Extended Abstract Journal of Pharmacy and Pharmaceutical Research 2021
Vol.5 No.2

# PROTECTIVE PROPERTIES OF SILYMARIN AGAINST THE TOXIC EFFECTS OF VALPROIC ACID IN THE HEART

**Ibrahim Aktas**
University of Adiyaman, Turkey

**Introduction**:
Epilepsy is a type of disease that brings a significant financial burden on both the health system and patients. On the other hand, valproic acid (VPA) is used to treat psychiatric disorders such as mania, migraine, bipolar and epilepsy due to its therapeutic benefits and low cost. Its chemical structure comprises an eight-carbon fatty acid called dipropylacetate. It acts by inhibiting the recovery of gamma aminobutyric acid (GABA) from presynaptic terminals by inhibiting GABA transaminase and increasing synaptic cleavage (2). VPA binds to plasma proteins at high levels when administered at therapeutic concentrations. This makes them prone to fluctuations in therapeutic effects during treatment, more importantly to unpredictable toxicity and drug interactions. Therefore, significant side effects have been reported during prolonged treatment with VPA. The main ones are pancreatitis, elevated liver enzymes, leukopenia, thrombocytopenia and cardiovascular disease (CVD). Myocardial infarction (MI), especially known as heart attack, results in death as a result of permanent heart muscle damage. It increases serum cardiac enzymes and lipid peroxidation from the first month of chronic treatment. According to histopathological and biochemical studies, VPA causes cardiac necrosis, apoptosis and oxidative stress. The production of excess reactive oxygen species (ROS) directly damages cellular macromolecules such as proteins, lipids and DNA. It changes normal signaling pathways by stimulating redox sensitive transcription agents. They are also aggressively involved in oxidative heart injury and become the center of cellular damage that seriously affects the myocardium. Various types of inflammatory cells in the heart affected by this ROS formation are cardiomyocytes and endothelial cells. Detoxification of ROS requires enzymatic and non-enzymatic antioxidant mechanisms.

**Objectives**:
During autopsy, the hearts of all rats used in the experiment were taken, made macroscopic and 10% neutral formalin was used for fixation. After fixing the tissues, the formalin was removed by washing in the stream. It was passed through a series of graded alcohols for dehydration and kept in xylene for transparency. It was then put into paraffin. From these obtained blocks, 3-4 micron sections were cut with microtome (RM2125RTS, Leica, Germany) and these sections were stained with Hematoxylin-Eosin for histopathological evaluation. The structural data in the heart tissue of groups were evaluated according to the notes of Refaiy et al. Modified semi-quantitative scale were used for the evaluation of histopathological changes: none, mild, moderate, severe grade. Samples were evaluated and imaged by imaging binocular light microscopy (ECLIPSE Ni-U, Nikon and Tokyo, Japan).

**Results**:
LDH, CK-MB, ALT and AST levels were significantly increased in VPA group compared to control and VPA + SLY groups. Treatment with SLY resulted in a significant decrease in LDH, CK-MB, ALT and AST levels elevated by VPA. According to the data and significantly higher MDA level and significantly lower GSH levels were detected in the VPA group. SLY treatments resulted in a significant decrease in VPA-induced MDA and a significant increase in VPA-induced GSH. Normal heart histological tissue was confirmed in the control group.In VPA group, mononuclear cell infiltrations in myofibrils, lipocytic infiltration and adipocytes, haemorrhagic areas, degeneration in myofibrils were moderately observed. These histopathological findings were less common in the SLY group. VPA + SLY given group; heart tissue sections; a decrease in histopathological findings was observed compared to VPA group (H – E, a-b-c x20,a1-b1-c1 x40).

**Conclusions**:
Our study demonstrated that SLY improves biochemical and histological disorders in VPA-induced heart injury. In addition, the mechanism of this effect may be inhibition of lipid peroxidation and stimulation of antioxidant enzymes. This suggests that SLY may be effective in the treatment of heart damage. Further studies are needed to fully elucidate the mechanism of the antioxidant effect of SLY.

This work is partly presented at Joint Event on 7th International Conference and Exhibition on PHARMACOLOGY AND ETHNOPHARMACOLOGY & 5th GLOBAL PHYSIOTHERAPY, PHYSICAL REHABILITATION AND SPORTS MEDICINE
March 27-28, 2019 | Amsterdam, Netherlands