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Prevalence of Tuberculosis in Chronic Hepatitis CPatients

KEYWORDS: Mycobacterium tuberculosis,Hepatitis C virus, Co-infection

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ABSTRACT *Background: Little is known about the characteristics of tuberculosis (TB) in chronic hepatitis C (CHC). We aimed to investigate the co-infection between TB and HCV and estimating their common impact on progression rates of fibrosis. Methods: A total of 558 individuals constituted this study (TB=126; CHC=322; Healthy=110). Western-blot and ELISAwere used for identifying TB-55kDa and HCV-NS4 antigens.Results: A single immunoreactive band was shown at 55-kDa and 27-kDa corresponding to TB-55kDa and HCV-NS4, respectively, due to binding with their respective antibodies.TB-55kDa provided area under ROC curve (AUC) of 0.90 for identifying TB patients with sensitivity=82% and specificity=100% while HCV-NS4 provided AUC=0.96 for identifying HCV with sensitivity=97% and specificity=90%. TB-55kDa significantly correlated with the progression of liver disease (r=0.50, P<0.0001) and its detection rate was 6%, 27%, 35% in patients with fibrosis, cirrhosis and hepatocellular carcinoma, respectively, with an increase in its level. Furthermore, HCV was detected in 66% ofTB-infected patients indicating that TB-patients are susceptible to HCV. Conclusion: Detection rate of TB-55kDa was found to increase with the progression of liver pathology indicating that advanced liver stages are more likely to be susceptible to TB. Moreover, TB may be a potential risk factor on liver fibrosis progression.*

Analytical Methods

PAPER

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Investigation of antimalarial drug pyrimethamine and its interaction with dsDNA by electrochemical and spectroscopic techniques

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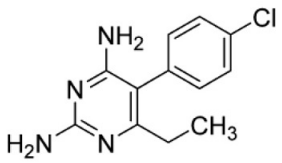
The electrochemical behavior of the antimalarial drug pyrimethamine (PMT) was examined at a screen printed carbon electrode (SPCE) in different aqueous supporting electrolytes using cyclic voltammetry (CV) and differential pulse voltammetry (DPV). The oxidation process of PMT was found to be pH dependent and irreversible proceeding under the diffusion controlled mechanism. CV, DPV and UV/vis spectroscopy were employed to probe the interaction between PMT and salmon sperm double strand DNA (ss-dsDNA) under physiological conditions (pH 4.0 and 7.4). The binding constants between the PMT drug and DNA were calculated to be 5.4×10^5 M^{-1}, 5.9×10^5 M^{-1} and 4.9×10^5 M^{-1} in pH 4.0 and 3.9×10^5 M^{-1}, 4.1×10^5 M^{-1} and 3.3×10^5 M^{-1} in pH 7.4, using DPV and UV/vis spectroscopy, respectively. The diffusion coefficients were found to be 3.1×10^{-7} for PMT and 2.8×10^{-9} cm^2 s^{-1} for PMT to DNA using the CV data. Based on the electrochemical and spectroscopic results, the binding of PMT–DNA was through a contribution of electrostatic interactions and/or hydrogen bonding along with intercalative binding. DPV determination of PMT at a SPCE surface modified with the ss-dsDNA layer was described. The method was applied for the determination of PMT in spiked serum.

Introduction

Pyrimethamine (PMT) 2,4-diamino-5-(3-chlorophenyl)(6-ethyl-pyrimidine) (Scheme 1) is a potent folic acid antagonist which forms a standard therapy for prophylaxis and treatment of malarial infections. PMT is a drug widely used in the treatment of diverse parasitic sicknesses[1,2] such as congenital toxoplasmosis. The treatment of this problem usually begins in the early post-natal period and could last throughout the first year of life.[3–5] PMT interferes with folic acid metabolism by inhibiting dihydrofolate reductase (DHFR), an enzyme responsible for the formation of tetrahydrofolate (H_4F) from dihydrofolate (DHF).[6] This provokes lack of substrates for the formation of purines and pyrimidines, thereby impeding cell replication.[1,7] DHFR is found to be present in the parasite and host but PYR is 1000 times more active in the parasite enzyme.[8,9] Nevertheless, DHFR is not exempted from toxicity, and in some cases could lead to thrombocytopenia, anaemia and leucopenia that usually bring about the suspension of the treatment.[10–12]

Nucleic acids play an important role in cellular processes including cell division (DNA replication) and protein synthesis (transcription and translation). DNA is the material of inheritance and controls the structure and function of cells. The studies on molecular interactions of drugs with DNA have great importance to understand their biological activity and have become an active research area in recent years.[13–17] The interaction of small molecules (drugs) with the DNA is of major importance to design effective chemotherapeutic agents. There are several types of interactions associated with drugs that bind to the DNA. These include electrostatic interactions (generally non-specific) with the negatively charged nucleic acid sugar–phosphate structure, intercalation, and minor and major DNA groove binding interactions. Especially, small molecules bind to the DNA by two predominant binding modes, intercalation and minor groove-binding. The intercalators bind to the DNA by insertion of a planar, aromatic substituent between base pairs, with concomitant unwinding and lengthening of the DNA helix. In minor groove-binding, the crescent-shaped ligand fits into the minor groove with little steric hindrance and with little distortion of the DNA structure. Minor groove binding makes intimate contacts with the walls of the groove, and as a result of this interaction, numerous hydrogen binding and electrostatic



Scheme 1 Chemical structure of PMT.

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Original Article

CLOVE OR GREEN TEA ADMINISTRATION ANTAGONIZES KHAT HEPATOTOXICITY IN RATS

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ABSTRACT

Objective: Khat consumption has become a common problem that affects the health aspects of life in Yemen and other parts in the world. The liver has been suspected to be particularly vulnerable to the harmful effects of khat use and until now khat hepatotoxicity effects are still controversial. This study was conducted to investigate the hepatoprotective effects of aqueous extracts of clove and green tea, as medicinal herbs with established antioxidant properties, against controversial hepatotoxicity effects of khat in rats.

Methods: Rats received a daily oral dose of khat extract alone or in combination with green tea or clove extract for six weeks. To study the effects on liver cells, histopathology, routine liver function tests, malondialdehyde (MDA), total antioxidant capacity (TAC) and the activities of superoxide dismutase (SOD) and catalase (CAT) enzymes were investigated.

Results: Khat administration showed marked liver injury; congestion in the portal vein with fibrous tissue proliferation, extended from the portal area and forming intralobular Porto-portal bridging fibrous septae. Besides significant routine liver function tests alterations, lipid peroxides elevation, and TAC reduction with significant inhibition of SOD and CAT activities.

Conclusion: Combined administration of khat with clove or green tea protected hepatocytes via oxidative stress inhibition. They significantly counteracted the alterations in liver function tests, decreased lipid peroxidation and restored the antioxidant status to near normal levels. These results confirm khat hepatotoxicity and suggest that clove or green tea administration has strong hepatoprotective effects against khat induced hepatotoxicity in rats via antioxidant mediated mechanism.

Keywords: Khat, Medicinal herbs, Hepatotoxic, Hepatoprotective.