The use of an adapted model allows contributing to the “Reduction” of mice used in experimental protocols: the case of the apoE-deficient (apo E\(^{-/-}\)) mice in a model of atherosclerosis control.

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Atherosclerosis is a chronic vascular disease whose development is influenced by several mediators \(^1\). Among them, the prostanoids large family lipids generated from the metabolism of arachidonic acid by the action of COX includes various types of PGs and thromboxane. Thromboxane A\(_2\) and PGI\(_2\) are present in abnormally elevated concentration in atherosclerosis \(^2\)-\(^3\). To exert its effects TXA\(_2\) and its precursor PGH\(_2\) act at a specific receptor termed TP receptor \(^4\). As a result, TXA\(_2\) synthase inhibitors and TP antagonists have been developed to reduce and to prevent TXA\(_2\) production and actions, respectively.

The present study was undertaken in order to investigate whether BM-573, an original sulfonylurea derivate synthesized in our lab \(^5\), and aspirin would be effective in preventing the progression of atherosclerosis in an apo E deficient mouse model.

Mice are highly resistant to atherosclerosis. The only exception in mice is the C57BL/6 strain fed with a very high content of cholesterol diet However the vascular lesion in these mice differ from the human in the histological nature and location \(^6\). So, in this study, apo E deficient mice model was chosen to test the efficacy of BM-573 and aspirin in atherogenesis because of its propensity to spontaneously and quickly develop sever atherosclerotic lesion very similar to those present in human, when fed with chow diet. The effect of 10 weeks of treatment with BM573 (2-2.5mg/kg/d) and aspirin (20-25mg/kg/d) on early aortic atherosclerotic lesions of apo E deficient mice was assessed. These mice presented spontaneous increase of total plasma cholesterol and triglycerides. In this experiment, while BM-573 and aspirin did not affect body weight, only BM-573 significantly decreases early atherogenesis lesions confirmed by macroscopic, microscopic and biochemical analysis. These results confirm that selective antagonism of TP receptor is more effective in reducing atherosclerotic lesion in
apo E deficient mice than COX-1 inhibition. Consequently, BM-573 could be a potential drug for prevention of atherosclerosis and this hypothesis will be tested in further investigation. This works emphases on the fact that severe selection of the mice strain chosen for the experiment allows producing reliable results with an adapted reduction in number of animals used.