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Anti-cancer Characteristics of Bee Venom and Assess its Anti- Tumor Effect Against Hepatocellular Carcinoma Induced in Male Albino Mice

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Abstract

HEPATOCELLULAR carcinoma (HCC) is one of the world's most prevalent and serious diseases, known for its high mortality rate. In recent years, there has been a strong trend towards herbal-based alternative medicine as an effective and safe treatment for various diseases. Herin, the efficiency of bee venom in HCC mice and evaluation its potential as a cancer resistance agent were investigated. In our study 50 mice were divided into 5 groups. The Negative control group, the Positive group was injected with CCl_4 only, the treatment group received CCl_4 followed by bee venom (0.1mg/kg), the protective group received bee venom (0.1mg/kg) followed by CCl_4 and the chemotherapy group received CCl_4 followed by cisplatin. Liver tissue and blood samples were collected from the mice after the experiment was completed. The positive group exhibited histological characteristics of HCC, while mice treated with bee venom and cisplatin showed partial restoration of normal liver architecture. Administration of bee venom resulted in a significant decrease in liver enzymes compared to the positive group. Furthermore, a significant decrease in Tumor Growth Factor (TGF-β1) (55.5±4.33), Tumor Necrosis Factor (TNF-α) (48.5±5.485), and Anti-liver Kidney Microsomal Antibody (LKMA) (11±1.155) levels compared to the positive control group (242.3±10.68) (499±9.815) (80.33±7.219) ($P \leq 0.05$) respectively. Additionally, there was a significant increase in Interleukin-12 (IL-12) (198±10.39)compared to the positive group (50.33±2.603)($P \leq 0.05$). In conclusion, the results indicated a significant therapeutic effect of bee venom against HCC, as evidenced by improvements in serum liver enzymes, pro-inflammatory cytokines, antitumor cytokines, and immunological marker.

Keywords: HCC; Bee venom; TGF-β1; TNF-α; LKMA; IL-12.

Introduction

The liver is one of the most important organs that contributes to many biological operations such as lipid and carbohydrate metabolism. Additionally, the liver can detoxify various toxins and waste products resulting from metabolic actions. Continued exposure of the liver to certain harmful factors can lead to liver damage and hepatocellular carcinoma [1]. Hepatocellular carcinoma (HCC) is a serious health condition with increasing incidence and mortality rates [2, 3]. The main risk factors for liver cancer include genetic changes, increased alcohol intake, exposure to carcinogenic chemicals, viral infections such as hepatitis B and C, and metabolic conditions like obesity and diabetes [4, 5].

In its early stages, liver cancer does not produce many symptoms and is hard to detect. This leads to a lack of timely diagnosis of the disease [6]. Accordingly, patients with late-stage cancers are not eligible for surgical processes, and chemotherapy reveals low availability efficiency for HCC patients diagnosed in advanced stages, as HCC is regarded as a highly malignant tumor [7]. After assessing the seriousness of the effects of radiotherapy and chemotherapy and their harm to the body [8].

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Scientists have turned to using natural products as alternative or an adjunct to treatment. Natural products including certain species' venom show great inhibition for the development of cancer mechanisms, causing a stimulating effect on disease prevention mechanisms through antitumor activation, antiproliferative, anti-inflammatory, and anti-oxidant systems [9]. Bee venom is classified as a complex material. Apis mellifera is the producer of this substance. It is noted that bee venom is widely used in the treatment of several diseases most notably, cancer [10]. The use of live bee stings, BV injections, and BV acupuncture are only a few of the long-established BV therapeutic techniques.

It is a safe form of acupuncture and has intriguing pharmacological features from a biotechnological perspective, notwithstanding its clinical issues, toxicity, or allergies. BVA is a widely used medication because of the bioactive chemicals extracted from BV and its pharmacological effects. In the last 20 years, a significant amount of research on BVA has emerged, and it has gradually gained popularity as an alternative therapy [11]. Melittin, apamin, mast cell degranulating peptide (MCD), hyaluronidase, phospholipase A2, and physiologically active amines like histamine and dopamine are the primary components of bee venom [12].

Recently, numerous effects of B.V. have been documented, including necrosis, cytotoxicity, effects on proliferation, induction of apoptosis, and reduction of the growth of various cancer cell types. Even through B.V. proteins can target a variety of cancer cells, including those in the kidneys, liver, prostate, lung, breast, and blood [13, 14].

The anti-cancer effects of bee venom and its major component melittin may be explained in several ways. Firstly, the anti-tumor effect may be mediated via the induction of extrinsic and intrinsic pathways of apoptosis. It has been reported that bee venom and melittin increase the expression and levels of various proapoptotic and apoptotic mediators.

The anti-tumor effects of bee venom and melittin may also be mediated via the inhibition of anti-liver Kidney Microsomal Antibody (LKMA) signaling pathways. This inhibition, in turn, results in a decrease in tumor growth and survival through suppressing cell proliferation, angiogenesis, anti-apoptosis, invasion and metastasis [15].

The central aim of this search has been finding products with inhibitory activity against tumor cell growth and metastasis and able to induce and control apoptosis. Several studies reported that bee venom and its components present some of these properties, like apoptosis induction, necrosis, and growth inhibition of different tumor cells. The research on the effect of bee venom on HCC was limited, and this search is considered the first to detect anti-immunological marker (LKMA1) for this purpose. According to a study, there is a link between autoimmune hepatitis (AIH) and a higher risk of developing HCC. Anti-LKMA1 is the standard antibody for diagnosing AIH.

This study was conducted to create an improved formulation to increase the related drug's anti-cancer characteristics and assess its anti- tumor effect against HCC in an effort to enhance cancer therapeutic regimens.

Material and Methods

All methods were carried out in accordance with relevant guidelines and regulations.

Bee venom

The Carniolan bee venom (Apis mellifera carnica) specimen was purchased from the Department of Beekeeping Research under the Research Institute of Plant Protection of the Centre of Agriculture Research in Dokki, Giza governorate, Egypt.

Chemical and drugs

Carbon tetrachloride (CCl_4) was supplied by Sigma Chem. Co., (St. Louis, U.S.A), whereas Cisplatin was purchased from (Sigma Aldrich).

Experimental Animals

The study is reported in accordance with ARRIVE guidelines for the reporting of animal experiments. The experimental optimal design and the handling of animals were approved via the Ethical Committee of Zagazig University with the approval number of (ZU-IAUUC/1/F/25/2020). Fifty albino mice were used: BALB/c mice (n = 50) from animal house of faculty of medicine zagazig university had body weights ranging from 20-25g (male, 2–3 weeks age). Mice placed in the house of animal presented in the faculty of medicine, Zagazig University. Mice keeping conditions were in the temperature range (20–25 C^0). The humidity of the environment was (60-65%). Mice also kept in 12h dark / light cycle.

Mice received free access to water and also a regular chow diet ad libitum.

Experimental design

Fifty male albino mice were used: BALB/c mice (n = 50). Before starting the experiments, albino mice were acclimatized for one week. The mice were divided into five experimental groups (n =10), Negative control group: normal mice, received water and diet only for 8weeks, positive control group: HCC induction was performed using carbon tetra chloride (CCl_4) 2ml/kg was conducted IP twice a week for three months to induce HCC[16], Treatment group: mice treated with Bee venom (0.1mg/kg/orally) for 45 day [17] after induction of HCC, protective group: mice received Bee venom (0.1 mg/kg /orally) daily for 45day then received carbon tetra chloride(CCl_4) for 2 months and Cisplatin group: mice treated with chemotherapy drug (cisplatin) (1.5 mg/kg /i.p) [18] after induction of HCC .

After treatment was completed, the animals were sacrificed with urethane injection. All the animals in the various experimental groups received their blood and liver tissues. Centrifugation was used to separate the serum (at 2500 rpm for 10 minutes) and was preserved until further analysis. For histological and biochemical investigation, a sample of the liver tissue was kept for 24 hours in 10% buffered formalin.

Measurement of serum biochemical parameters and Liver function parameters

Liver function parameters: ALT, AST and ALP, Pro-fibrinogenic cytokine: TGF-β1, Pro-Inflammatory cytokine: TNF-α, Anti-tumor cytokine: IL-12 and Immunological marker: LKMA1. The principles to evaluate the liver enzymes were Colorimetric determination, (alanine aminotransferase (ALT). Catalogue Number MET-5123, aspartate aminotransferase (AST) Catalogue Number MAK055, and alkaline phosphatase (ALP) Catalogue Number MAK446, tumor growth factor (TGF-β1) Catalogue Number RAB0460, tumor necrosis factor (TNF-α) Catalogue Number 10602-MM01, anti-liver kidney microsomal antibody (LKMA1) and interleukin-12. These kits were based on sandwich enzyme-linked immune-sorbent assay technology.

Histopathological Examination

An automated tissue processor was used to process the formalin-preserved hepatic tissue specimens. At the beginning the procedure involved two steps of fixing and dehydration. Fixation using submersion of tissue in 10% buffered formalin for 48 hours, followed by elimination of fixative in distilled water for 30 minutes.

Dehydration was then carried out by running the tissues through a graded sequence of alcohol (70%، 90%and 100%). on the first the tissue was exposed to 70% alcohol for 120 minutes followed by 90% alcohol for 90 minutes and then two absolute alcohol cycles, each for one hour. Dehydration was then followed by clearing the samples in various changes of xylene. It consisted of tissue submersion for an hour in a comprising a mixture 50% alcohol and 50% xylene، followed by pure xylene for one and a half hour. After that, samples were infused with molten paraffin wax, then embedded and blocked out.

Hematoxylin and eosin (HE) was used to stain the paraffin slices (4-5 µm). before being stained and studied under a microscope [19].

Histochemical study

Masson's Trichrome Staining Protocol for Collagen Fibers: Collagen fibres in liver tissue can be found using this technique. on formalin-fixed, paraffin-embedded sections, and may be used for frozen sections as well. The backdrop will be stained red, the nuclei will be stained black, and the collagen fibres will be stained blue. Fixation: 10% formalin or Bouin's solution. Section: paraffin sections at 5 µm [20].

Statistical analysis

The results of statistical analysis were analyzed using the Excel program. Data were displayed as mean ± SEM. Statistical significance was determined using a Two-Factor Without Replication ANOVA test. P values less than 0.05 ($P \leq 0.05$) were regarded as statistically significant [21] (Fig. 1).

Results

Effect of Bee venom on biochemical parameters in all groups

Detection of liver function.

When compared to the positive control group, the levels of the liver function test (ALT, AST, and ALP) in the therapeutic and protective groups significantly decreased ($P < 0.05$) (Table 1).

Detection of pro-fibrinogenic cytokine

There was a significant decrease in pro-fibrinogenic cytokine (TGF-β1) in the therapeutic and protective groups compared to the group that served as the positive control ($P < 0.05$) (Table 1).

Detection of pro-inflammatory cytokine

There was a significant reduction in pro-inflammatory cytokine (TNF-α) in the therapeutic and protective groups compared to the positive control group ($P < 0.05$) (Table1).

Detection of Anti-tumor cytokine

There was a significant decrease in anti-tumor cytokine (IL-12) in the therapeutic and protective groups compared to the group that served as the positive control ($P < 0.05$) (Table 1).

Detection of immunological marker

When compared to the positive control group, there was a considerable rise in the immunological marker (LKMA1) in the therapeutic and protective groups ($P < 0.05$) (Table 1).

Histopathological finding

Liver sections reveal the Photomicrograph from liver of. G.1(control group): showing apparently normal hepatic cords. G.2(positive group): Marked hepatic inflammation apoptotic and necrotic changes hepatocellular dysplasia and malignant change. G.3(treatment group): Regenerative changes in hepatocytes, mild inflammatory cells infiltration and degenerated malignant cell. G.4(protective group): Biliary proliferation, mild portal round cells infiltration, apparently normal portal area and hepatocytes. G.5(Cisplatin group): normal portal area, mild portal round cells infiltration, focal necrotic and apoptotic changes and apparently normal and regenerating hepatocytes. Megakaryocyte -like cells are seen in hepatic tissue of all groups. H&E X 400 (Figure 2).

Histochemical finding

Concurrently and going parallel with the study of immune-histochemistry. Histo-chemical findings were of great interest. Results of the present study demonstrated that no fibrous tissue was seen in any of the examined liver tissue of control negative group, meanwhile large deposition of collagen fibres which appeared light to dark green fibrils particularly at the vicinity of the portal areas. The amount of deposited collagen fibrils dramatically decreased in the bee venom the treated and protective groups to very low limits. Few amounts of such collagen fibrils were noted intermixed with the few infiltrated residues of inflammatory cells seen in and at the vicinities of the portal triads and around bile ducts.

The amounts of deposited collagen fibrils were minimally recorded at the vicinity of the portal triads in cisplatin treated mice (Figure 3).

Discussion

HCC is one of the cancers that kills the most people worldwide and has limited therapeutic options. It has a terrible prognosis with an overall survival rate of less than 9%. In the event that the tumor cannot be surgically removed, HCC has few therapeutic choices because it does not respond well to chemotherapy and responds well to radiotherapy. This increases the possibility of using natural remedies and compounds that have been shown to have hepatoprotective and anticancer properties, or their secondary metabolites [22].

Traditional medicine and herbal medicines have long made use of natural products. They contain several different bioactive components. Natural products are less expensive than experimental methods and produce effective outcomes with no adverse effects. In our research, we enhanced the bee venom anti-cancer effects against HCC caused by CCl_4 in a mouse model. To prove our hypothesis, we compared the components of bee venom and cisplatin. Cisplatin is a well-known chemotherapeutic drug that inhibits the growth of cancer cells using specific mechanism. Once inside the cell, it binds to DNA, forms intra-strand DNA adducts, prevents DNA synthesis, and lead to programmed cell death by binding to DNA. Despite the effectiveness of the treatment, some cancer patients have died due to chemotherapy's inability to eradicate cancer cells [18].

Strongly hepatocarcinogenic CCl_4 disrupts nucleic acid repair processes and produces reactive oxygen species (ROS), leading to oxidative stress. In the current investigation, we tested the hepatoprotective and anticancer effects of bee venom and used CCl_4 to create mice model of HCC [16]. The balance of cytokines, oxidative marker status, and normal liver architecture were successfully restored by BV.

Tests for liver enzymes can reveal whether or not the liver is functioning properly. As indicator enzymes, ALT, AST and ALP are significant indicators of liver disease. Since it is generally known that ALT activity is the most prevalent

biomarker of hepatotoxicity when its level is elevated in serum, determining this enzyme's concentration is a more accurate way to check for liver problems because it mainly distinguishes the necrosis of the hepatocellular [23].

The liver enzymes ALT, AST, and ALP rise in reaction to a hepatotoxic substance and are a sign of hepatic insufficiency [23]. In the present study, elevated levels of the liver function tests ALT, AST, and ALP with CCl_4 treatment were reduced following bee venom administration. Bee venom was given to mice pre- and post-treatment with CCl_4, a liver toxicant, and helped restore ALT, AST, and ALP levels to close to normal.

The treated group, demonstrated the effectiveness of bee venom in reducing the impact of CCl_4 by preserving hepatocyte integrity. In the treated and protected groups, bee venom significantly reduced the activity of liver enzymes to normal levels.

Transforming growth factor (TGF- β) is a protein that plays crucial roles in liver physiology and pathology, influencing all stages of liver disease progression. TGF-β acts as a tumor suppressor in early carcinogenesis stages but can become pro-tumorigenic as cells develope resistance to its tumor-suppressing effects, promoting invasiveness and metastasis [25]. Due to its pleiotropic properties and elevated levels in tumors and stroma, the TGF- β pathway is a potential therapeutic target in HCC [26]. In the current study, the level of TGF-β decreased in the treated and the protective group compared to positive group.

This result aligns with a study that revealed that HCC-induced rats exhibited a significant upregulation of TGF-β gene expression. However, in the HCC -induced group treated with bee venom, there was a significant downregulation of TGF-β gene expression [27]. Therefore, the antifibrotic effect of bee venom through the downregulation of TGF-β is one of the mechanisms underlying its hepatoprotective effects. Additionally, a significant amount of literature has confirmed that inhibiting the TGF-β1/Smad pathway could effectively reduce liver fibrosis injury and, consequently, liver cancer [28].

The liver is remarkable in that it can completely renew itself, setting it apart from other organs that recover by leaving a scar. Although chronic injury attracts inflammatory cytokines like TNF-α, whose excessive production is harmful, the ability for regeneration is minimal. Cancer is associated with inflammation and some of the inflammatory markers such as TNF-α become increased in HCC and after CCl_4 administration, as both are associated with inflammation. According to reports, TNF-α is produced during the early stages of hepatic metastasis as a result of the host's pro-inflammatory reaction to tumor cells. TNF-α is cytotoxic, but it also encourages adhesion molecule expression, tumor cell invasion, migration, and survival, as well as an angiogenic response, which aids in the development of hepatic metastases. Increased levels of TNF-α in the bloodstream trigger TNF- α receptors on cell surfaces, which activates stress-related protein kinase and increases the synthesis of more inflammatory cytokines. TNF-α suppression is thus seen as a way to alleviate liver damage [29].

In the current study, the value of TNF-α was decreased in the sera of the treated and protective groups compared to the positive group.

There is a study investigated that CCl_4 administration induced a significant upregulation of TNF-α gene expression. However, in the HCC-induced group treated with bee venom, there was a significant downregulation of TNF-α gene expression. TNF-α inhibition and deletion reduced the tumor incidence in a rat model of CCl_4-induced HCC by promoting apoptosis and decreasing hepatocyte proliferation, indicating that TNF-α upregulation promotes tumor growth and poor prognosis in HCC. Therefore, one of the molecular aspects of the hepatoprotective effects of bee venom is its anti -proliferative activity via the downregulation of TNF-α gene expression [27].

It is well recognized that members of the IL-12 family of cytokines are crucial for controlling both innate and adaptive immune responses. Numerous studies have been conducted on the roles played by members of the IL-12 family of cytokines in the context of infection and autoimmune disorders. There has been a lot of research on how these cytokines affect immune responses in cancer. Promising options for the regulation of anti-tumor immunity are the IL-12 cytokines [30]. In hepatocellular carcinoma (HCC) patients, IL-12 expression was significantly reduced in patients [31]. In the current study, the levels of IL-12 were significantly reduced with CCl_4 treatment but increased following Bee venom administration.

It was stated that the levels of IL-12 were reduced significantly with CCl_4 treatment but increased following bee venom administration [32].

A study found a connection between autoimmune hepatitis (AIH) and an increased risk of HCC [33]. Anti-LKMA1 is the standard serological marker for the diagnosis of AIH. AIH is marked by positive anti-liver kidney microsomal antibody type 1 (LMKA1) [34]. In the current study, the value of LKMA was decreased in the sera of the treated group compared to the positive group.

These results align with several studies that have reported that BV and its components possess properties such as inducing apoptosis, necrosis, and inhibiting the growth of various tumor cells [35].

The current study's findings showed that giving CCl_4 for five weeks resulted in the loss of the typical hepatic architecture, with the majority of liver cells showing few vacuoles and darkly pigmented nuclei. Organell**e** edema caused this structural damage. In the current study, a large increase in the area % of collagen fibers in Masson trichrome stained served as a blatant indicator of liver cancer. Since collagen constitute the majority of the ECM, liver fibrosis results. Thus, Masson's trichrome staining was used to examine collagen accumulation [36].

Our results demonstrated that the liver tissues in the normal control group exhibited a normal lobular structure without apparent collagen accumulation around the blood vessels. However, after receiving CCl_4, there was a significant accumulation of collagen in the liver tissues. Additionally, it was evident that bee venom therapy reduced the amount of collagen build-up.

This result aligns with a study that explains that Masson’s trichrome staining revealed that the IR+PBS group showed significant increases in collagen deposition and the number of fibrotic foci. Treatment with bee venom phospholipase A2 (bvPLA2) significantly reduced collagen deposition [37].

In this study, we hypothesized that the antioxidant and anti-inflammatory characteristics of bee venom could be responsible for its antineoplastic efficacy. Remarkably, crude bee venom has shown anti-tumor activities against various cancer cell lines. Thus, bee venom is a potentially effective therapeutic supplement. The results of this study suggest that larger randomized trials should be conducted in the future to ensure that bee venom is used safely. More research is needed to elucidate the mechanisms of action, dose, formulation, and possible side effects and interactions.

Conclusion

The study's main goal is to provide an overview of the importance of bee venom's putative anti-cancer properties, which are abundant in many physiologically active substances. Based on improvements in hepatorenal cellular function and its antioxidant, anti-inflammatory, and anticancer properties, the current study indicates that bee venom is a valuable adjunct to liver cancer treatment in Albino mice. It could be concluded from the present study that CCl_4 intoxication damaged the liver. From the obtained results, CCl_4 induced liver cancer in male Albino mice caused a significant alteration in liver tissues. Overall, the results indicated a significant therapeutic effect of bee venom against CCl_4-induced liver cancer in mice by improving serum liver enzymes (ALT, AST and ALP), serum pro-inflammatory cytokines (TGF-β1 and TNF-α), serum antitumor cytokine IL-12, immunological marker anti-LKMA1. Thus, bee venom is a potentially effective therapeutic supplement. These investigations did show promising anti-cancer qualities.

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Funding statement

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Declaration of Conflict of Interest

The authors declare that there is no conflict of interest.

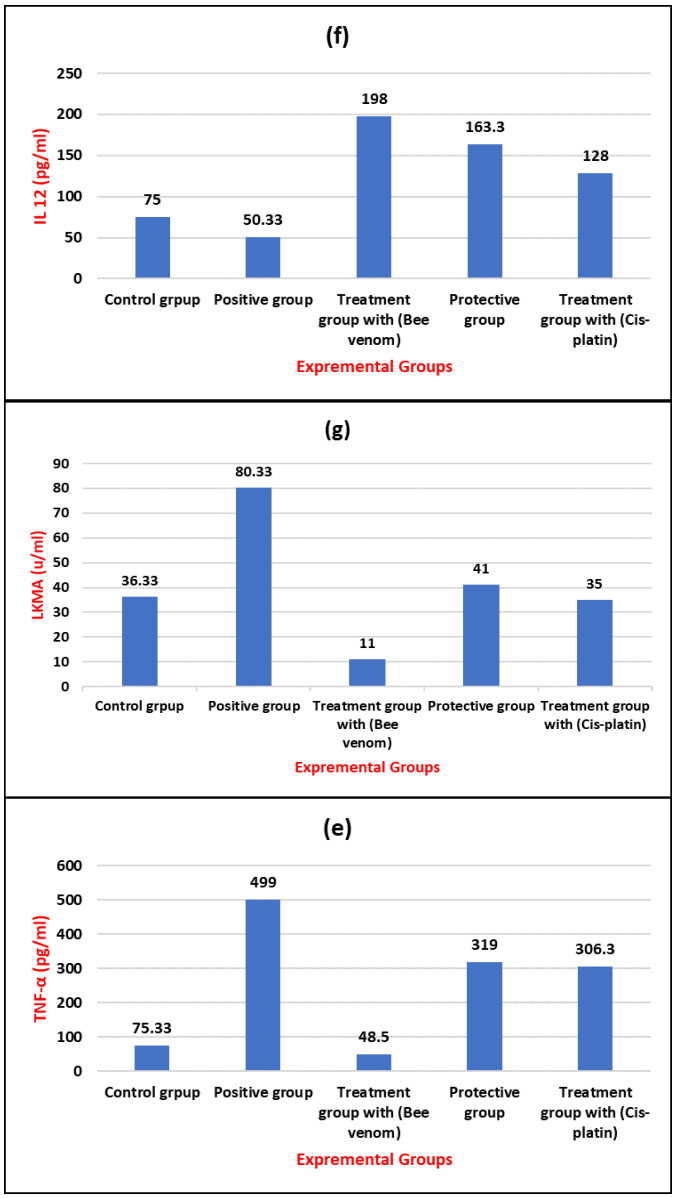
Ethical of approval

The experimental optimal design and the handling of animals were approved via the Ethical Committee of Zagazig University with the approval number of (ZU-IAUUC/1/F/25/2020).

TABLE 1. Effect of Bee venom on biochemical parameters in all groups for detection of therapeutic activity. Data were displayed as a mean ± SEM, n = 10.

Groups	ALT	AST	ALP	TGF-β 1	TNF-α	IL 12	LKMA
Control (NC)	170.733±4.12^{*a}	107.7±64.18^{*a}	93.5±6.062^{*a}	109.3±38.46^{*a}	75.33±7.219^{*a}	75±22.81^{*a}	36.33±26.43^{*a}
Positive (PC)	397.9±47.67	366.3±28.81	275.7±14.72	242.3±10.68	499±9.815	50.33±2.603	80.33±7.219
Treatment (BV)	144.6±4.273^{*b}	222±20.03^{*b}	205±6.351^{*b}	55.5±4.33^{*b}	48.5±5.485^{*b}	198±10.39^{*b}	11±1.155^{*b}
Protective (PBV)	160±34.37^{*b}	50.62±41.94^{*b}	113.3±12.41*^{b}	65.67±39.01^{*b}	319±25.98^{*b}	163.3±59.62^{*b}	41±6.928^{*b}
Treatment (CP)	214.4±11.69^{*b}	313.3±8.603^{*b}	138±6.928^{*b}	115±12.12^{*b}	306.3±10.68^{*b}	128±7.506^{*b}	35±4.041^{*b}

Comparisons across all five groups represented statistical significance as a P-value of≤ 0.05 indicating significant difference and a P-value of ≤ 0.001 indicating a highly significant difference. (*a) indicate a significant difference between negative group and positive group. (*b) indicate a significant difference between treatment groups and positive group.



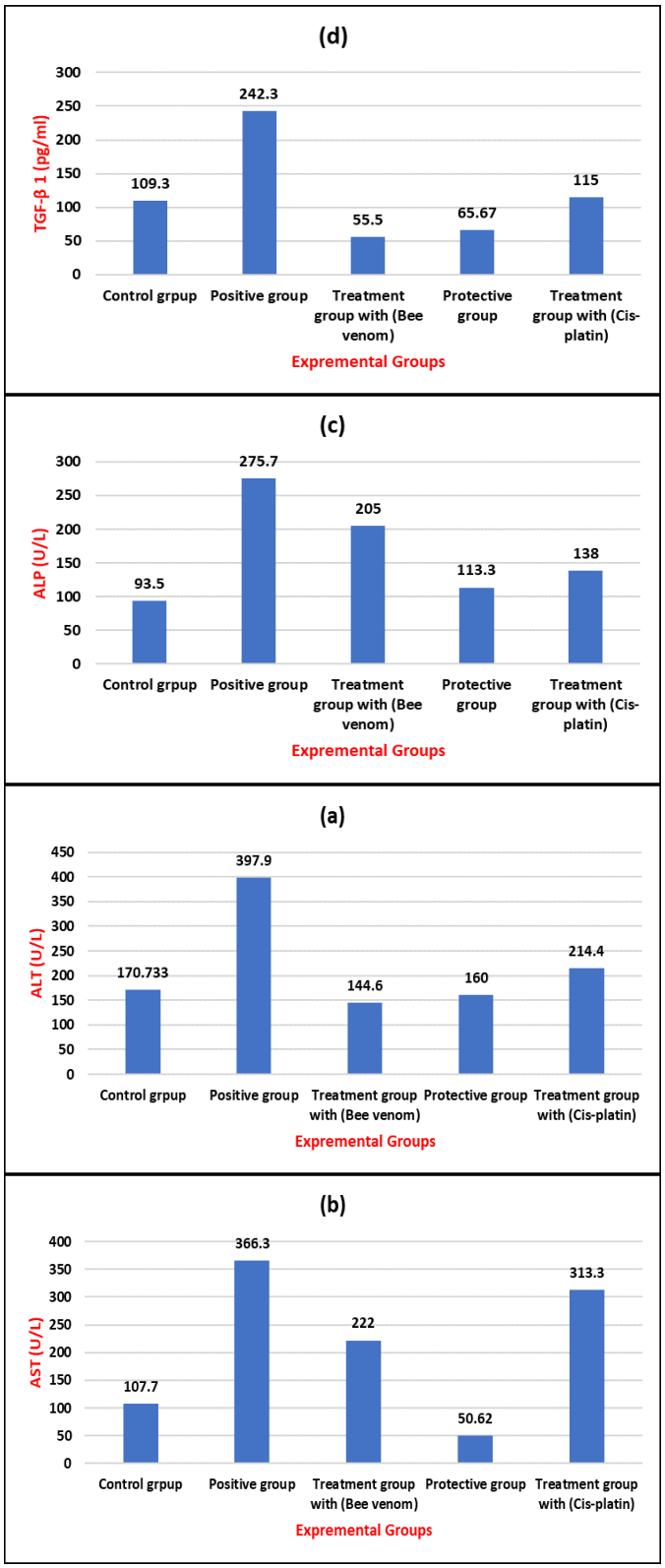


Fig. 1. Activities of all biochemical variables in the groups; (a) ALT activity in the groups; (b) AST activity in the groups; (c) AlP activity in the groups; (d) TGF- β1 activity in the groups; (e) TNF- α activity in the groups; (f) IL-12 activity in the groups; (g) LKMA activity in the groups.

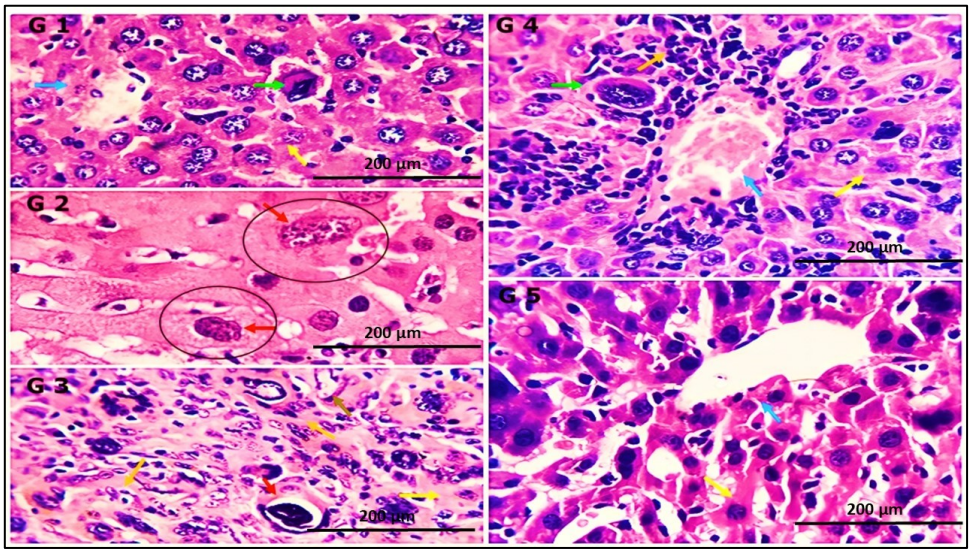


Fig. 2. Histopathological Findings; Photomicrograph from liver stained with hematoxylin and eosin(H&E). G.1 (negative control group): showing apparently normal hepatic cords (yellow arrow and portal triads (blue arrow). G.2 (positive control group): Marked hepatic inflammation (congestion and round cells aggregations. Orange and blue arrows) apoptotic and necrotic changes (brown arrows), hepatocellular dysplasia and malignant change (black circles and red arrows). G.3(treatment group): Regenerative changes in hepatocytes (yellow arrows), mild inflammatory cells infiltration (orange arrows) and degenerated malignant cell (red arrow). G.4(protective group): Biliary proliferation (black arrow), mild portal round cells infiltration (orange arrow), apparently normal portal area (blue arrow) and hepatocytes (yellow arrows). G.5(cisplatin group): normal portal area (blue arrow), mild portal round cells infiltration (orange arrow), focal necrotic and apoptotic changes (brown arrow) and apparently normal and regenerating hepatocytes (yellow arrows). Megakaryocyte -like cells are seen in hepatic tissue of all groups (green arrows). H&E X 200.

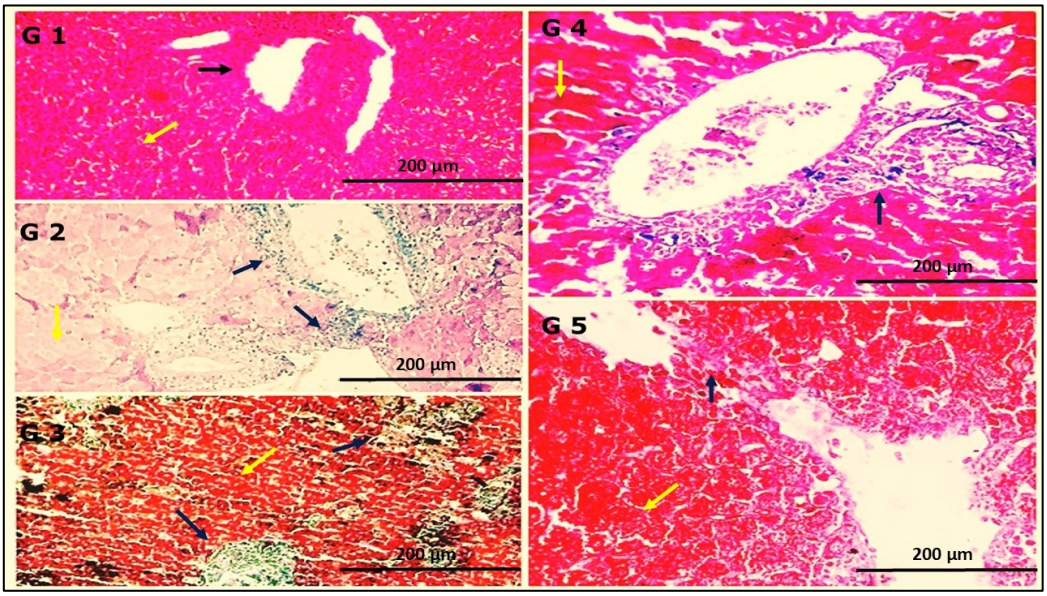


Fig. 3. photomicrograph demonstrating the amounts of collagen fibrils (dark blue arrows) deposited in the hepatic tissue of different experimental groups. Normal hepatic tissue pointed by yellow arrows. Masson trichrome stain X 200. No fibrous tissue was seen in any of the examined liver tissue of negative control group(G1), meanwhile large deposition of collagen fibers in positive control group (G2) which appeared light to dark green fibrils particularly at the vicinity of the portal areas. The amount of deposited collagen fibrils was dramatically decreased in the bee venom treated(G3) and protective(G4) groups to a very low limit. The amounts of deposited collagen fibrils were minimally recorded at the vicinity of the portal triads in cisplatin treated mice(G5).

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الخصائص المضادة للسرطان لسم النحل وتقييم تأثيره المضاد للورم ضد سرطان الخلايا الكبدية المستحث فى ذكور فئران الألبينو

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الملخص

يعتبر سم النحل مزيج من المواد الى تم استخدامها فى الطب البديل والتى تم اجراء العديد من الدراسات عليها بسبب خصائصها البيولوجية. وقد سلطت العديد من الأبحاث الضوء على تأثيره المضاد للالتهابات وتأثيراته المناعية. لذلك فإن سم النحل ذو دور فعال فى حماية وعلاج الكبد من التليف الكبدى وحدوث السرطان المحدث فى الفئران باستخدام مادة رابع كلوريد الكربون وأدى استخدامه على الحفاظ على نسب القياسات الحيوية فى الدم والأنسجة لما يقارب النسب الطبيعية. علاوة على ذلك، تشير نتائج هذه الدراسة إلى ضرورة اجراء تجارب مستقبلية أكثر توسعاً لضمان استخدام سم النحل بشكل أكثر أماناً ، كما أن هناك حاجة إلى اجراء مزيد من الأبحاث لتوضيح أليات العمل والجرعة والتركيبات والآثار الجانبية والتفاعلاتالمحتملة لهذه المادة.

الكلمات الدالة: سم النحل، سرطان الخلايا الكبدية، مادة رابع كلوريد الكربون.