CHALCONES AS POTENTIAL INHIBITORS OF PANCREATIC LIPASE

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INTRODUCTION

Obesity is a global disease that has been escalating to epidemic proportions over the past years. A recent report from World Obesity Federation predicts that, in 2030, 1 billion people will be obese[1]. Thus, it is mandatory to develop new therapeutic options that are able to manage and control obesity. One of the most promising research paths is the inhibition of pancreatic lipase (PL), responsible for the hydrolysis of 50 to 70% of total dietary triglycerides (Figure 1)[2].

Polyphenols are natural occurring and structurally diverse compounds with different biological activities, such as anti-inflammatory, antioxidant, antidiabetic, and anti-obesity activities[3]. Chalcones are the precursors of flavonoids, consisting of two benzene rings connected by a three-carbon α,β-unsaturated carbonyl structure, that have been explored as potential anti-obesity molecules[4].

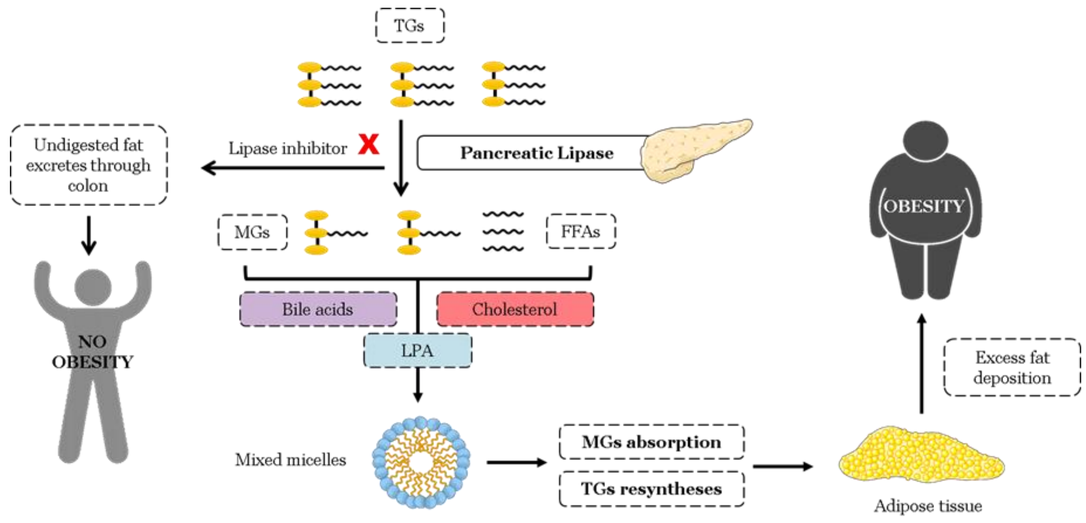
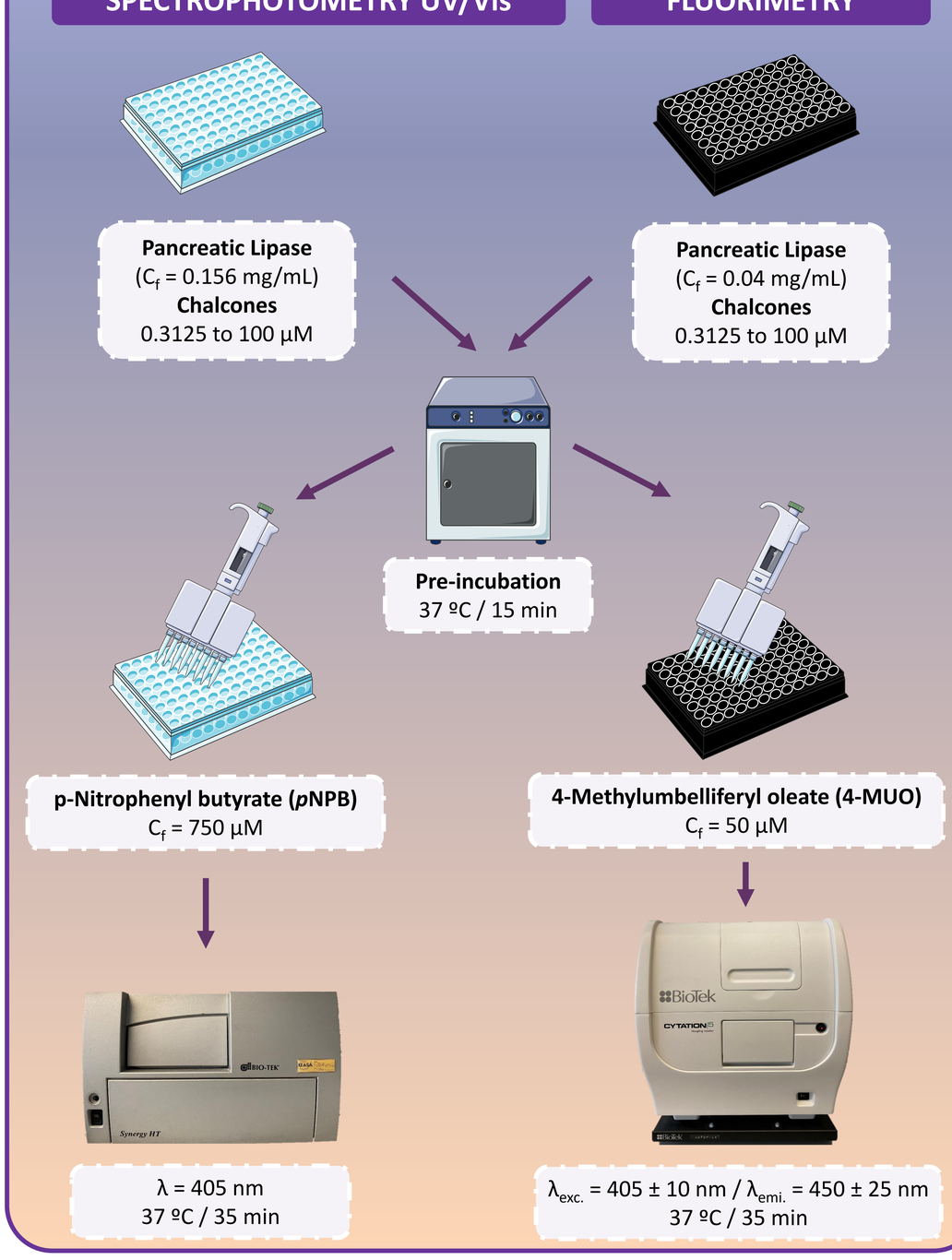


Figure 1. *Lipids absorption and PL activity inhibition consequences.*

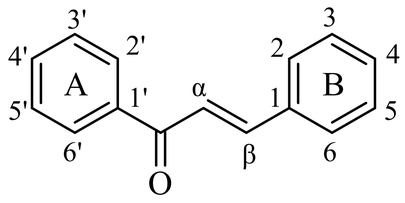
AIM

To evaluate the activity of seven chalcones with hydroxy (OH) and chloride (Cl) substituents (*Table 1*) as potential inhibitors of PL using spectrophotometric and fluorimetric microanalysis systems.

METHODS



RESULTS



						*p*NPB	4-MUO
	R_3	R_4	R_5	$R_{2'}$	$R_{4'}$	IC_{50} (µM) or PL inhibition (%)	
1	-	-	-	-	-	< 30% 100 µM	45 ± 7 % 50 µM
2	-	-	-	OH	-	< 30% 100 µM	**60 ± 6**
3	OH	OH	-	-	-	34 ± 5 % 100 µM	< 30% 25 µM
4	OH	OH	-	OH	OH	< 30% 100 µM	< 30% 6.25 µM
5	OH	OH	OH	OH	-	< 30% 50 µM	< 30% 12.5 µM
6	-	Cl	-	-	-	< 30% 100 µM	< 30% 50 µM
7	Cl	-	-	OH	-	**90 ± 5**	35 ± 2 % 25 µM

Table 1. *Inhibitory activity of the tested compounds against pancreatic lipase (IC50, µM ± SEM, or % inhibition at the maximum concentration tested).*

CONCLUSIONS

The obtained results PL inhibitory activity of chalcones are concentration-dependent manner.

Considering the spectrophotometry and fluorimetry methodologies used, our results proved that:

- ✓ both instrumental techniques are effective for the evaluation of PL catalytic activity and the inhibitory effects of isolated compounds;
- ✓ the fluorimetric assay was shown to be more sensitive than the spectrophotometric UV/Vis assay.

From the results obtained in the fluorimetric assay, the compound that demonstrated the highest inhibitory activity was compound **2**, that has an OH group at position 2' of ring A, with an IC_{50} = 60 ± 6 µM. It also appears that the OH groups in both rings A and B decrease the inhibitory capacity of chalcone to inhibit PL. The same conclusions cannot be taken with Cl substituents since we did not test enough compounds to make conclusions.

It was also observed that chalcones with OH groups have high interferences with fluorimetry, requiring further refinement of the performed assay.

These findings bring new insights into the structure design for the modulation of PL and, although some compounds show some potential for PL inhibition, further studies are still needed to further explore these compounds as potential anti-obesity molecules!

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