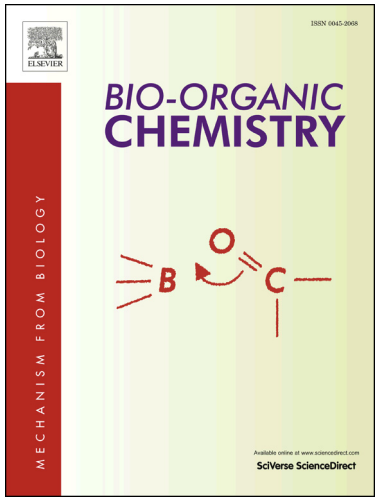

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Synthesis, Structure-Activity Relationships Studies of Benzoxazinone Derivatives as α-Chymotrypsin Inhibitors

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Abstract

A series of benzoxazinones **1**-**28** were synthesized *via* reaction of anthranilic acid with various substituted benzoyl chlorides in the presence of triethylamine in chloroform. Compounds **1**-**18** showed a good inhibition of α-chymotrypsin with IC_{50} ± SEM values between 6.5 to 341.1 μM. Preliminary structure-activity relationships studies indicated that the presence of substituents on benzene ring reduces the inhibitory potential of benzoxazinone. Also the increased inhibitory potential due to fluoro group at phenyl substituent was observed followed by chloro and bromo substituents. Compounds with strong electron donating or withdrawing groups on phenyl substituent, showed a good inhibitory potential at *ortho*>*meta*>*para* position. Kinetics studies showed diverse types of inhibition, except uncompetitive-type inhibition. The Ki values ranged between 4.7 to 341.2 μM. Interestingly, most of these compounds were non-cytotoxic to 3T3 cell line at 30 μM, except compounds **6**, **14** and **15**. Competitive inhibitors of chymotrypsin are like to inhibit other α-chymotrypsin-like serine proteases due to structural and functional similarities between them. The inhibitors identified during the current study deserve to be further studied for their therapeutic potential against abnormalities mediated by chymotrypsin or other serine protease.

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