

# The Effect of Excessive Ginger Intake on the Health of Mice and Liver Tissue

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## Abstract

**Introduction:** Spices are one of the main ingredients frequently used in Arab and Asian kitchens. Therefore, we must research their harms in the service of society. **Objective:** This study aimed to investigate the effect of excessive ginger consumption on the phenotypic and histological structure of the mice liver. It is important to have a clear view of the spices that play a major role in damaging organs. **Methodology:** About 20 mice were used. I was orally (1g) to ginger for 50 days. that anesthetization, separating the liver, fixing by formalin, using the routine method to preparation block and sectioning (5um) then coloured with H&E. **Results:** Symptoms was the loss of weight, high temperatures, as well as the Gangrene at ends of the Ear, Tail. the liver appearance of severe congestion with a dark red colour, accompanied by bleeding and the appearance of fluid-filled swelling in the liver, forming what is called the liver abscess. Microscopy indicated a loss of the normal structure of the liver tissue. The sections also showed the emergence of the stages of programmed death of cells. **Conclusion:** We concluded that consuming spices in large quantities will lead to toxic liver toxicity, but it is not dangerous.

**Keywords:** Ginger, Health, Liver, Mice, Tissue

## Introduction

The liver is organ that controls the various chemical and physiological processes in the body of an organism . However, in the long term, multiple cases of injuries and for different reasons, in addition to taking medications continuously, can cause injuries that lose the ability to regenerate<sup>1</sup>. And since a person has grown accustomed from ancient times to adding vegetable parts in their fresh form or after drying them to some of his food dishes, including ginger, it has been observed lately that people have become more interested in them either for use in cooking or as herbal remedies instead of chemical treatments as a result of their common perception of

herbs that they do not cause effects Sideways according to their beliefs and the cheapest prices<sup>2</sup>.

Many studies have discussed the healing and preventative potential of ginger. It has been shown that ginger and some of its components can prevent inflammation in isolated macrophage cells, scrape free radicals, suppress abnormal cancer cell proliferation and induce apoptosis in a dose-dependent manner<sup>3</sup>. The fact that the liver is considered to be in rodents is one of the main target members in assessing toxicity safety by clinical studies and the generation of preclinical toxicity and oncogenicity tumours<sup>4</sup> is a measure of toxicity as it is affected by removing toxic effects and various metabolites of different drugs and spices, including the spice used, where the effect begins on it from the beginning of its action until it or one of its metabolites reaches the toxic limit, which leads to some liver cells losing their function or death, which leads to obstruction of liver function<sup>5</sup>. And for the use of spices in many international kitchens, this study aimed to find out the extent of the damage caused by continuing to eat these

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products and their effects as a result of eating them on human health through conducting laboratory research on laboratory animals, so it found several side effects and the most important finding of this study is to summarize Palatine .

### **Materials and methods :-**

#### **Animals:-**

This study was carried out in the laboratories of the Diyala University and the laboratories of Hospital, it included 20 mice weighing (30-26g).

#### **Animal dosing:-**

The animals were administered orally by (1g) per ginger powder mixed with (10ml) of distilled water , period lasted for 50 days. The groups were divided into two groups, which included 10 mice for each group, as follows. Separating the liver by using the Pellet Wild method , then put into formalin after washing it with saline solution, for a period ranging between (12-16h). Using routine preparation and sectioning by manual rotating microtome of the type (HM325) and that coloured with Delafield haematoxylin and Eosin<sup>6</sup>.

### **Results and discussion**

#### **Clinical symptoms**

Current study was carried out in a manner contrary to what was stated in previous studies. To demonstrate the effect of excessive consumption of ginger in the livers of mice (Swiss albino). Their ability to eat remains normal before and after dosing, although they are accompanied by a decrease in weight: this indicates an increase in the metabolic rate in the body in addition to an increase in activity after the dosing, but during the dosing, simple signs of bleeding from the mouth appeared Also, some mice died by 20% also showed necrosis in the end tail and ear , as well erosion of the tissue and the formation of the cyst (Fig.1). different results appeared in the study<sup>7</sup>, regarding weight gain of rabbits when dosed with ginger. While in the study<sup>8</sup>, its results showed compatibility with some of the results of the current study, when exposing pregnant mice to glue smoke at a concentration of 2500 mg/kg of body weight, behavioural symptoms were

### **Examination of the morphology**

Clinical results showed liver congestion as a result of increased blood pooling in addition to paleness of the limbs and the formation of a cystic in some lobes, which led to the erosion of liver tissue. As shown in (Fig.1) This is identical to what is found in the study<sup>8</sup>, where the livers of pregnant mice exposed to glue smoke at a concentration of 2500mg/kg of body weight were noted, their irregularity, congestion and the appearance of white scars on the surface of the lobes, but less severe than what was found in the livers of mice for the study Current

#### **Microscopical apperants changes:-**

The microscopic examination of the tissue livers sections, in general shows the presence of a distortion represented by the radial arrangement of the hepatic cords in the central lobular region and the surrounding areas in the dosed groups, in addition to the appearance of hepatitis with infiltration of neutrophil granulocytes . Blurred boundaries between the cytoplasm and the nucleus of hepatocytes, the asterisk indicates areas of liver congestion and cell necrosis (Fig.2) and this Similar to a study<sup>9</sup> that clarifies the role of T cells in the work of liver abscess caused by *Bacteroids fragile* as it has been found to play a key role in its formation. On the seventh day of infection of the mice with bacteria, the emergence of polymorphic leukocyte infiltration (kupffuer cell) with the destruction of the liver structure was found. According to the study . my result similar to the effect of .

The results of mice exposed to glue smoke at a dose of 1500 and 2500mg/kg showed congestion of blood vessels between lobules, massive infiltration of mononuclear inflammatory cells near blood vessels, vacuole degeneration and thrombotic necrosis of cells, but upon exposure to a dose of 3500mg/Kg of body weight of glue, which results in congestion of blood vessels and heavy infiltration of inflammatory cells around them<sup>8</sup> .

The current study also occurrence of vascular dilatation among the hepatic lobules, due to acute vein congestion . which led to the filling of the central vein and the portal area with blood components and their

infiltration into the hepatic sinusoid (monocyte). as shown amyloid with infiltration of mononuclear (kupffer cells) inflammatory cells in the necrotic area, and blurred borders between the cytoplasm and the nucleus of hepatocytes, in addition to the appearance of bile droplets and cell enlargement (Fig.3,4), and this is similar to the effect of Tamoxifen on the liver cells of the female white mice mentioned by<sup>10</sup> as well as similar results<sup>11</sup> when Dosage of mice with parkazole. The changes caused by the doses of 250,350 and 450mg/kg of body weight were distorted by microscopic examinations such as vascular congestion between the lobules, expansion of sinusitis, thrombotic necrosis of hepatic cells, congestion of central veins and focal infiltration of inflammatory cells around the blood vessels.

These changes are also similar to the results of the study<sup>12</sup>, who found that chronic exposure to inhalation of thinners by mice led to focal necrosis, granuloma and inflammation portal inflammation which are characteristic changes of hepatitis toxic and these changes may be due to oxidative stress It is a dangerous problem during drug development and use of many known drugs. For example, an overdose of acetaminophen (APAP) is currently the most common cause of acute liver failure in the United States and Great Britain .Drug-induced liver injury indicates that mitochondria are critical targets for drug toxicity, either directly or indirectly through the formation of reactive metabolites. These events together lead to cell apoptosis . The main mechanism of toxicity is the induced metabolism activation of cytochrome P450, which generates the reactive metabolite (N-acetyl-p-benzoquinone imine (NAPQI) formed after an APAP overdose depletes cellular glutathione (GSH), and adds proteins including mitochondrial proteins, which It causes oxidative stress inside the organelle and then begins to signal creeps resulting in programmed necrosis of cells, DNA fragmentation and subsequent inflammatory response, including the release of inflammatory cytokines and activation of immune cells. In contrast to APAP infection, oxidative stress-mediated by immune cells is critical in liver infection caused by conditions such as ischemia, wherein associated molecular patterns (DAMPs) from liver cells induce the production of free radicals and chemokine from Kupffer cells in the hepatic sinuses, This then causes neutrophils to infiltrate

the disease area and further oxidative stress near the liver cells, which ultimately results in mitochondrial oxidative stress and results in cell necrosis.

The effect of ginger on the liver is similar to that of the study<sup>13</sup>, which included dosing mice with varying concentrations (50-100-200)g/kg of sweet seed (Fennel) *Foeniculum vulgare*.

He found that the dose with a weight of (100-200) g/kg shows the expansion of hepatic sinusoids, hepatic cell degeneration, inflammatory cell dysfunction with vascular congestion and necrosis of the liver tissue .

Besides, the livers of white male mice suffered from degeneration and distinct deformation in the hepatocytes, the emergence of blood congestion, infiltration of inflammatory cells and emptying in the cytoplasm of hepatocytes due to the effect of the aqueous extract of coriander leaves at the dose of 250mg.

These results indicate that an oral dose of aqueous coriander leaf extract has effects. Toxicity in the liver at a dose of 250 mg per kg of body weight <sup>14</sup>

The sections revealed the presence of enlargement and significant necrosis at the site of the lobe that contains the pyogenic cyst, which showed significant erosion and necrosis of the hepatocytes as in (Fig.5,6). It is accompanied by slightly contracted and irregularly shaped hepatocytes with the cytoplasm of the fibres of the acidic pigment and a fragmented small nucleus representing the initial stages of apoptosis, accompanied by the presence of small spherical cells with a small single nucleus and the fibrous cytoplasm of the acid dye as well. These represent the late stages of apoptosis <sup>4,15</sup> .

In other passages, bile droplets were infiltrated and retained inside the hepatocytes, as shown in (Fig.3). The current study differed wit<sup>16</sup>, where it was found that the effect of the aqueous ginger extract by 400mg/kg antioxidant and prophylactic in the liver of diabetic mice after being injected with oxen known as its ability to damage pancreatic and hepatic tissue, and the reason for this difference may be dependent on the amount of Given dose <sup>3</sup>. also showed positive results for evaluating the preventive therapeutic activity of 6-gingerol and 6-shogaol on prostate cancer cells and their anti-

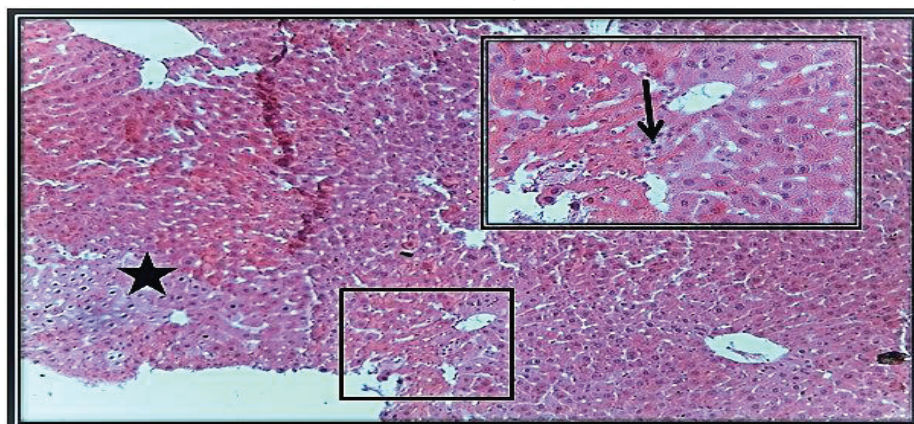
inflammatory effect on otitis media in mice, caused by the use of the active component of Croton oil, (12-otetradecanoyl-phorbol-13-acetate TPA) as the active ingredient is used to induce an inflammatory response in mice.

It is a powerful inducer of tumours, hyperplasia, inflammation and excessive expression of cyclooxygenase and cytokines when applied to mouse skin. Most of the morphological features of programmed cell apoptosis are present, such as segmented nuclei, chromatin condensation, and the presence of apoptotic bodies. It has also been observed that 8-gingerol, the shogaol mixture and 6-shogaol are more effective

in causing programmed cell death in both prostate cancer cell lines (androgen-dependent line (LNCaP) and androgen-independent cell line(PC-3)by activating the internal pathway)or the mitochondrial pathway for apoptosis. From the researcher’s point of view, it was found from this scientific evidence that the spice studied in our research has some pharmaceutical and chemical properties similar to classes of drugs capable of causing liver damage if given in high doses and thus explains its ability to affect the observed tissue structures. Therefore, based on the results of this study, it was found that excessive consumption of ginger is capable of causing liver damage and therefore should be taken with caution.

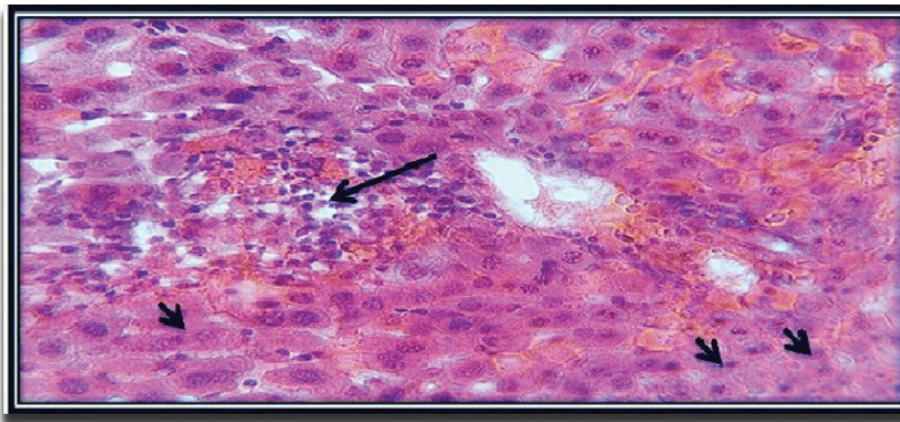


**(Figure1):**Macroscopically a mouse with a ginger spice showing signs of erosion of the ear and the tip of the tail , macroscopical the liver of the shielded mouse with ginger spice showing erosion of the tissue and the formation of the cyst(arrow)

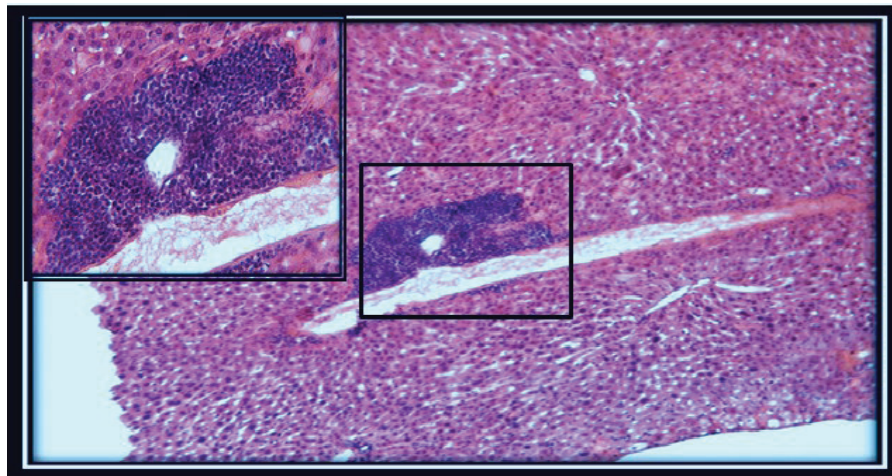


**(Figure2):**Liver dosed with a spice of ginger showing hepatitis with infiltration of neutrophil granulocytes (black arrow). Blurred boundaries between the cytoplasm and the nucleus of hepatocytes, the star indicates areas of liver congestion and cell necrosis (black star) at a strength of (X40)

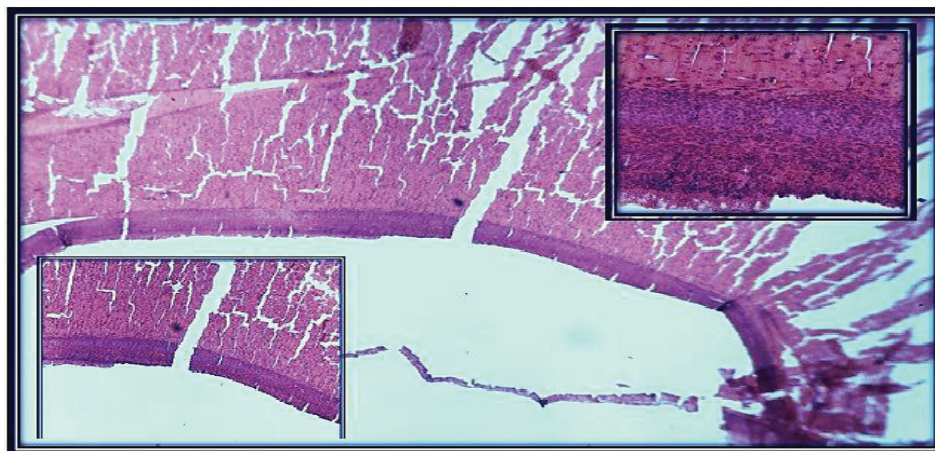




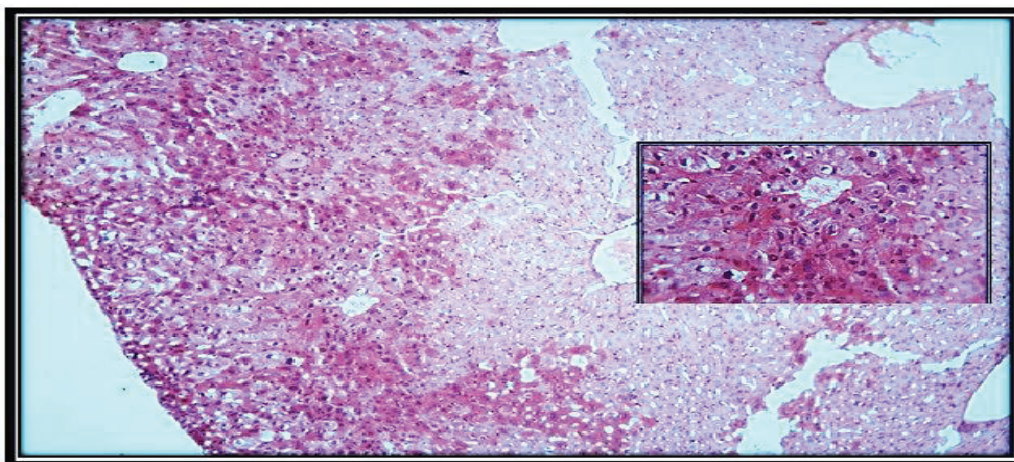
**(Figure3):**Liver dosed with a spice of ginger showing amyloid with infiltration and proliferation of neutrophils, lymphocytes in the necrotic area (black arrow) and blurred borders between the cytoplasm and the nucleus of hepatocytes (arrowhead), in addition to the appearance of bile droplets and cell enlargement. Hepatic at a power of(X40)



**(Figure4):**Liver dosed with ginger spice showing vascular congestion, infiltration of mononuclear (kupffer cells) inflammatory cells, vacuole degeneration, and hepatocellular necrosis accumulated in the extremities. (X40).



**(Figure5):**Liver dosed with a ginger spice showing the area of coagulative necrosis and tissue erosion, of (X4 , X10 andX40)



(Figure6):Liver dosed with a ginger spice showing the presence of dark areas coagulative necrosis and faded ones with and there is loss cellular detail with infiltration inflammatory cell ( kupffer cell ) (X4 , X10).

### Conclusions

To begin with, we say too much of something is harmful, no matter how beneficial it is, as it has been proven that eating ginger in high and repeated doses leads to the damage that was discovered in the livers of experimental animals. It damages the structural structure of liver tissue and the damage may reach erosion in parallel with the experimental results and the reported cases. These results coincide with the term “Toxic hepatitis”. But despite all these symptoms and compared to the dose administered with the weight of the mice, the mortality amount was If you compare the dose scale given with the bodyweight of the mice, we find that the death amount is low or the resistance of the mice to it may be high.

### Recommendations

1. Carry out a biochemical and physiological study to see the effect of spice
2. Conducting a study at the level of the electron microscope to find out the effect of spice on the cellular structure

**Ethical Clearance** - Taken from Ethics Committee of Diyala Medical College

**Source of Funding** - Self founded

**Conflict of Interest** - Nil

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