ABSTRACT

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Drug-drug interactions (DDI) and pharmacodynamic effects of metformin

Metformin is a widely used medication in the treatment of type 2 diabetes and is being increasingly used in the treatment of other conditions. Metformin is concidered the 1st line treatment in type 2 diabetes due to its effectiveness, minimal drug-drug interactions and rare self limiting side effects.

Metformins full mechanism of action is still unknown. The molecular mechanism of metformin action has been proposed in the liver related to AMPK activation and up-regulation of SHP. SHP suppresses functions of several nuclear receptors and transcriptional factors involved in the regulation of hepatic metabolism including PXR, which is a major regulator of drug/xenobiotic metabolism.

Therefore it was hypothesized that SHP is an important link between hepatic drug/xenobiotic metabolism regulated by nuclear receptors such as PXR and intermediary metabolism controlled by AMPK pathway.

In the diploma thesis we summarize the recent finding regarded the proposed mechanism of metformin action and its putative role on PXR in regulation of cytochrome P450 enzymes. Metformin's various roles and the common drug-drug interactions, specifically with competitive cationic drugs will be summarized and the potentially lethal effect of co-administration with contrast dyes.