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Garlic Aqueous Extract's Hepatoprotective Effect Against Ciprofibrate-Induced Hepatotoxicity In Male Albino Rats

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ABSTRACT

Background: The danger of liver growth is increased because the liver is exposed to too many hazardous compounds every day, either from the environment or from a variety of other sources like preservatives or medications. Ciprofibrate belongs to the chemical family of peroxisome proliferators, which stimulates hepatic cells and causes the hepatic cells to proliferate uncontrolled, leading to liver enlargement. Drugs and other xenobiotics, such as the long-term hypolipidemic treatment that causes cancer in rats, can cause the liver cell to divide. However, this has not yet been proven in people.

Objectives: The current study's objective is to assess the possible protective effects of garlic administration against the biochemical and histological changes that ciprofibrate-induced liver damage in male rats.

Materials and Methods: Eight groups of six male rats each were utilised in the current study: control, oil, garlic, ciprofloxacin 50 and 100 mg/kg body weight, ciprofloxacin 50 mg/kg body weight plus garlic, ciprofloxacin 100 mg/kg body weight plus garlic. For 21 days, the rats received daily oral gavage treatments. The animals were killed on the final day of the experiment, and then blood samples and liver tissue were taken. Serum Alanine Aminotransferase (ALT), Aspartate Aminotransferase (AST), Alkaline Phosphates (ALP), and serum total and direct bilirubin concentrations were measured to assess liver function. For all groups, a histological analysis of the liver tissues was done.

Results: Male rats treated with ciprofibrate at doses of 50 or 100 mg/kg body weight experienced a substantial rise in their serum levels of the enzymes ALT, AST, and ALP as well as total and direct bilirubin. Histological examination of the central vein area and portal zones indicated necrosis in liver cells, damage to the epithelium lining the central vein, and congestion in blood sinusoids. The liver's structural changes were greatly improved and the levels of blood ALT, AST, and ALP activity, total bilirubin, and direct bilirubin were significantly reduced when garlic aqueous extract and ciprofibrate were administered together.

Conclusion:Conclusion: Treatment with ciprofibrate increased liver function tests and caused significant histological abnormalities, however in male rats, garlic aqueous extract was able to shield the liver from these side effects. Therefore, it should be recommended to patients who are on ciprofibrate treatment to take garlic aqueous extract.

Keywords:
Ciprofibrate, Hypolipidemic agent, Garlic aqueous extract, Hepatotoxicity, Hepatic pathophysiological changes

INTRODUCTION :

The liver, which is crucial in the transformation and elimination of chemicals, is vulnerable to the toxicity of these substances. Certain medications have the potential to harm the organ when taken in excess or occasionally even when administered within therapeutic parameters. When the liver functions regularly, the body's numerous metabolic processes are balanced and regular; however, taking some medicines may result in liver issues. Due to its function in the elimination and metabolism of substances, the liver is a particular target for drug toxicity. Drugs can enter the body through the nose, intramuscular injection, intravenous route, cutaneous absorption, or intravenous route [1]. It is well recognised that the liver's primary job is to remove any toxins that could otherwise enter the body.

This method leaves vulnerable tissue injured, which might manifest as bleeding, congestion, necrosis, or other liver injury disorders [2]. Chemicals known as peroxisome proliferators have a variety of impacts on rats and mice, including enhanced DNA synthesis and cell proliferation (peroxisome proliferation).

Peroxisomeproliferator-activated receptors (PPARs), which function as nuclear transcription factors themselves, are nuclear membrane receptors that are activated by ligands in order for these substances to have an effect [3, 4]. The PPs cause a cellular process in which the size and number of peroxisomes dramatically increase, which is correlated with both hepatocyte hypertrophy (an increase in the size of liver cells) and hyperplasia, or an increase in the number of liver cells, during replicative DNA synthesis and cell division [5]. The various substances

known as peroxisome proliferators vary in their ability to Although they differ somewhat in structure, all produce recognisable effects in the treated rats' and mice's livers [6]. Chemicals like hypolipidemic medicines, plasticizers, and organic solvents are examples of peroxisome proliferators. They all promote liver cancer in laboratory rodents by a non-genotoxic mechanism.

Ciprofibrate is a member of the low-fat lipoprotein family, which slows down the conversion of high-density lipoprotein HDL to LDL cholesterol. Additionally, it boosts triglyceride analysis and decreases triglyceride production. These outcomes lower the chance of having arterial heart disease and stroke due to sclerosis. Even though ciprofibrate has been used in medicine since 1930, its exact mode of action was still unclear in 1990. Growth of the liver and replicative DNA synthesis go hand in hand with peroxisome proliferation.

most of These peroxisome proliferators have acidic properties that can control the metabolism of fatty acids [7]. Hepatocyte hyperplasia (increased replicative DNA synthesis and cell division) and hypertrophy are both causes of the liver enlargement brought on by peroxisome proliferators [8]. Along with additional pleiotropic effects including the proliferation of peroxisomes and the stimulation of specific cytosolic and peroxisomal enzymes in the liver, peroxisome proliferators also promote the growth of liver cells [9].

A disruption in the equilibrium between the generation of free radicals, also known as reactive oxygen species (ROS), is known as oxidative stress. The theory behind the oxidative stress is that chronic administration of peroxisome proliferators causes rodent hepatocytes to experience prolonged oxidative stress as a result of an imbalance.

when hydrogen peroxide is created and broken down [10]. One is based on the idea that active oxygen species are produced more frequently as a result of unbalanced peroxisomal enzyme production; it has been suggested that these reactive oxygen species induce indirect DNA damage that leads to the development of tumours [11]. In recent decades, the usage of antioxidants has become more popular because research has shown that they are effective against a number of ailments. Here are a few of them that were utilised for this investigation. Garlic, also known as Allium sativum, is a member of the Lilliaceae family of herbs. The oldest plant that has been domesticated, garlic has been used as a spice, food, and folk remedy for more than 4,000 years [12]. The use of garlic as a treatment for many illnesses was described in ancient Egyptian documents [13]. It has possesses therapeutic qualities such as immunomodulation, hepatoprotection, antioxidant, antimutagenic, antibacterial, and anticarcinogenic activities and has been utilised as a traditional medicine in the treatment of heart conditions, malignancies, and headaches [14].

Additionally, it is said to have antifungal [15], hypoglycemic [16], hypolipidemic [17], and anti-atherosclerotic [18] effects. In the past, people have used garlic to treat a variety of ailments, including earaches, leprosy, deafness, severe diarrhoea, constipation, and parasitic infections, as well as to reduce fever, combat infections, and ease stomachaches [19]. The mineral germanium, calcium, copper, iron, potassium, magnesium, selenium, and zinc, as well as at least 33 sulphur compounds, many enzymes, vitamins A, B1, and C, fibre, and water are all present in garlic. The 17 amino acids found in garlic, including lysine, histidine, arginine, aspartic acid, threonine, swine, glutamine, proline, glycine, and alanine, are also present in it.

Leucine, isoleucine, tryptophan, phenylalanine, cysteine, valine, methionine, and isoleucine [20]. The primary sulphur compounds found in garlic include allicin, ajoene, diallyl disulfide, and diallyl trisulfide. Flavonoids, phenolics, and anthocyanins [21–23], as well as SAC sulfoxide. Additionally, it contains vitamins B1, B2, B6, C, and E as well as proteins, fatty acids, glycolipids, phospholipids, fiber, saponins, and glycosides lectins [24].

DISCUSSION:

The liver is a key organ for detoxification and a main location for intensive metabolism in general. As a result, exposure to toxins can cause a variety of illnesses [29]. In recent decades, liver function tests have emerged as the most crucial tools for evaluating the liver's resistance to damage. The severity of the liver injury is often assessed by liver performance indices such ALT, AST, and ALP [30]. In hepatotoxicity investigations brought on by chemicals, serum aminotransferase activities are known as toxicity markers, and an increase in these enzymes' activities is referred to as the early detection of toxic hepatitis [31].

The release of these enzymes into the bloodstream can be caused by necrosis or damage to the cell membrane [30]. Biochemical indicators showed variation in liver function testing.It has been underlined that, when compared to the control group, ciprofibrate 50 and 100 mg had negative effects on the activities of the serum Alanine aminotransferase, Aspartate aminotransferase, alkaline phosphates, total bilirubin, and direct bilirubin in male albino rats. With both concentrations, the AST level was shown to rise in the current study; take notice that it was slightly higher with Cipro at 50 mg/kg body weight. Additionally, ALP enzyme is present in the same circumstances, but its concentration is substantially higher than AST, particularly at 50 mg/kg [5].

Garlic was employed to confirm their therapeutic and/or preventive action in order to lessen the adverse effects of ciprofibrate. According to reports, garlic regulates free radical reduction, improves liver biomarkers, ameliorates hepatic marker enzymes, lessens the degree of fibrosis, and normalises the structure of hepatocytes. The hepatic activation of DNA replication begins as early as 24 hours in male rats, according to earlier investigations in vivo and in vitro using Wistar and Fischer rats (F344/NHsd) dosed with peroxisome proliferators (nafenopin and Wyeth-14,643) [5, 10, 32, 33].

The peroxisome proliferator (ciprofibrate) has been shown to significantly accelerate the replication of hepatic DNA in male Fischer rats, leading to hepatocarcinogenesis in rats [34]. When exposed to substances known as free radicals, liver cells are harmed.

which considerably form in the body as a result of exposure to a certain type of medication, such as peroxisome proliferators. It is important to note that free radicals injure healthy cells and contribute significantly to the occurrence of cancer, but garlic, which is a potent antioxidant, lessens the harm done by these agents. Garlic extract shown a favourable effect on cell proliferation and dramatically decreased serum liver functions in this investigation [35]. by ciprofibrate in rats [36]. Additionally, Banerjee et al. [1] claimed that numerous clinical investigations had demonstrated the beneficial effects of garlic [37]. Additionally, the garlic significantly reduced the total bilirubin level. Garlic's therapeutic effects as a potential preventive measure for free radical-mediated liver injury may be increased by the hepatoprotective impact it was shown to have in this study [38]. According to Shaarawy et al. [13], giving rats garlic considerably lessened the liver damage that was brought on by Nnitrosodiethylamine (NDEA) and carbon tetrachloride (CCL4). According to Nasr et al. [39], pretreated rats with aged garlic extract (250 mg/kg once daily for 21 days) showed a substantial decrease in AST and ALT serum levels when cisplatin (7.5 mg/kg once intraperitoneal) was administered. Additionally, histopathology showed that the toxicity caused by cisplatin had significantly improved. the anatomy of the liver. Aged garlic extract possesses anti-inflammatory and antioxidant properties.

In the present investigation, co-administration of garlic extract with ciprofibrate at doses of 50 or 100 mg/kg body weight resulted in a substantial reduction in serum ALT, AST, and ALP. A similar study discovered that taking garlic (both therapeutically and preventively) greatly decreased the liver damage brought on by Rats' liver structure and oxidative stress were both induced by cisplatin. In order to lessen the hazardous side effects of anticancer medications, it could be taken as a dietary supplement. The intra-gastric infusion of crude garlic extract considerably reduced the circulation activity of AST, ALT, and ALP, according to Akinyemiju et al. [23]. According to the reversal of abnormal antioxidant enzyme activity back to normal levels, garlic extract was found to prevent and regulate oxidative stress caused by immobilisation stress. The organ sulphur components in garlic, such as allicin, alliin, and the two main organ sulphur molecules SAC and Sallylmercaptocysteine, which are strong free radical scavengers, may be to blame for this [40].

CONCLUSION:

The current study looked at the protective benefits of garlic against liver damage brought on by peroxisome proliferators (ciprofibrate). The prospective effects of ciprofibrate on liver enzymes and the histological consequences are accurately analysed in this study. Through examination of biochemical markers and histological alterations, the study produced valuable data. Peroxisome proliferators have been the subject of prior research, and the current study largely supported those findings. Garlic was also utilised in this experiment to lessen the drug's toxicological effects. In rats, liver damage brought on by hepatotoxicity was inhibited by garlic.

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