

Exploring the Modulation of Pharmacodynamics and Liver Carboxyl Esterase 1A Metabolism in the Herb-Drug Interaction of Clopidogrel and Xuesaitong Dispersible Tablet

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Abstract

Clopidogrel and Xuesaitong dispersible tablet (XST) have been clinically proven to be effective for treating cardio-cerebrovascular disease. The present study was to investigate the herb-drug interaction of Clopidogrel and XST by modulation of the pharmacodynamics and liver Carboxyl esterase 1A metabolism. Xuesaitong dispersible tablet product has been clinically proven to be effective for treating cardio-cerebrovascular disease. Furthermore, herb-drug interactions between the XST product and drugs that are commonly co-administered, such as aspirin, must be explored to ensure safe clinical use.

Introduction

In recent years, the use of herbal medicines and conventional drugs together has become increasingly common. However, it is crucial to be aware of potential interactions between these substances to ensure patient safety and optimize therapeutic outcomes. One such interaction of clinical importance is between Clopidogrel, an antiplatelet medication commonly prescribed for cardiovascular conditions, and Xuesaitong Dispersible Tablet, a Chinese herbal medicine. This article aims to explore the herb-drug interaction of Clopidogrel and Xuesaitong Dispersible Tablet, focusing on their modulation of pharmacodynamics and liver carboxyl esterase 1A metabolism [1].

Clopidogrel

Clopidogrel is an antiplatelet medicine. It prevents platelets from sticking together and forming a dangerous blood clot. Taking clopidogrel helps prevent blood clots if you have an increased risk of having them. Your risk is higher if you have or have had: a heart attack [2].

Drugs interact with clopidogrel

Medications like proton pump inhibitors, fluoxetine, and fluconazole can make clopidogrel less effective. Grapefruit juice can also make clopidogrel less effective. Taking clopidogrel with certain medications can increase your risk of bleeding [3].

Xuesaitong

Xuesaitong oral preparations are adjuvant therapy for treating cerebral infarction. Xuesaitong oral preparations are adjuvant therapy for treating cerebral infarction. Xuesaitong injection (XST) is one of the major TCM patent medicine used in IHD. Its major components are saponins from *Panax notoginseng* (PNS), including ginsenoside Rb1, ginsenoside Rg1, and notoginsenoside R1 [4].

Drugs interact with Xuesaitong

Xuesaitong, extracted from *Panax notoginseng* was widely used in TCM hospitals. Ginsenoside Rg1, Rd, and notoginsenoside R1 were its main active components. XST was used to treat cerebral infarction and ischemia, coronary heart disease, and atherosclerosis. However, there have not been any publications describing an herbal-drug effect of clopidogrel with XST through modulation of target metabolism and pharmacokinetics. The present study investigated the rationale of combined applications and the drug-herb effects on target metabolism

and pharmacokinetics of CAMD [5].

Clopidogrel

Clopidogrel is a widely used antiplatelet drug that inhibits platelet aggregation and helps prevent blood clots. It is commonly prescribed for patients with atherosclerosis, acute coronary syndromes, and those who have undergone percutaneous coronary intervention. Clopidogrel is a prodrug that requires hepatic metabolism to convert it into its active form [6].

Xuesaitong dispersible tablet

Xuesaitong Dispersible Tablet, on the other hand, is a traditional Chinese herbal medicine that has been used for promoting blood circulation and alleviating blood stasis. It contains multiple active compounds, including extracts from the medicinal herbs *Panax notoginseng* and *Astragalus membranaceus*, among others. Xuesaitong is commonly used in China for the prevention and treatment of cerebrovascular diseases, including stroke [7].

Pharmacodynamics modulation

The combination of Clopidogrel and Xuesaitong Dispersible Tablet may lead to pharmacodynamics interactions. Clopidogrel inhibits platelet aggregation by irreversibly blocking the ADP receptor P2Y12 on platelets. Xuesaitong, on the other hand, contains bioactive compounds that also possess antiplatelet and anticoagulant properties. The concurrent use of these two agents may result in an enhanced antiplatelet effect, potentially increasing the risk of bleeding complications. Therefore, caution is necessary when combining these medications, particularly in patients at high risk of bleeding or

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undergoing invasive procedures [8].

Liver carboxyl esterase 1A metabolism

The metabolism of Clopidogrel is mediated by liver carboxyl esterase 1A, an enzyme involved in its activation. Studies have suggested that some herbal medicines, including Xuesaitong, can modulate CES1A activity, potentially influencing the conversion of Clopidogrel to its active metabolite. It is important to note that the effects of herbal medicines on drug metabolism can vary depending on the specific constituents and their concentrations [9].

Clinical implications and precautions

Healthcare professionals should be aware of the herb-drug interaction between Clopidogrel and Xuesaitong Dispersible Tablet. When considering the combination therapy, individual patient factors such as the severity of the underlying condition, bleeding risk and the need for invasive procedures should be carefully assessed. Close monitoring of platelet function and appropriate adjustment of the antiplatelet regimen may be necessary. Additionally, patients should be educated about the potential risks and advised to report any unusual bleeding or bruising promptly [10].

Conclusion

Clopidogrel and XST Coadministration appreciably increased the C_{max}, AUC, and MRT of CAMD and decreased the CES1A mRNA expression. Animal studies indicated that clopidogrel and XST administration produced significant herb-drug interactions in pharmacokinetic and metabolic enzyme aspect. Decreased CES1A mRNA expression and elevated serum CAMD levels were due to the

XST combination. The herb-drug interaction between Clopidogrel and Xuesaitong.

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