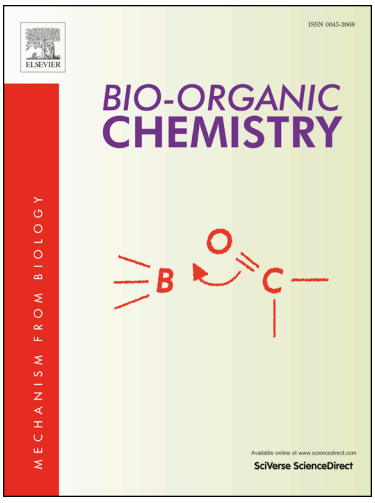

Synthesis, molecular docking and biological evaluation of Some Benzimidazole Derivatives as potent pancreatic lipase inhibitors

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Synthesis, molecular docking and biological evaluation of Some Benzimidazole Derivatives as potent pancreatic lipase inhibitors

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Abstract.

In this study, a new series of benzimidazole and bisbenzimidazole derivatives were prepared via the reaction of iminoester hydrochlorides and *o*-phenylenediamines and then screened for their lipase inhibition properties. Among the synthesized molecules, compounds **7a, 8a** and **8c** showed the best inhibitory effect against lipase enzyme with IC_{50} values of 1.72±0.12 µM, 1.92±0.28 and 0.98±0.07 µM, respectively. Moreover, molecular modeling studies were performed in order to understand to the inhibitory activity of the molecules. Binding poses of the studied compounds were determined at the target sites using induced fit docking (IFD) algorithms.

1. Introduction

Obesity is defined as an excessive fat accumulation in the body due to the result of high level of food intake and low energy consumption [1, 2]. Today, obesity is increasingly becoming a global health threat. Obesity is considered to be associated with many metabolic diseases, including cardiovascular disease, diabetes mellitus, atherosclerosis, hyperlipidaemia, high blood pressure and various cancers [3-5]. Anti-obesity drugs have various objectives, including reduction of food intake, alteration of metabolism and increase of thermogenesis [6]. Lipases are key enzymes for the hydrolysis of fat to glycerol during fat digestion and free fatty acids which can be used for energy production or stored in adipose tissues [7, 8]. Thus, if the human pancreatic lipases were inhibited, fat absorption would be controlled [9].

Drug discovery is a very time-consuming and expensive process. Approximately every 10.000 compounds which are evaluated in animal studies, 10 will make it to human clinical trials in order to