Repurposing piroxicam for antithrombotic and cardiopulmonary protection: Pharmacological rationale and therapeutic potential

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Abstract:

BACKGROUND: Recent research indicates that non-steroidal anti-inflammatory drugs may interfere in coagulation process and platelet aggregation. However, the potential of piroxicam in thrombotic and cardiopulmonary disorders remained unexplored.

OBJECTIVES: To bridge this knowledge gap, the current study was conducted to assess the potential of piroxicam as antithrombotic and cardiopulmonary protective agent using multi-level approaches.

MATERIALS AND METHODS: Piroxicam was docked against 16 key proteins involved in thrombotic and cardiopulmonary conditions. Its antiplatelet effect was evaluated by arachidonic acid (AA) and adenosine diphosphate (ADP)-induced aggregation while its effect on coagulation parameters were also evaluated. Cardiopulmonary protective effect in rats was investigated through isoproterenol induced myocardial infarction (MI) and self-embolus induced pulmonary embolism (PE).

RESULTS: Strong binding interactions were identified, with docking energies of ≥-9.0 kcal/mol noted for cyclooxygenase (COX) 1, glycopotein-IIb/IIIa, antithrombin-III, COX-2, and nuclear factor Kappa-B (NFkB). Piroxicam significantly inhibited AA and ADP-induced platelet aggregation (IC50: 0.68 and 24.9 μM) and also prolonged the prothrombin, activated partial thromboplastin, thrombin, and clot lysis time. Piroxicam markedly and in a dose-related manner lowered MI and PE associated serum markers in experimental rats. Piroxicam further safeguarded cardiac and pulmonary tissues from infarction and histopathological injury through the suppression of oxidative imbalance and inflammatory activity. This protective outcome was also due to reduced expression of tissue necrosis factor-α, NFkB, COX-2, NLRP3, and platelet-derived growth factor-β, verified using immunohistochemistry, enzyme-linked immunosorbent assay, and real-time polymerase chain reaction RT-PCR techniques.

CONCLUSIONS: These results indicate the prophylactic potential of piroxicam in cardiopulmonary thrombotic disorders.

Keywords:

Antiplatelet, coagulation, myocardial infarction, piroxicam, pulmonary embolism