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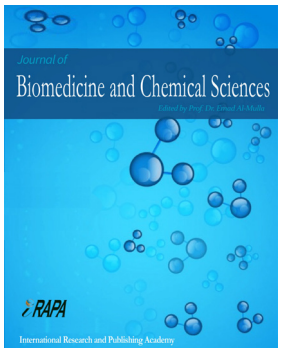

Histological Changes of Liver Tissue Triggered by Antibiotic Drug Azithromycin and the Ameliorative Effects of Garlic in Male Albino Rats

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ABSTRACT

The garlic plant can be used as a spice in cooking or as a treatment for several common disorders. Garlic's four primary constituents are allicin, alliin, diallyl sulfide (DAS), and S-allyl cysteine (SAC). Anti-inflammatory, anti-cancer, antidiabetic, and antioxidant qualities are among its biological attributes. By using histological analysis of liver tissue, the work aimed to determine the harmful effects of the antibiotic Azithromycin, as well as the protective function of garlic. In the animal house of the Faculty of Science, University of Kufa, 24 mature male albino rats (*Rattus norvegicus*) weighing between 180 and 270 grams on average were employed in this study. The rats were between 2.5 and 3 months old. According to the study, two weeks after oral administration of 500 mg/kg of azithromycin and 240 mg/kg of garlic to animals, histological changes in liver tissue were estimated. Compared to the control group, which acquired distilled water and garlic, several negative effects on liver tissue were observed in the groups that received azithromycin and azithromycin + garlic. Furthermore, compared to the group that was given azithromycin alone, the results displayed a minor alteration in liver tissue in the group that received azithromycin plus garlic.

INTRODUCTION

One cytotoxic medication, azithromycin is also referred to as a broad-spectrum bacteriostatic antibiotic, it has a high capacity for tissue penetration, it has been widely used to treat infections of the respiratory, enteric, and genitourinary systems (Doan, et al., 2018). Because of azithromycin's potent anti-inflammatory properties and strong activity against Gram-negative organisms, macrolide antibiotics are broadly used to treat a range of chronic inflammatory pulmonary diseases, where an altered inflammatory response leads to the development of damage to the host tissues. Azithromycin is generally considered bacteriostatic and is produced by Streptomyces species. (Doyle, et al., 2015).

In accordance with Sinha et al. (2017), additional antibacterial, antiviral, and immunomodulatory properties of azithromycin which may help treat viral infections like covid-19, these properties include reducing inflammation, controlling neutrophil and macrophage activity, and regulating cytokine production. Additional notable inhibitory effects on cell survival, tumor necrosis factor-α, interleukin-2, and interleukin-8 are among the cell cytokines that azithromycin has been observed to produce, along with total antioxidant capacity (Feng, et al., 2019). By directly causing cytotoxic effects on the infected cells, azithromycin can also cause tissue damage, in intensive care, the host's inflammatory response is usually linked to morbidity and mortality (Oliver & Hinks, 2020). According to Olayinka and Ore (2014), low concentrations resulted in damage to the liver and kidneys as well as reduced liver and kidney function.

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One of the Liliaceae family's members is garlic (Allium sativum), has been used as a culinary spice and a medicinal remedy for several common diseases since ancient times. It contains organosulfur compounds, which are thought to be its primary constituents, such as [S-allyl-L-cysteine sulfoxide and glutamyl-S-allyl-L-cysteine] (Sheikh Raisuddin et al., 2018). Garlic has four main components, according to various studies: allicin, alliin, diallyl sulfide, and S-allyl cysteine (SAC), population studies and extensive in vitro or in vivo research have mentioned that garlic possesses a variety of biological functions, such as antioxidant, anti-inflammatory, and anti-cancer qualities (Sheikh Raisuddin et al., 2018). Garlic performs through a variety of mechanisms. For instance, it may inhibit oxidative stress by eliminating reactive oxygen species, prevent lipoprotein oxidation and tumor growth, increase antioxidant enzyme activity by triggering endogenous antioxidant enzyme expression, reduce inflammation, lower blood sugar, encourage apoptosis, and restrict the cell cycle (Shukry et al., 2020).

Another essential function of garlic in cells is its antioxidative properties, they include decreasing blood pressure and cholesterol levels to reduce the risk of cancer and heart disease and preventing the development of lipid peroxides. (Sheikh Raisuddin et al., 2018). The current study conducted a histological test that included liver tissue to examine the toxicity effect of the antibiotic azithromycin and the substantial protective impact of garlic.

MATERIALS & METHODS

Experimental Animals

This study, which involved 24 male rats (Rattus norvegicus), was carried out in the animal house owned by the Faculty of Science University of Kufa between October and November of 2023. Between two and three months of age, with an average weight of 180 to 270 grams, before the trial began, they were kept in an animal home with a normal light-dark cycle and fed and watered for at least two weeks.

Experimental Design

In this work, four groups of six individuals each were utilized. Animals in group one was not given any medication, while those in group two were given merely 500 mg/kg of body weight of azithromycin. For a period of two weeks, the fourth group received 500 mg/kg of azithromycin plus 480 mg/kg of garlic, while the third group received around 480 mg/kg of garlic.

Ethics Statement

Following permission from Kufa University's Central Committee for Bioethics, all animal experiments were carried out in accordance with the guidelines for the use and care of lab animals.

Drugs

For a period of two weeks, 500 mg/kg body weight of azithromycin and 480 mg/kg body weight of garlic were administered orally in 13 milliliters of distilled water, respectively.

Histopathological study

In accordance with Bancroft and Gamble (2008), liver tissues were preserved in 10% formalin for a minimum of twenty-four hours. After that, tissue samples were made to investigate histological alterations in the liver tissue of experimental animals, they had been wrapped in paraffin wax, and cut into slices that were six millimeters thick using a rotary microtome. After staining the sections with hematoxylin and eosin dyes, the liver histological alteration was viewed under a light microscope.

RESULTS & FINDINGS

The liver tissue of male albino rats administered the antibiotic azithromycin for two weeks showed histological changes when compared to control group (figures 1, 2, 3, and 4). As seen in Figure 5, the findings also demonstrated garlic's preventive properties and ability to lessen the histological alterations in liver tissue.

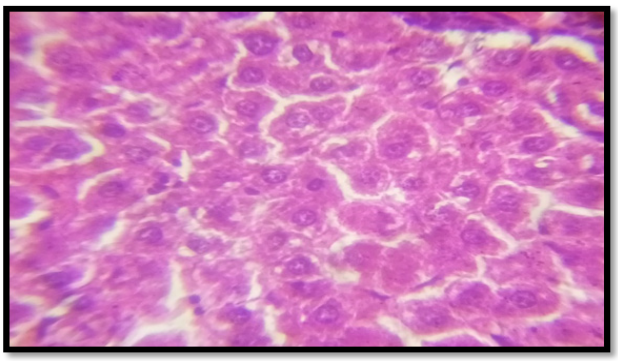

Fig. 1. Cross section of liver tissue showing normal architecture from control group. Sections of tissue were taken at 400 X magnification after being stained with H&E.

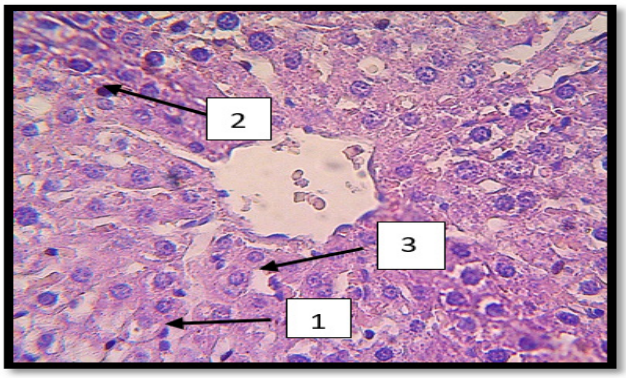

Fig. 2. Cross section of liver tissue showing 1: activated kupffer cell 2: pycknosis 3: vacuolated hepatocytes from group given by Azithromycin. Sections of tissue were taken at 400 X magnification after being stained with H&E.

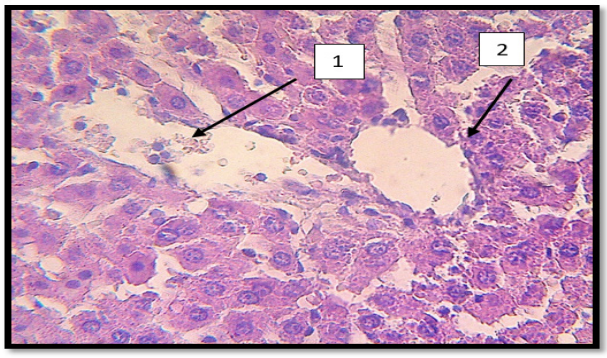

Fig. 3. Cross section of liver tissue showing 1: great degradation of hepatocytes 2: infiltration of leukocytes from group administrated by Azithromycin. Sections of tissue were taken at 400 X magnification after being stained with H&E.

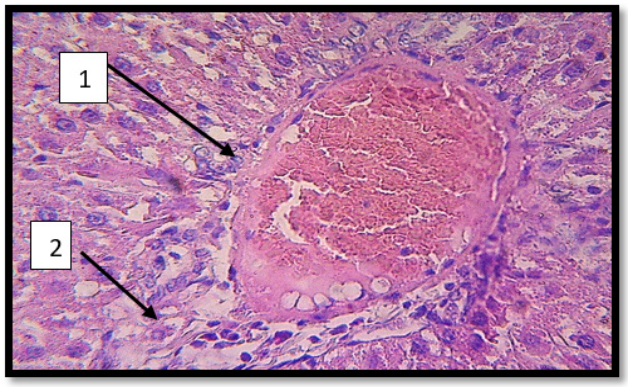

Fig. 4. Cross section of liver tissue showing 1: haemorrhage in blood vessels 2: infiltration of leukocytes. Sections of tissue were taken at 400 X magnification after being stained with H&E.

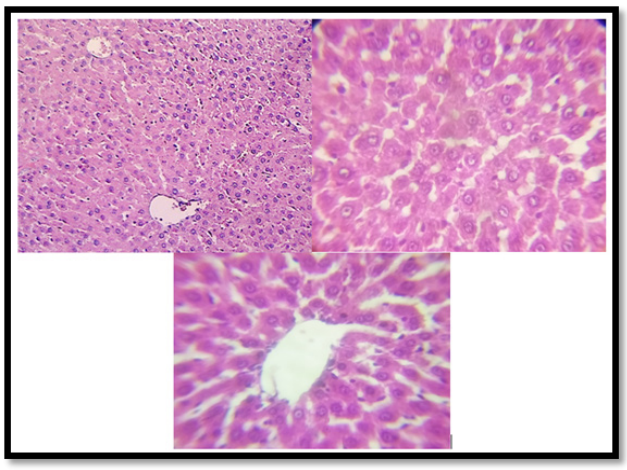

Fig. 5. Cross section of liver tissue showing slight changes in liver tissue and semi normal architecture from garlic treated group. Sections of tissue were taken at 400 X magnification after being stained with H&E.

Discussion

According to Woodhead et al. (2019), azithromycin is one of the macrolides that causes liver toxicity and raises liver enzyme levels. The results shown in figures 1, 2, 3, and 4 supported these findings. Furthermore, the findings were corroborated by Omara et al. (2021), who noted that necrosis in the parenchyma was one of the numerous histological alterations in liver architecture brought on by azithromycin. Additionally, the study confirmed by Liu et al. (2020) revealed Azithromycin altered the function of glycose and lipid metabolism as well as the proliferation and differentiation of cells, causing liver apoptosis. Moreover, the results verified the outcomes of Dabdoub et al. (2022), who explained azithromycin damages the liver by decreasing the rise in liver enzyme activities such as ALP (alanine aminotransferase), AST (aspartate aminotransferase), and gamma-glutamyl transferase. Likewise, the results incorporated with Radwan et al. (2021).

They clarified despite being a broad-spectrum antibiotic, because of the hepatotoxicity of azithromycin, which causes degenerative changes in the hepatic cords, dilatation of central blood arteries, infiltration of inflammatory cells, and an increase in collagen fibers, its therapeutic indications are limited. Furthermore, the results correspond with those of (Ellison & Blackwell, 2021), who found that the administration of azithromycin to an animal model resulted in direct hepatocellular damage and perhaps severe liver damage. Furthermore, the findings were further supported by Li et al. (2016), who noted that azithromycin caused oxidative stress and liver damage in mice. Figure 5's findings in similarity with Sheikh Raisuddin et al., (2018), they found garlic's primary pharmacological component, allicin, has anticancer properties by preventing the proliferation of different cancer cells.

Furthermore, the results supported the findings of Shukry et al. (2020) that garlic has antioxidant activity within the cell by suppressing free radical production as well as supporting body-protective systems by destroying them. According to studies by Farhat et al. (2021), garlic possesses chemoprevention mechanisms that include improving carcinogen detoxification and having a strong effect on scavenging electrophiles and ROS (reactive oxygen species). In the opinion of Aly et al. (2019), garlic's main compounds, known as organosulfur substances, have anticancer properties through inhibiting carcinogen activation, accelerating phase 2 detoxification activities, which mainly results in cell cycle arrest between the growth 2 and mitotic phases, stimulating apoptosis, aiding in DNA repair, suppressing proliferation, and reducing inflammation.

CONCLUSION

According to the study's findings, garlic has several health benefits and can be utilized as an antioxidant. It also had a strong protective effect against the cytotoxicity and histological alterations caused by azithromycin in the liver tissue of male albino rats.

Competing Interest

The authors had no competing interests.

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