In vitro cytotoxicity of 7,3',4'-trihydroxyflavones in lung fibroblasts

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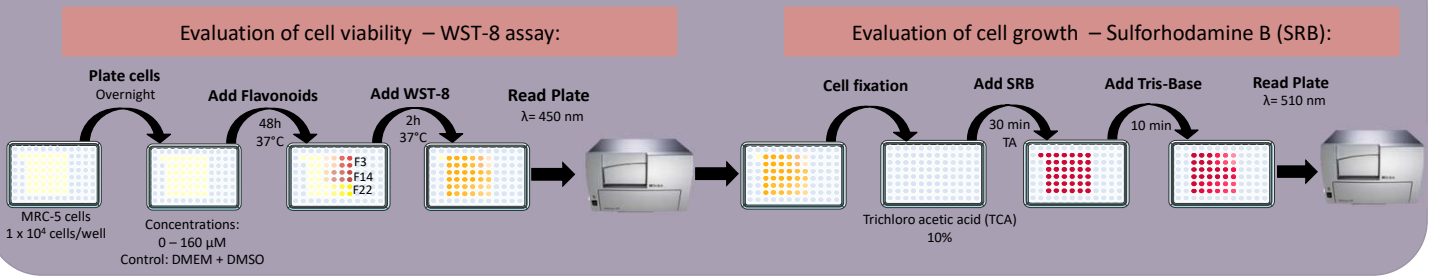
Introduction

Cancer is the second leading cause of death worldwide[1]. Nowadays, the current therapeutic approaches include surgery and a combination of chemotherapy with radiotherapy[1]. These strategies are associated with adverse side effects and may become less efficient over time. Thus, the research to find new more effective and safer anticancer agents may have huge societal impact. In this scope, flavonoids, a class of natural products with medicinal benefits, are being widely explored as they enclose a wide range of biological activities such as anti-inflammatory, anticancer and antioxidant[3,4,5]. The majority of the *in vitro* studies report the cytotoxic effects of flavonoids in cancer cell lines[4]. However, their corresponding effects in healthy cell lines are to unveil.

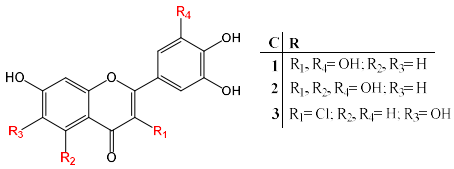
Aim

The present work aims to evaluate the cytotoxic effects of flavonoids hydroxylated at positions C-7, C- 3' and C-4', in human lung fibroblasts, following the assessment of cell viability and growth.

Methods



Results



C	R
1	R_1, R_4= OH; R_2, R_3= H
2	R_1, R_2, R_4= OH; R_3= H
3	R_1= Cl; R_2, R_4= H; R_3= OH

Figure 1. Chemical structure of the flavonoids used in the cytotoxicity assays.

Table 1. Half maximal inhibitory concentration (IC_{50}) values of C1, C2 and C3. Cells were exposed to the mentioned flavonoids for 48 h and IC50 values were determined following WST-8 and SRB assays.

	IC_{50} (µmol/L) ± SEM[1]	
Compounds tested	WST-8 assay	SRB assay
C1	65 ± 7	57 ± 6
C2	71 ± 26	66 ± 24
C3	82 ± 12	59 ± 18

[1]SEM- Standard Error of Mean

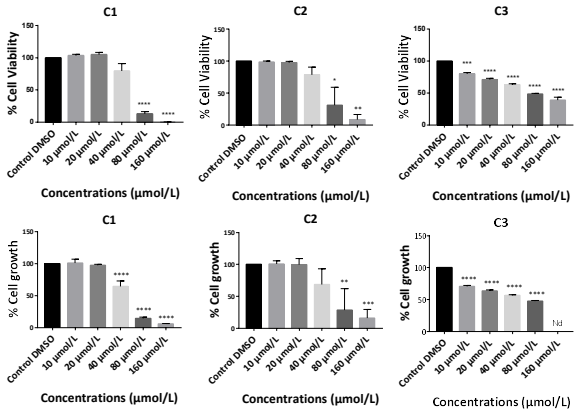


Figure 2. Cytotoxic effects of flavonoids (C1, C2 and C3) in MRC-5 cells. Cells were analyzed for cytotoxicity by WST-8 (cell viability panels) and SRB (cell growth panels) assay. The data are mean ± SEM (n ≥ 3). Nd- not determined. Significant differences (asterisks) are shown relative to 0.1% DMSO control; * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$, and **** $p < 0.0001$ (one-way ANOVA).

Conclusions

- Structurally similar compounds C1 and C2, presented no cytotoxic effects at 10 and 20 µmol/L, while C3 presented cytotoxic effects from 10 µmol/L. Moreover, compared to incubation with C1 compound, incubation with C2 compound, hydroxylated at C-5, was less cytotoxic at higher doses.
- Despite the differences in cytotoxicity profiles, the IC_{50} values determined were similar between compounds.
- The low toxicity compounds identified can serve as basis for the design of novel and safer anticancer agents.

Acknowledgments

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