Abstract

Lenvatinib is a multi-targeted kinase inhibitor capable of inhibiting these kinases at nanomolar concentrations. For this reason, it is used as a drug in the treatment of various types of cancer. Like many other xenobiotics, lenvatinib is metabolized by cytochromes P450, which can cause occurrence of drug interactions with other substances. Identification of the most important and clinically relevant drug interactions is essential to ensure the safety of patients already suffering from reduced quality of life due to cancer.

The main aim of this bachelor thesis was to investigate the effect of lenvatinib on cytochromes P450, specifically on isoforms of subfamily 2C in humans and rats. The inhibitory effect was measured *in vitro* using marker rections on rat liver microsome samples for the CYP2C6 isoform and on human recombinant CYP2C9 isoform samples expressed in Superosomes™ or Bactosomes®. Furthermore, the effect of lenvatinib on CYP2C11 and 2C6 expression in the liver of rats exposed to lenvatinib was investigated.

Lenvatinib caused a decrease in the activity of the human recombinant CYP2C9 isoform, whereas no effect was observed on the activity of the CYP2C6 isoform in rat liver microsomes. One of the other objectives was to determine the IC_{50} for CYP2C9, but the objective was not met. When investigating the effect of lenvatinib on CYP2C11 and 2C6 expression in the liver of male rats, it was observed that a single dose of 30 mg lenvatinib/kg of weight caused no changes in the expression of the isoforms examined.

Lenvatinib has an inhibitory effect on the human recombinant CYP2C9 isoform, but this effect is not significant. Therefore, lenvatinib is unlikely to have a significant impact on drug interactions that might occur with drugs metabolised by the isoforms under investigation.

Keywords: lenvatinib, CYP2C6, CYP2C9, CYP2C11, inhibition