Iraqi Journal of Science, 2026, Vol. 67, No. 6, pp: 3250- 3263
DOI: 10.24996/ijs.2026.67.6.15

ISSN: 0067-2904

Effect of Bitter Almond Extract on Some Physiological and Histological Parameters in Male Rats

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Received: 21/12/2024 Accepted: 29/6/2025 Published: 30/6/2026

Abstract

Bitter almond is a peach fruit from the Rosaceae family. Despite its diverse health benefits, some harmful and toxic properties can be produced in the body as it contains hydrocyanic acid, which gives a bitter taste. This study was conducted to investigate the harmful toxic properties of bitter almonds that can be produced in the body as they contain hydrocyanic acid; despite its many beneficial secondary metabolites. Methods: Whole bitter almond seeds collected in Iraq were extracted and dosed to rats. 20 Westar albino male rats weighing (200- 250) gm were obtained from the Biotechnology Center / AL-Nahrain University. The animals were divided into 4 groups (control group administered distill water orally only, T1 = first tested group administrated 100 mg /kg body weight, T 2 = second treated group administrated 200 mg / kg B.W. and T 3 = third treated group administrated 300 mg / kg B.W. All groups were treated by oral route every day for four weeks. Then, samples were collected for histological study of the organs of the liver and kidneys. Results: There was a significant ($P \leq 0.05$) rise for ALT, AST, ALP, LDH, urea, creatinine, uric acid, cholesterol, triglyceride and a significant ($P \leq 0.05$) increase in LDL for both T2 and T3 in comparison with T1 plus control group. The total serum bilirubin explained no significant ($P \leq 0.05$) difference between treated groups with the control. The HDL cleared a significant ($P \leq 0.05$) decrease in T3 with comparison with the control group, T1 and T2. After examining tissue sections with a compound microscope, it was found that various changes occurred, such as; bleeding, cell necrosis, congestion and damage to blood vessels in both organs.

Keywords: bitter almond. Liver enzyme, kidney, liver, rats.

تأثير مستخلص اللوز المر في بعض المعايير الفسيولوجية والنسيجية في ذكور الجرذان

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الخلاصة

اللوز المر هو ثمرة خوخ من العائلة الوردية. على الرغم من أن اللوز المر له فوائد صحية مختلفة، إلا أن له آثار ضارة وسامة على الجسم، وذلك لاحتوائه على حمض الهيدروسيانيك الذي يسبب الطعم المر. بالإضافة إلى المكونات النشطة مثل الجلوبيولين والألبومين والأحماض الأمينية وغيرها.طرق العمل : تم استخلاص بذور اللوز المر الكاملة التي تم جمعها في العراق وتم إعطاؤها بجرعات مختلفة للجرذان. تم

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الحصول على 20 جرذ ألبينو ذكر وزنة (200− 250) غم من مركز التقنيات الاحيائية / جامعة النهرين. تم تقسيم الحيوانات إلى 4 مجموعات: (مجموعة السيطرة أعطيت الماء المقطر عن طريق الفم فقط، T1 = المجموعة المعاملة الأولى أعطيت 100 ملغم / كجم من وزن الجسم ، T 2 = المجموعة المعاملة الثانية أعطيت 200 ملغم / كجم من وزن الجسم وT3 = المجموعة المعاملة الثالثة أعطيت 300 ملغم/كغم من وزن الجسم. كل المجاميع المعاملة اعطيت الجرع عن طريق الفم يومياً لمدة 4 أسابيع. ثم جمعت العينات للدراسة الفسلجية و النسيجية لأعضاء الكبد والكلى. النتائج : أظهرت النتائج زيادة معنوية ($P \leq 0.05$) في مستويات ALT، AST، ALP، LDH، اليوريا، الكرياتينين، حامض اليوريك، الكوليسترول، الدهون الثلاثية وزيادة معنوية ($P \leq 0.05$) في LDL في T2 و T3 مقارنة مع T1 ومجموعة السيطرة. نتائج البيليروبين أظهرت عدم وجود فروق معنوية ($P \leq 0.05$) بين المجموعات المعاملة مع السيطرة. انخفض مستوى HDL بشكل ملحوظ ($P \leq 0.05$) في T3 مقارنة مع مجموعة السيطرة، T1 وT2. وبعد فحص المقاطع النسجية بالمجهر المركب، تبين حدوث تغيرات مختلفة، مثل النزيف ونخر الخلايا والاحتقانات وتلف الأوعية الدموية في كلا العضوين.

1. Introduction

Almonds; are crop belonging to the Rosaceae family. Usually positioned in the subfamily Amygdaloideae or Prunoideae, however occasionally, it is located in their family (Prunaceae) or (Amygdalaceae). Almond trees are small, deciduous trees that grow to 4 - 10 m in height, and up to 30 cm in trunk in diameter [1]. Three kinds of almonds yield nuts, some are eatable, and others are not. The first kind yields sweet nuts, which are eatable. The other yields toxic bitter nut, and the third kind yields a combination of the two. Two main types of almonds are cultivated commercially, which are, *Prunus amygdalus dulcis* (sweet almonds) and *Prunus Amygdalus amara* (bitter almonds). Both produce plants that could be set apart according to the base of flowers, as the sweet almond flowers are white, even though flowers of bitter almonds are in color pink [2]. Bitter almond is a fruit that has considerably excessive amounts of poisonous phytochemicals termed glycoside amygdalin. Therefore, its excessive consumption (toxic human acceptable dose) can lead to possible poisoning and sometimes death. Bitter almond shoots are pink and somewhat shorter and flatter fruits than sweet almonds with white shoots [3]. Several researches have been led to explore the advantages of bitter almonds as to avoid diseases and heal them [4]. The bioactive elements in almonds are many, for instance, albumin globulins, amino acids for instance; histidine, arginines, phenylalanines, lysines, valine, leucine, methionine, tryptophan, besides cysteine [5]. Almonds consist of proteins and some minerals such as magnesium and calcium. Moreover, their richness in dietary fiber, vitamin B, essential minerals and monounsaturated fat [6]. Bitter almond is an incredible antioxidant, antimicrobial, and antitumor in vitro, in which effects of water, methanol, and ethanol kernels extracts were revealed [7]. Almonds contain some phytochemicals with antioxidant properties. Bitter almonds are rich in flavonoid and phenolic compounds and fat-soluble vitamins. E vitamin is a vitamin with ideal antioxidant effects [8]. Amygdalin is one of the main ingredients of bitter almonds, has been called B17 in the last years, and has been acknowledged to be a unique ingredient for cancer healing for nearly a century. Studies confirmed that bitter almond aqueous, ethanolic, and methanolic extracts can prevent cancer cell line growth [9]. Bitter almonds are used for anti-depressant effects, memory enhancing effects and anti-aging activity. Bitter almonds have antifungal activity, anxiolytic activity, hyperlipidemia activity, anti-diabetes activity, laxative activity, anti-depressant activity, hepatoprotective activity, antiparkinsonian effect, immunostimulant properties, hyperlipidemia activity, and inflammation [10]. Liver is considered the biggest internal organ in human's body as it acts as key part of the metabolism and detoxification of many drugs, chemicals, and any other toxic compounds. Oxidative stress (OS) is a

biochemical disorder that happens in the body, making several kinds of reactive species, for instance, reactive oxygen species (ROS) plus reactive nitrogen species (RNS). OS is considered one of the pathological conditions that initiate and progress liver damage by inducing irreversible alterations of the lipid membranes, DNA and proteins and, more importantly, by modulating pathways that control biological functions [11].

Kidneys are organs with complex structures essential for human persistence since embryonic development. Each cell in renal parenchyma is very specialized in electrolyte, volume maintenance, and waste homeostasis. The kidney has different structures of nephrons, the functional part of the kidney. The glomeruli, plus the foremost part of urinary tubules, named the proximal-convoluted tubules (PCT), are situated in the cortex. After PCT comes to a loop-of-Henle (hairpin-like-structure), enters the medullas, then back to the cortex in order to bond with distal-convoluted-tubules (DCT). Lastly, nephrons drain into the collecting duct through connecting tubules. The glomeruli filter huge amounts of blood, as the tubular system converts it into urine by secretion and reabsorption of solutes and free water [12, 13].
This study was conducted to investigate the harmful and toxic properties of bitter almonds that can be produced in the body as they contain hydrocyanic acid, despite their many beneficial secondary metabolites.

2. Materials and Methods

2.1 Almond seeds extraction and HPLC analysis

Bitter almond seeds were collected in Iraq. The extraction was carried out using a Soxhlet apparatus using ethanol (80 %) extract [14]. Standard procedure was used to discover the active ingredients by chemical tests of plant methanolic extracts. Mayers and Wagners reagents were used to test for alkaloids, while flavonoids were tested by using the lead acetate test plus NaOH test, and saponins presence was tested by foam test and $HgCl_2$ test. On the other hand, tannins and terpenoids tests were done using H_2SO_4 and chloroform tests [15]. Samples of extract were analyzed using High-performance layer chromatography analysis-HPLC, model (SYKAM, GERMANY) to investigate various ingredients seen in fractions. Pump-model (S2100 quaternary-gradient pump), auto sampler-model (S5200), detector (UV S2340), column-oven model (S41145). The mobile phase was methanol with formic acid and D.W (70:5:25), the column was C18- ODS (25cmx4.6mm), and the detector was UV 280nm at 1.0ml/min flow rate [16]. After that, different doses are given daily to rats' orally.

2.2 Animal management

This research paper was conducted between September 2023 and September 2024 in the Biotechnology Center / AL-Nahrain University under the improvement of the scientific research ethics committee of the biology department in the College of Science for Women. In this study, 20 Westar albino male rats weighing (200- 250) gm were obtained from the Biotechnology Center / AL-Nahrain University. All institutional and national guidelines for the care and use of laboratory animals were followed. The animals were kept in the same center, with the setting of controlled heat and 12 h. dark-light cycle.

2.3 Experimental design

Animals were divided into 4 groups, each group involved 5 animals, and three treated groups administrated the dosage of ethanoic extract orally for 4 weeks [17]. As shown in Table 1.

Table 1: animal groups and their dosages of bitter almond extract.

Groups	Dosage mg - kg
Control	Distill water
T 1	100
T 2	200
T 3	300

Blood sampling was done by heart puncture technique; blood samples were drawn from male rats after 4 weeks. The blood samples were placed in gel activated tube and centrifuged for 15 min. at 2000 rpm. The obtained serum was separated by pipette, placed in a sterile Eppendorf tube, and frozen at -20 ˚C for biochemical analysis.

2.4 Biochemical and histological analysis

The measured parameters are alanine- transaminase (ALT), aspartate-aminotransferase (AST), alkaline-phosphatase (ALP), lactate-dehydrogenase (LDH), total serum bilirubin, urea, creatinine, uric acid, cholesterol, triglycerides, high - density lipoprotein (HDL), and low - density lipoprotein (LDL). Treated animals were sacrificed after 4 weeks of experiments for histological study, kidney and liver were removed and then fixed in 10 % formalin. The tissues were routinely processed and sectioned by rotary microtome and stained with hematoxylin and eosin for histological studies. Then the sections were examined using a compound microscope.

2.5 Statistical-Analysis

Program of Statistics-Analysing System SAS (2018) was utilized to spot any different factors in the research variables. LSD test [ANOVA] was utilized to differentiate significance amongst means. Also, the Chi-square test was utilized to differentiate significance between percentages (0.0 5 and 0.01 probability) in the current study [18].

3. Results

The phytochemical screening of the bitter-almond extract revealed the presence of alkaloids, flavonoids, saponins, and tannins (Table 2). Bitter almond compounds were investigated by HPLC analysis, which showed the presence of 6 peaks (quercetine, naringenin, catechine ,kaempferol, gallic acid, and apigenin) (Figure 1) and its chromatograms compared to standards are illustrated in figure 2.

Table 2: The concentrations of the active compounds of bitter almond extract.

Compound	Gallic acid	Naringenin	Qurcetine	Kaempferol	Catechine	Apigenin
Concentration	41.5	35.9	30.2	20.1	18.9	14.9

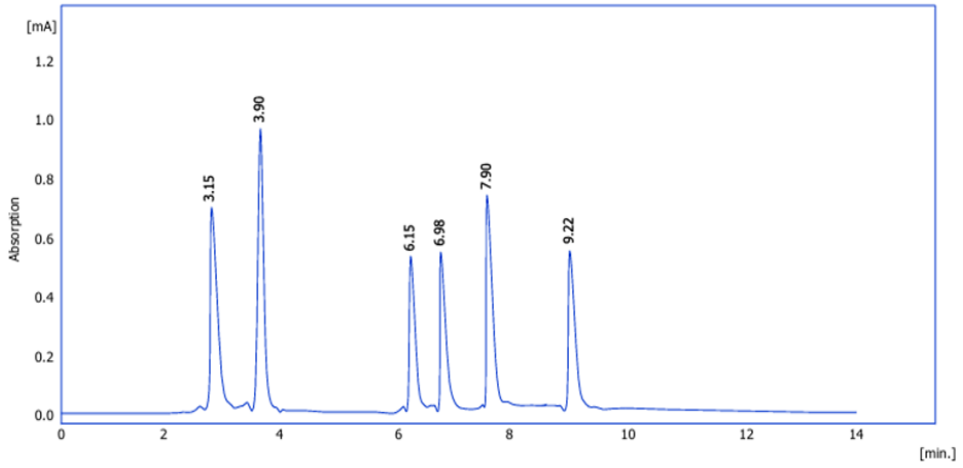

Figure 1: Chromatogram quercetine, naringenin, catechine, kaempferol, gallic acid and apigenin of bitter almond extract.

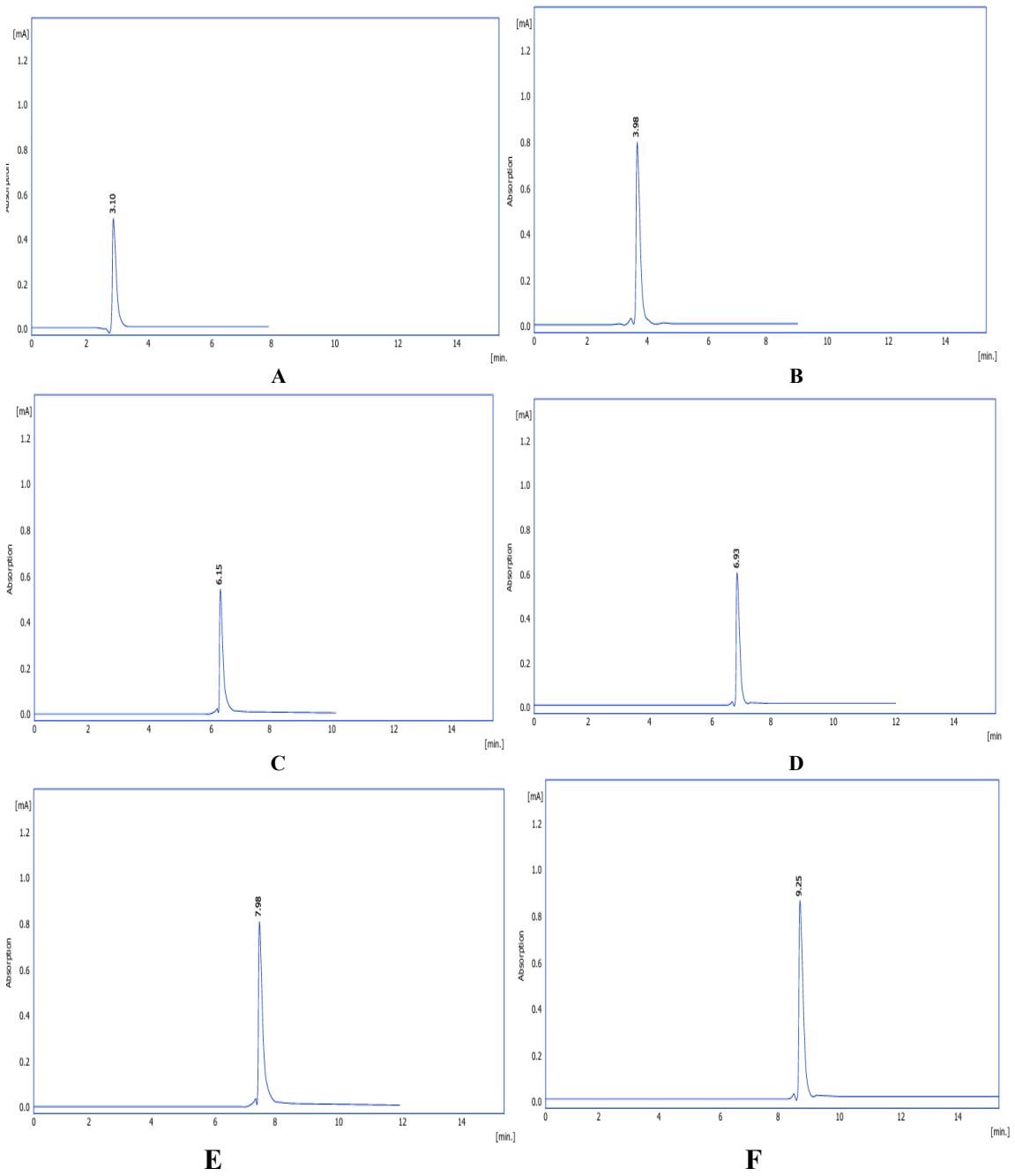

Figure 2: Chromatogram A: quercetine, B: naringenin, C: catechine, D: kaempferol, E: gallic acid and F: apigenin standard.

The physiological parameters of our results revealed a substantial (P≤ 0.05) raise of ALT in the T1 - treated group in comparison with the control. While T2 significant (P≤ 0.05) increase in comparison with the control, nonetheless, no significant (P≤ 0.05) difference with T1, and T3 significance (P≤ 0.05) rise in contrast per control with non-significantly (P≤ 0.05) difference with T2.

The AST explained a significant (P≤ 0.05) increase in comparison by means of the control, T2 is significantly (P≤ 0.05) improved in comparison by means of the control but non-significance difference (P≤ 0.05) with T1. Although T3 has a significant increase (P≤ 0.05) in comparison with the control with a non-significant difference (P≤ 0.05) with T1 and

T2. The ALP results showed T1 has a significant increase (P≤ 0.05) in comparison by means of the control, T2 and T3 have significant difference (P≤ 0.05) by means of T1 with no significant difference (P≤ 0.05) with the control. The LDH T1 and T2 cleared a significance (P≤ 0.05) raise in comparison with control plus T3, while T3 showed significant differences (P ≤ 0.05) with T1 and T2 with no significant differences (P ≤ 0.05) with control. The three treated groups of total serum bilirubin explained no significant differences (P≤ 0.05) with the control or significant differences (P≤ 0.05) between all treated groups, as shown in Table 3.

Table 3: Explained comparison between difference groups in liver enzyme, LDH, and T.S. Bilirubin

Groups	Mean ± SE				
	ALT	AST	ALP	LDH	Total Serum Bilirubin
Control	25.33 ±1.08 c	19.29 ±0.76 c	67.48 ±3.22 b	12.37 ±0.61 b	0.750 ±0.06
T 1	36.94 ±2.17 a	33.82 ±1.64 a	83.65 ±3.95 a	27.90 ±1.26 a	0.909 ±0.14
T 2	32.60 ±1.82 ab	29.99 ±1.07 a	70.38 ±3.16 b	27.21 ±1.42 a	0.791 ±0.10
T 3	30.53 ±1.69 b	23.95 ±1.15 b	65.46 ±3.52 b	14.89 ±0.56 b	0.667 ±0.04
LSD value	5.382 **	4.874 **	8.027 **	5.019 **	0.297 NS
P- value	0.0084	0.0006	0.0079	0.0001	0.081
Means different letters of similar columns differ significantly. **(P≤ 0.01)					

Urea in the T1 group showed a significant increase (P ≤ 0.05) in comparison with the control and T3. T2 showed a significant increase (P ≤ 0.05) in comparison to the means of the control with no significant difference (P≤ 0.05) by means of T1, and T3 is the lower significant (P≤ 0.05) differences in comparison with T1 and T2 with no significantly (P ≤ 0.05) differences by means of control. The group T1 revealed a significant increase (P ≤ 0.05) of creatinine in comparison with control, T2 and T3. While T2 and T3 resulted in significant differences (P≤ 0.05) with T1 with no significant differences (P ≤ 0.05) with control. The uric acid in the T1 explained a significant increase (P≤ 0.05) in comparison with the control, T2 showed a non-significant difference (P ≤ 0.05) with both control and T1. T3 resulted in significant differences (P≤ 0.05) with T1 and no significant difference (P≤ 0.05) with both control and T2, as shown in Table 4.

Table 4: Showed a comparison between different groups in creatinine, urea and uric acid.

Groups	Mean ± SE		
	Creatinine	Urea	Uric Acid
Control	0.352 ±0.07 b	15.87 ±0.78 b	4.167 ±0.32 b
T 1	1.080 ±0.25 a	26.29 ±1.28 a	5.778 ±0.57 a
T 2	0.549 ±0.11 b	25.67 ±1.04 a	4.909 ±0.29 ab
T 3	0.380 ±0.08 b	17.02 ±0.84 b	3.837 ±0.22 b
LSD value	0.4073 **	3.117 **	1.089 *
P- value	0.0018	0. 0001	0.0285
Means different letters of similar columns differ significantly. **(P≤ 0.01), * (P ≤0.05)			

Concerning cholesterol and triglycerides, T1 cleared significant differences (P ≤ 0.05) with both T2 and T3 with significant differences (P≤ 0.05) by means of the control. Although T2 and T3 exhibited significant differences (P≤ 0.05) with both control and T1.
The HDL in theT1 and T2 explained no significant difference (P≤ 0.05) by means of control but a significant difference (P≤ 0.05) by means of T3. Though T3 exposed significant differences (P≤ 0.05) with control, T1 and T2. The LDL in the T1 resulted in a non-significant difference (P ≤ 0.05) by means of the control, but a significant difference (P≤ 0.05) by means of T2 and T3. T2 has significantly increased (P≤ 0.05) in comparison with control and T1. T3 significantly (P≤ 0.05) improved in comparison with the control, T1, and T2 as shown in Table 5.

Table 5: Explained comparison between different groups in the lipid profile.

Groups	Mean ± SE			
	Cholesterol	Triglyceride	HDL	LDL
Control	171.15 ±7.02 b	171.32 ±8.52 b	36.14 ±2.41 a	104.29 ±5.47 c
T 1	188.01 ±7.64 b	197.31±11.37 b	39.11 ±2.59 a	112.32 ±7.21 c
T 2	245.72 ±14.59 a	237.47 ±13.08 a	40.32 ±2.65 a	153.71 ±8.93 b
T 3	248.69 ±17.94 a	266.39 ±15.78 a	27.04 ±1.24 b	172.07±12.37 a
LSD value	22.48 **	31.097 **	6.522 **	10.865 **
P- value	0.0052	0.0019	0.0001	0.0063
Means with different letters in the same columns differ significantly, ** (P ≤0.01)				

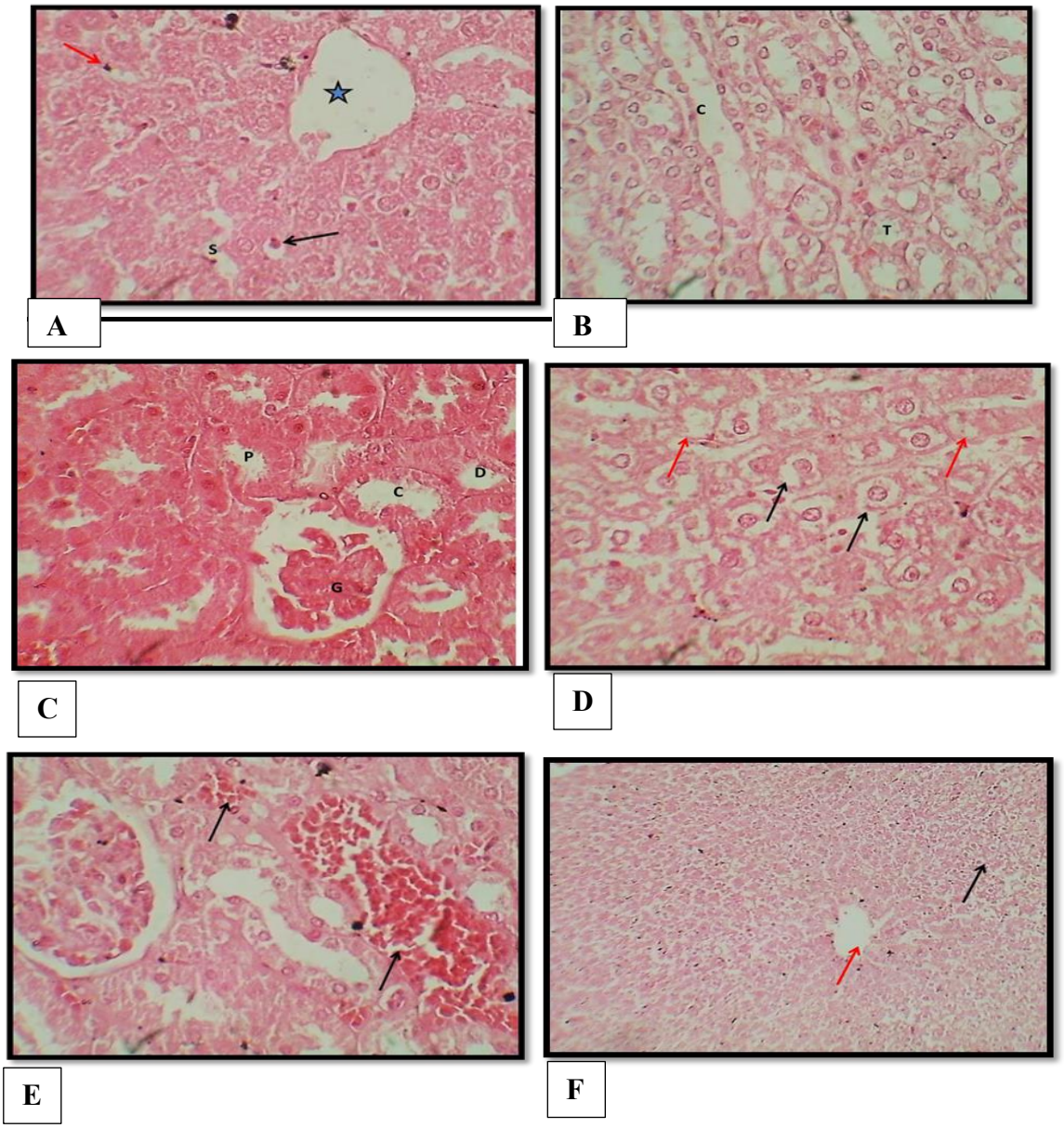

Figure 3: (**A**) histology of liver lobule [control] shows central-vein (asterisk), hepatocyte (black arrow), sinusoid (S) and kupffer-cell (red arrows). Hematoxylin Eosin stain. 400x. (**B**) section of the liver (T1) shows a normal central vein (red arrow) and a normal arrangement of hepatic cords with mild zonal cellular swelling of hepatocytes (black arrow). H and E stain.100x. (**C**) Section of the liver lobule (T1) shows: mild cellular swelling of some hepatocytes (black arrows) and necrosis (red arrow). H and E stain.400x. Histology of kidney (T2): (**D**) histology of the renal-cortex [control] indicates glomeruli (G), collecting-tubules (C.), proximal (P), and distal-convoluted tubule (D). Hematoxylin Eosin stain.400x.(**E**) histology of renal-cortex (T1) displays typical glomerulus and renal-tubules with mild interstitial tubular hemorrhage (arrows).H and E-stain.100x.(**F**) histology of the renal-medulla (T1) displays a typical form of the collecting-tubules (C), thick segments (T) of Henle's loop .H and E stain.400x.

The histological features of the liver and kidney of the T1 group are illustrated in Figures A-F. The liver displays a typical central-vein plus a normal arrangement of the hepatic cords with mild zonal cellular swelling of hepatocytes (Figure 3 B) compared to control (Figure 3

A) with mild cellular swelling of some hepatocytes and coagulative necrosis (Figure 3 C). The kidney revealed minor interstitial tubular hemorrhage (Figure 3 E) compared to control (Figure 3 D). While the figure of the renal medulla was similar to that of the control group (Figure 3 F).

In T2 groups, the liver showed enlargement and congestion of the central-vein (Figure 4 A). The hepatic cords revealed moderate zonal cellular swelling and necrosis of hepatocytes (Figure 4 B). Histopathological figures of T2 renal-cortex and medulla exhibited regular glomerulus and all tubular segments of nephron (Figure 4 C), with mild interstitial tubular hemorrhage (Figure 4 D).

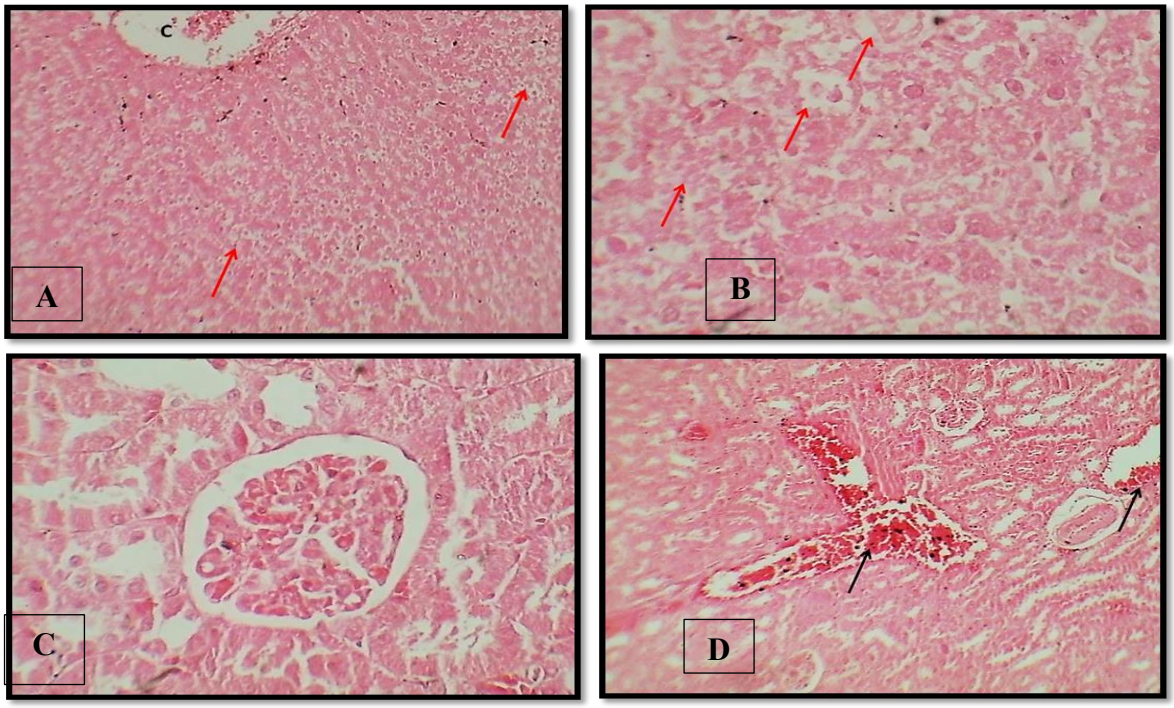

Figure 4: Histology of liver (T2) (A) Enlargement and congestion of central-vein (C) plus moderate zonal cellular swelling of hepatocytes (arrows). H and E stain.100x. (B) Section of the liver lobule (T2) shows cellular swelling and necrosis hepatocytes (arrows). Hematoxylin Eosin stain .400x. Histology of kidney (T2) (C) histology of renal-medulla (T2) displays a typical form of glomerulus, and renal-tubule. Hematoxylin Eosin stain.400x. (D) Histology of renal-cortex (T2) displays regular-renal tubules with mild interstitial tubular hemorrhage (arrows).H and E stain.100x.

The histopathological figures in the T3 group of the liver showed severe dilation and congestion of the central vein. The hepatic cords revealed severe diffused cellular swelling and necrosis of hepatocytes (Figure 5 A). A histopathological figure of the renal-cortex exhibited typical glomerulus with marked damaged epithelial renal tubules and vascular degeneration (Figure 5 B, and C).

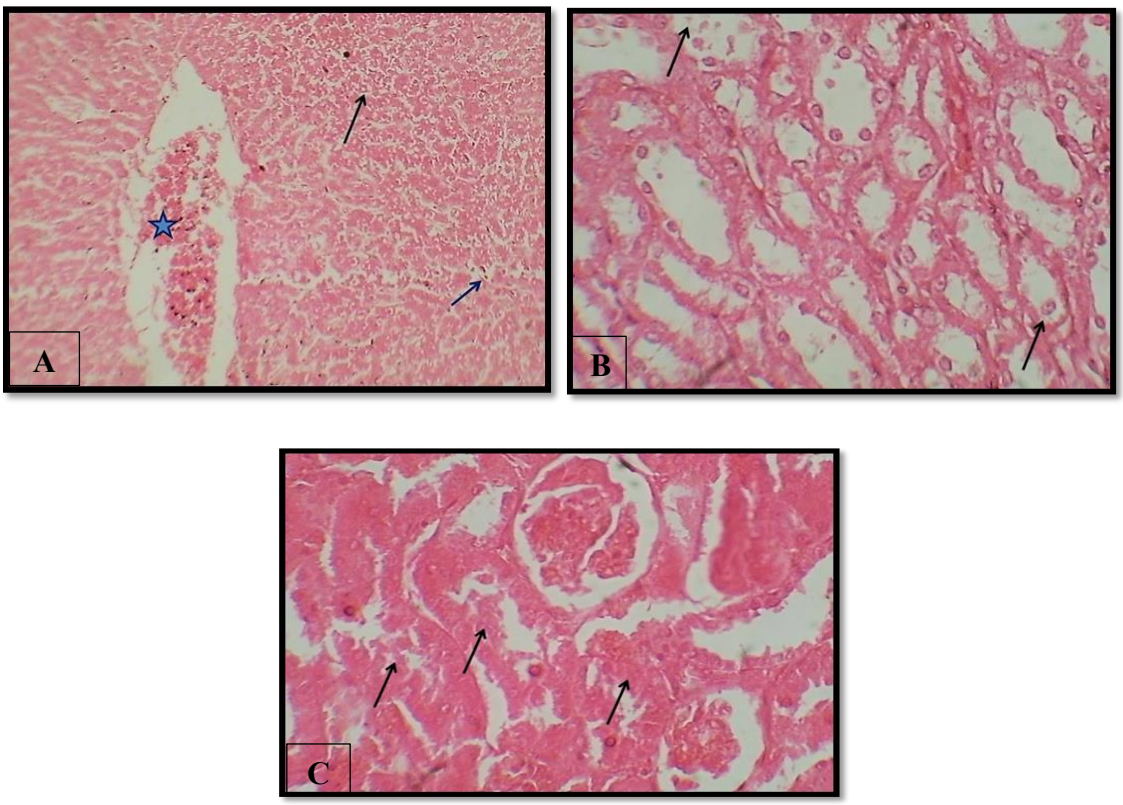

Figure 5 : Histology of liver (T3): (A) displays a severe enlargement and congestion of the central-vein (asterisk), cellular swelling plus necrosis hepatocytes (arrows). Hematoxylin Eosin stain. 400x. Histology of kidney (T3); (B): histology of the renal- cortex (T3) illustrates deterioration of renal tubules and damaged epithelial tubule (arrows). Hematoxylin Eosin stain.400x. (C): histology of renal-medulla (T3) illustrates vascular degeneration of renal-tubules (arrows). Hematoxylin Eosin stain.400x.kidney.

4. Discussion

Almonds have two types: sweet almonds and bitter almonds. The sweet ones are eatable whereas the bitter ones are non-eatable and noxious. Bitter ones are somewhat shorter and broader than the sweet ones. Sweet almonds comprise 50% fatty oil. Bitter almonds yield hydrogen cyanide [19]. The phytochemical screening of the current study of the bitter almond extract revealed the presence of alkaloids, flavonoids, saponins, and tannins. Previous studies of bitter almond analysis imply that seeds have fatty acids, mainly oleic and linoleic besides phenolic and flavonoid compounds. Many studies stated that bioactive compounds differ from one plant to another plant of the same genus and even in the same species in different parts, which is due to many factors such as soil and environment as it may create variant chemical compounds although in the same country [20, 21]. Previous almond phytochemical studies showed it implies phenolic compounds, especially flavonoids like myricetin, naringenin, and kaempferol, and phenolic acids such as caffeic acid, ferulic acid, vanillic acid, hydroxyl and cinnamic acid, also proanthocyanidin compounds are present [22].

Bitter almonds contain greater quantities of toxic phytochemicals named glycoside amygdalin, which it's too much use a toxic allowable dose for humans could initiate intoxication and sometimes death [23]. Amygdalin and prunasin are the core elements of bitter almonds. Prunasins are cyanogenic monoglucosids seen in several parts of almonds. Prunasin is produced early in fruit development and transforms into diglucoside amygdalin by nuclear development and maturation processes [24]. Cyanogenic-glycoside is formed by numerous plants and forms cyanide-hydrogen by hydrolysis. A method is known as

cyanogenesis, which occurs in bitter almonds [22]. Moreover, bitter almonds also contain great quantities of quercetin and catechins, which studies revealed could provoke liver toxicity with high doses [25]. Mammals have an efficient mechanism of detoxifying cyanide by alteration throughout intramitochondrial enzymes and rhodaneses to lessen lethal compounds such as thiocyanate SCN, which is eliminated mostly in urine. These enzymes are commonly dispersed all over tissues but essentially in the liver and kidney [21]. The study corresponding with Gauhar and Alam [22] that exposure to a long period of cyanide led to a significant rise ($p \leq 0.05$) in ALT, AST, creatinine, and urea. Our study showed a significant increase ($p \leq 0.05$) in AST, ALT, ALP, LDH, bilirubin, creatinine, uric acid, urea, cholesterol, HDL, and LDL in all treated groups in comparison with a control group, and this agrees with another study that explained same results [23].

The histopathological findings indicate significant hepatorenal toxicity in treated mice. These alterations suggest acute oxidative stress and cellular apoptosis mediated by cyanogenic compounds, most importantly amygdalin [24]. Additionally, renal cortical damage underscores the extract nephrotoxic potential, consistent with findings on amygdalin-induced mitochondrial dysfunction in proximal tubules [25].

Amygdalins (D-Mandelonitrile-6-O--D-glucosido-D-glucoside) are disaccharides that occur by nature, very concentrated in fruits kernels of Rosaceae species, such as bitter almonds, peach, and apricot [26]. Amygdalins are nouns as a cyanogenic glycoside as every molecule of it has a group of nitriles that are eliminated by means of toxic cyanide anions with the help of beta-glucosidases. Orally administered amygdalin discharges cyanide into the bloodstream and causes toxicity in the human body [27, 28]. A major part (80%) of cyanides is detoxified by the liver, caused by thiosulfate-sulfur-transferase enzymes (such as rhodanase [E. C. 2. 8.1 .1]), as it is extant in mitochondria of the liver [26]. Human's fatal dosage of intravenous injections of amygdalins is 5g. It is assumed that eating 50 bitter almonds in a short time could be a fatal dosage for adults; moreover, a dosage of 5 to10 bitter almonds could be lethal for a kid. The deadly dose for adults of amygdalins is valued 0.5–3.5 mg /kg B.W. [28].

Amygdalin induces reactive oxygen species (ROS) release, and the following benzaldehydes overproduction might trigger protein oxidation. Which can induce toxicity and negative effects on the hepatic tissues oxidative balance with obvious effects in mice histopathology [29]. The cyanides synthesized during amygdalin hydrolysis will binds with cytochrome-oxidase c plus a3, inhibit breathing plus DNA-synthesis by ROS, block cell nutrition, and then, lastly, induce autolysis. The anaerobic bacteria of the gut generate huge amounts of lactic acid by fermentation of pyruvate, which lifts glucosidase action, as it is hurtful due to amygdalins hydrolyzing to cyanides and augments toxicity [30].

The action mechanism of cyanides leads to intracellular hypoxia via binding reversibly within a mitochondrion to mitochondrial cytochrome-oxidase-a3, which is considered compulsory for oxidative-phosphorylation [31]. The attachment of cyanide to a ferric ion in cytochrome-oxidase-a3 obstructs the respiratory chain of a terminal enzyme, then ends electron-transportation plus oxidative-phosphorylation [32]. Cyanides induce toxicity because elevated dosages of bitter almonds need mutual disturbance and treatment in order to avoid disease [33]. When small quantities of cyanogenic elements are ingested, the general way of detox is hydrocyanic acid transformation to thiocyanates within the liver plus kidney [34]. Essentially, the cyanide concentrations are greater within erythrocytes than in the plasma [35]. Studies have revealed that levels of cyanide in various tissues of humans are about 0.03 in stomach juice, 0.50 in blood, 0.03 in liver, 0.11 in kidneys, 0.07 in brain, and finally 0.20

in urine (mg /100g) [36]. Kidney stones could be a health problem if numerous almonds are digested. Kidney stones are made when a high level of calcium oxalates is present and kept in the body, and they do not get excreted. Almonds are rich in oxalates, which are levels in nuts that have better absorption by the body than any other foodstuff. That, for the hazard of forming painful kidney stones plus bladder issues, should keep you away from eating too many almonds at once. Mainly for ones who are disposed to kidney problems, and have a history of formation of kidney stones or self-restraint issues [37].

5. Conclusion

Our current research has dealt with the study of the effect of ethanoic extract of bitter almond seeds to know its effect on the liver and kidneys. Therefore, it concluded from the results that the presence of amygdalin in bitter almond seeds, and what results from the metabolism of amygdalin, which is cyanide, has been observed to cause significant damage to the liver and kidney tissues, especially in high concentrations and long periods of consumption. In some cases, when the high dosages of cyanide was consumption so, it observed many circumstances of intoxication by cyanide due to excess seeds consumption of comprising amygdalins.

6. Recommendation

Future studies are recommended to investigate the action mechanisms of anticancer effects of bitter almond and amygdalin, the most important compound of this plant, in animal models to find nontoxic and therapeutically efficient doses. Next, these doses can be studied in clinical trials to treat different cancers.

Conflict of Interest: The authors declared no conflicts of interest regarding this manuscript publication.

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