Abstract

Propranolol (PRN) undergoes extensive first-pass metabolism by the liver resulting in a relatively low bioavailability (BA). Thus, multiple doses are required to achieve therapeutic effect, which causes increased side effects. Glucosamine (GlcN) is an amino monosaccharide that is used to treat osteoarthritis (OA) and rheumatoid arthritis (RA) in elderly patients due to its ability to maintain connective and cartilage tissues strength and flexibility. Therefore, this research aimed to study the effect of GlcN on PRN BA, as a possible event of drug-drug interaction that may occur in patients especially elderly patients receiving both drugs. As a result, this could help to recommend whether PRN dose adjustment should be necessary with GlcN administration. Initially, in order to investigate such drug interaction a validated HPLC method of PRN in rat serum and Krebs buffer was developed and validated. Later, *in vivo* experiments were carried out to determine the effect of GlcN on PRN. PRN area under curve (AUC) and maximum concentration (C_{max}) were significantly decreased by 43% ($p<0.01$) and 34% ($p<0.05$), respectively for the highest GlcN dose 200 mg/kg. On the other hand, 100 mg/kg of GlcN did not change PRN AUC and C_{max} ($p>0.05$). Additionally, 200 mg/kg of GlcN decreased intestinal permeability (P_{eff}) and increased PRN clearance by 50%. Rifampin is an enzyme inducer which potently induces many CYP450, whereas cimetidine is an enzyme inhibitor that effectively reduces the metabolism of concomitant drugs. Therefore, it is used as a control in many of literature studies documenting its role in drug interactions. The results showed that rifampin, at 9 mg/kg did not change PRN AUC and C_{max} ($p>0.05$), whereas 5 mg/kg of cimetidine increased PRN C_{max} significantly by 86% ($p<0.01$) and AUC by 20% ($p>0.05$). However, in