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Hepatoprotective Potential of Apigenin versus Vitexin: A Comparative Study in an Acetaminophen-Induced Acute Liver Injury Rat's Model

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Abstract

Acetaminophen (Paracetamol) poisoning is a global issue that can result in severe liver failure and permanent liver damage, necessitating the need for liver transplantation. The aim of our study was to assess and compare the preventive effects of Apigenin and vitexin against acetaminophen-induced acute liver damage in rats. Twenty male rats were divided into four groups (5 per each) and treated for seven consecutive days. Group I (negative control group) received 5% DMSO, Group II received a single acetaminophen dose, Group III received 10 mg/kg Apigenin i.p, while Group IV received 40 mg/kg vitexin i.p. On the seventh day, all groups except Group I received a single oral dosage of 3000 mg/kg acetaminophen three hours after their final Apigenin or vitexin dose. After 24 hours of acetaminophen administration, the animals were sacrificed, and their blood and livers were taken for biochemical and histopathological examination. The results demonstrated that acetaminophen treatment led to notable increases ($p < 0.05$) in blood biochemical markers (alanine aminotransferase, aspartate aminotransferase, and alkaline phosphatase), in contrast to the negative control group. However, rats who received Apigenin exhibited a notable decrease ($p < 0.05$) in the level of these biomarkers. For vitexin pretreatment, the levels of these enzymes were reduced, but this reduction was significant only for alkaline phosphatase levels compared to the acetaminophen group. Furthermore, Apigenin pretreatment was able to restore normal liver histopathology, while vitexin was not. In conclusion, our research validated the hepatoprotective properties of Apigenin against acetaminophen hepatotoxicity and provided insight into potential distinctions in the effects of a flavonoid versus its glycosylated form.

Keywords: Apigenin, Vitexin, Hepatoprotection, Acetaminophen, Paracetamol, Liver Damage

Introduction

Drug-induced liver injury (DILI) is still a major issue in clinical practice, necessitating the research for potential protective agents [1]. DILI ranges from asymptomatic rise in liver enzymes to acute liver failure (ALF). DILI remains the predominant cause of ALF in Western countries [2]. Acetaminophen-induced hepatotoxicity is an example of a dose-dependent and predictable DILI [3]. In the United States, acetaminophen overdose causes roughly 40% of all cases of ALF, while idiosyncratic drug reactions account for approximately 13% of cases[1,4].

Acetaminophen was discovered in 1878 and became popular as an over-the-counter analgesic and antipyretic in the 1950s. Since then, multiple studies have found a dose-dependent link between acetaminophen use and liver injury. These consequences can be exacerbated in the presence of other risk factors such as alcohol misuse, starving ketosis, or concurrent illnesses [5]. When taken in therapeutic amounts, over 90% of acetaminophen is transformed into harmless byproducts by sulfation and glucuronidation processes and then excreted through the kidneys. However, when a dangerously high amount of acetaminophen is taken, the body's mechanisms for processing the medication get overwhelmed. This results in a higher proportion of the drug being eliminated without any changes (~10%) and being metabolized into a harmful substance called N-acetyl-p-benzoquinone imine (NAPQI) (>15%) by CYP450 enzymes [6]. After undergoing glutathione conjugation, NAPQI is ultimately removed since it is converted into innocuous metabolites [6,7]. The effect of acetaminophen on glutathione levels depends on the dosage, with greater dosages leading to prolonged depletion of glutathione [8]. When glutathione is depleted, oxidative stress triggers the activation of