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Inhibition of pancreatic α-amylase activity by a group of hydroxyxanthones

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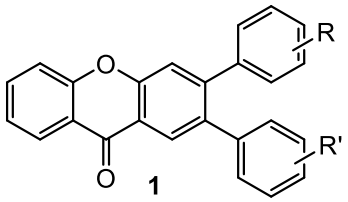
Diabetes *mellitus* is a non-infectious and non-transmissible life threatening disease. It is one of the fastest growing health challenges of the current century, in which the number of adults living with diabetes have more than tripled over the past 20 years. According to the International Diabetes Federation, 1 in 11 adults (20-79 years) have diabetes (463 million people) and 2 in 3 people with diabetes live in urban areas.[1] This may be closely related to genetic and lifestyle factors such as physical inactivity, unhealthy diets, obesity, raised blood cholesterol and glucose, stress, etc.[2]

Diabetes *mellitus* is an endocrine disorder that occurs when pancreas does not produce enough insulin, when the body cannot use insulin efficiently or both situations, leading to chronic hyperglycemia. Thus, the control of postprandial blood glucose level via the inhibition of digestive enzymes, such as α-glucosidase and/or α-amylase, is a relevant strategy for the management of type 2 diabetes and its complications.[3]

During the last two decades, in the pursuit for novel anti-diabetic drugs, a wide variety of natural and synthetic xanthone derivatives have been applied in the inhibition of α-glucosidase enzyme activity, however, the effects of this class of compounds on the activity of α-amylase enzyme is scarce.[4] With this ratio in mind and as part of our on-going project, the aim of the present study is to investigate the effect of a series of hydroxyxanthones **1** on pancreatic α-amylase activity to find out the relevance of this group of compounds in controlling blood glucose levels for the treatment of disorders related with the carbohydrate uptake.



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Different concentrations of xanthones **1** were incubated with the enzyme and the hydrolysis of the substrate 2-chloro-*p*-nitrophenyl-α-D-maltotriose was monitored spectrophotometrically at 405 nm. Acarbose was used as the standard inhibitor. In addition, the study of the inhibition type was carried out through nonlinear regression Michaelis-Menton enzymatic kinetics and the corresponding Lineweaver-Burk plot.[5]

The results pointed out that the IC_{50} values obtained ranged from 23 to 90 μM, considerably higher than the values obtained for the positive control acarbose (IC_{50} = 0.62 ± 0.07 μM). For the active compounds, two of them revealed a competitive type of inhibition while for the remaining ones a noncompetitive type of inhibition was recorded. More details concerning the structure-activity relationship will be presented and discussed in this communication.

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