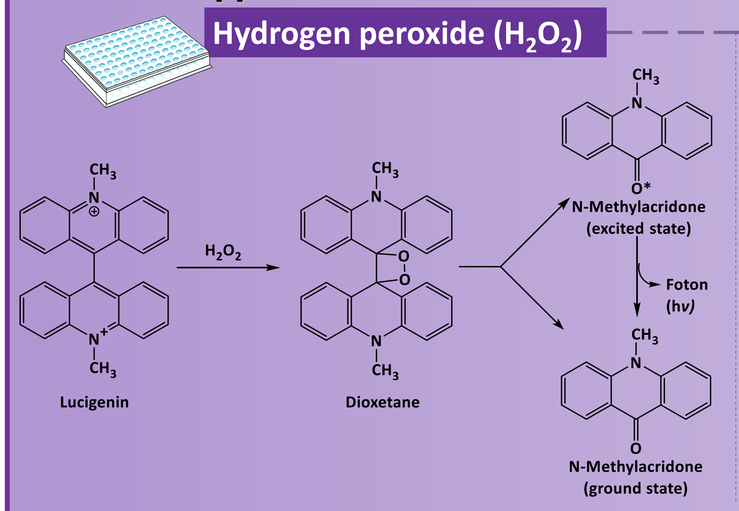
B

C1) R_1, R_3 = H;R_2 = OH
C2) R_1, R_2 = H; R_3 = OH
C3) R_1, R_2, R_3 = OH

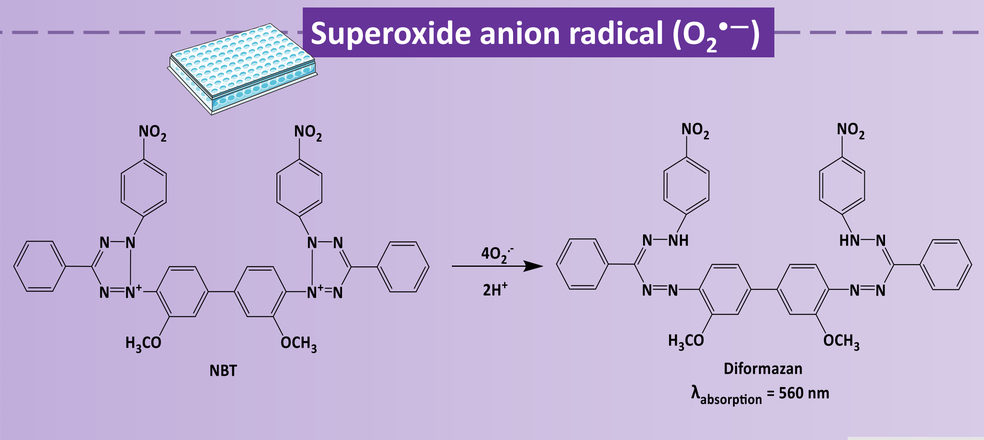
Fig. 1 Chemical structures of the studied 2-SC (**A**) and chalcones (**B**).

Methods [4]

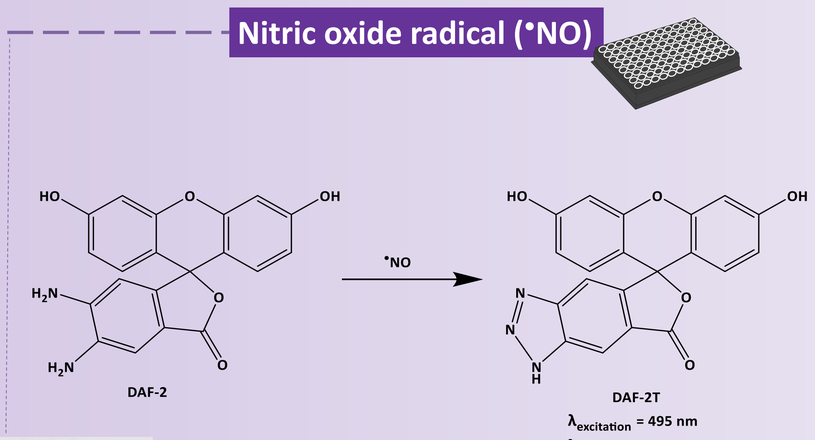
Hydrogen peroxide (H_2O_2)



Superoxide anion radical ($O_2^{\bullet -}$)



Nitric oxide radical ($^{\bullet}NO$)



Non-celular *in vitro* microanalysis using chemiluminometric, colorimetric and fluorimetric detection methodologies.

NBT - Nitro blue tetrazolium
DAF-2 - 4,5-Diaminofluorescein
DAF-2T – DAF-2's oxidation product

Results

Hydrogen peroxide (H_2O_2)

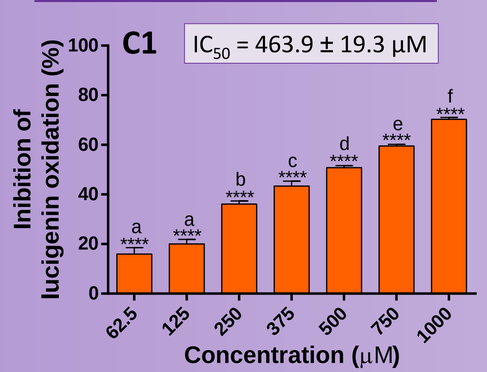


Fig. 2 Inhibition of H_2O_2 - induced lucigenin oxidation by **C1** (62.5 – 1000 µM), the most active compound found.

Superoxide anion radical ($O_2^{\bullet -}$)

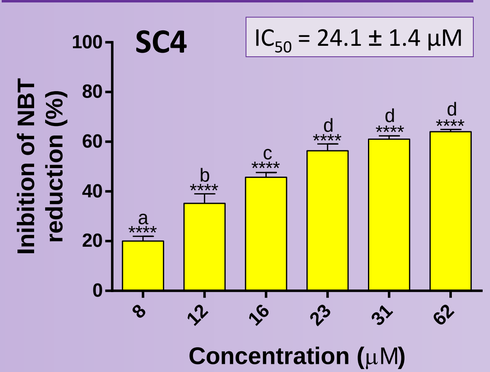


Fig. 3 Inhibition of $O_2^{\bullet -}$- induced NBT reduction by **SC4** (8 – 62 µM), the most active compound found.

Nitric oxide radical ($^{\bullet}NO$)

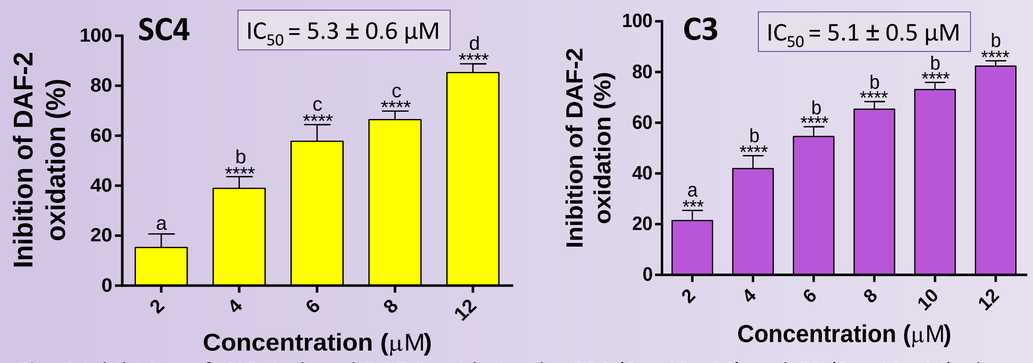


Fig. 4 Inhibition of $^{\bullet}NO$- induced DAF-2 oxidation by **SC4** (2 – 12 µM) and **C3** (2 – 12 µM), the most active compounds found.

Results are expressed as the mean ± standard error of the mean (SEM). ****$p \leq 0.0001$, compared with the control (without prooxidant reactive species).
Letters above the bars indicate either statistically similar data, if letters are the same ($p > 0.05$), or statistically different data, if letters are diferent ($p > 0.05$).

Conclusions

► The 2-SC **SC4** was the only one able to scavenge more than one reactive specie, $O_2^{\bullet -}$ and $^{\bullet}NO$

► The chalcone **C1** demonstrated some selectivity as it scavenged H_2O_2, but not $O_2^{\bullet -}$ or $^{\bullet}NO$

► The presence of hydroxy groups on the B-ring seems to contribute to this activity, in both 2-SC and chalcones scaffolds, namely at C3', C4' and C5'

► Overall, chalcones seemed to be slightly more active than 2-SC

References

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