Synthesis of Chalcones and prenylated Flavanone with antioxidant and antiproliferative activity

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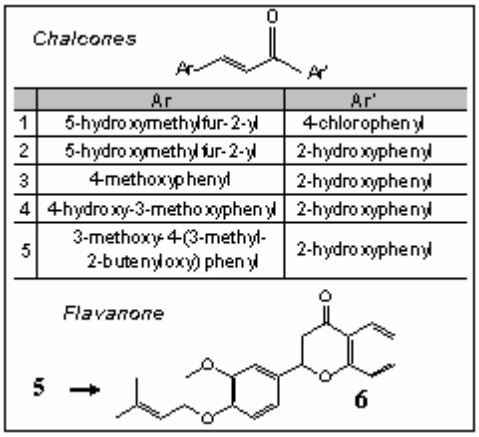
Introduction

Chalcone-based natural products are widely explored because of their array of biological activities[1-2]. Here, we discuss the antitumoral and antioxidative activities shown by some unexplored chalcones and by a prenylated flavanone.

Results and Discussion

We have prepared a number of chalcones (**1-5**) by base-catalysed Claisen-Schmidt condensation conditions of appropriate substituted acetophenones and aryl aldehydes. Flavanone (**6**) was obtained from isomerization of 2´-hydroxychalcones in presence of NaAc and EtOH under reflux of 8 hours.



	Ar	Ar'
1	5-hydroxymethylfur-2-yl	4-chlorophenyl
2	5-hydroxymethylfur-2-yl	2-hydroxyphenyl
3	4-methoxyphenyl	2-hydroxyphenyl
4	4-hydroxy-3-methoxyphenyl	2-hydroxyphenyl
5	3-methoxy-4-(3-methyl-2-butenyloxy) phenyl	2-hydroxyphenyl

Figure 1. Synthesized chalcones and flavanone.

Five compounds have been examined for their *in vitro* cytotoxic activity.

The furan derivatives **1** and **2** exhibited cytotoxic activity against all tested tumor cell lines. Compound **1** demonstrated expressive cytotoxic activity and selectivity against breast cancer cell line T47D. At the same concentration, it has not revealed activity against normal fibroblasts.

Compound **2** was also mainly active against T47D but presented lower activity when compared to compound **1**. Interesting, compound **3** exhibited ***proliferative*** properties.

Following these results, it was prepared a screening test of antiproliferative activity to compounds **1**, **2**, **4** and **6** using cell counting and MTT methods.

Table 1. Examples IC_{50} values in µg/ml of synthesized compounds.

Cell Line	Compounds			
	1	**2**	**4**	**6**
MIAPaCa2*	10	> 200	18	57
CRO2B**	50	> 200	12	6
SW620***	0.85	9.7	17	84
CaCo2***	17.5	> 200	12	18
WI38****	4.9	20	8.3	8.2

*pancreas; ** carcinoid; *** colonic; ****fibroblasts.

Compounds **1**, **4** and **7** were very active against almost all tested human tumor cell line. Compound **2** was less active than **1**, but more selective. Compounds **4** and **7** demonstrated significant activity against fibroblastic cell lines.

Compounds were also analyzed to their radical scavenging property using DPPH test. Compound **4** exhibited excellent radical scavenging activity (98% of effectiveness).

Conclusions

- All compounds were obtained through efficient and simple synthetic approach and were active against, at least one of the tested tumor cell lines and with IC_{50} values up to 87 µg/ml.
- Compound **1** exhibited the most promising profile as antitumoral agent.
- Compound **4** also exhibited a significant radical scavenging activity and can be explored as antioxidative agent.

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