Therapeutic Effects of Barks Group (Cinnamon and Chinchona) on Liver Cancer

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Abstract

Cinnamon (*Cinnamomum zelancum*), originates from South Asia and India, made from the barks of *Lauracea* family, growing in Europe and Philippine. Chinchona (*Cinchona officinalis*), made from the barks of *Rublacea*, it is a big green tree growing in South America woods, Europe, India and parts of Africa. In order to study the therapeutic effects of barks group, each one alone, on liver cancer, 0.1 ml/gm aflatoxin B_1 (AFB_1) was administrated intraperitoneal in male Wister Albino rats for a period of 10 days to cause liver cancer. Cinnamon and chinchona, each one alone, was given to rats for a period of 20 days. The animals were killed at the end of the study and blood was tested for some key enzyme such as: aspatate aminotransferase (AST), alanine aminotransferase (ALT), gamma- glutamyl transferase (GGT), and other biochemical parameters which include bilirubin, urea, uric acid, creatinine, cholesterol, triacylglycerols, glucose and hemoglobin. Part of the liver samples were taken to determine the content of deoxyribonucleic acid (DNA), ribonucleic acid (RNA) and total proteins, the other part was used for histological examination. The results from this study demonstrated that cinnamon was prevented the proliferation of liver cancer at the initiating stage by inhibiting AFB_1 effects on DNA and regeneration of hepatocyte cells, chinchona gave same results but to lesser extent.

Introduction

Chemoprevention is a concept defined as prevention of cancer by the administration of natural or synthetic pure chemical, or by daily foods enriched with cancer preventive components. Several compounds have been discovered with inhibitory effects on the tumor-promoting stage, and interestingly many of them were derived from plants (**1**). Today, one of the most urgent problems of public health is the development of effective methods to block the carcinogenesis sequential events. Liver cancer (Primary hepatocellular carcinoma) is a major public health hazard in the developing countries of Africa and Asia. The etiology of this disease implicates both infectious (hepatitis B and C) factors, contaminant of foods by aflatoxin B_1 (AFB_1) which has been linked to high incidence of liver cancer in these regions (**2**).

Cinnamon is the bark of the (*Cinnammomum zelanicum*) tree from the *lauraceae* family. True cinnamon is a native of Srilanka and grows almost exclusively in this country. As much as 68% of the oil consists of cinnamic aldehyde, which is a powerful irritant that can blister the tongue. Cinnamon contains only about 1% of aldehyde and is not an irritant under ordinary circumstances (**3**), also contain antioxidant phenolic and flavonoids (**4**), its effects the antioxidant enzymes in heart and liver (**5**). Cinnamon extracts act as antimicrobial and associated with the pathogenesis of gastritis, duodenal ulcer and gastric lymphoma (**6**). It consists of 23% hydrocarbons and 74% oxygenated compounds, a total of 26 compounds consistuting approximately 97% of the oil was characterized. 41.98% cinnamyl acetate, 7.97% trans-alpha-bergamotene, 7.2% caryophyleene oxide and are found to be major compounds (**7**). The antioxidant in cinnamon inhibited lipid peroxidation (**8**). The essential oils have more inhibition of fungal growth and mycotoxin production depends on the concentration of these essential oils.

Chincona or quinine bark, grows in South America, Europe, India and Parts of Africa (**9**). Weak cytotoxic activity was due to the presence of quinovic acid which has antitumor activity (**10**). Chincona contains alkaloid compounds, primaquine, chloroguanide, pyrimethamine, mefloquine, praguanil which used as treatment of malaria (**11**), other alkaloid

compounds are quinine, quinidine, cinchonine and cinchonidine (**12**). Quinidine is the common alkaloid of chinchona barks and still used in rhythmology today (**13**). The ability of cinchonine to reverse doxorubicin drug resistance in leukemia cell line was wel known (**14**). Quinine has an important effect as a treatment of dysenteria and liver disease (**15**).

The aim of this study is to find out the biochemical changes of liver cancer caused by aflatoxin B_1, on the blood and liver tissues of male Wister Albino Rats. Also, to study the effects of two herbs extracts used for treatment of liver cancer as well. Also, to study the histological changes of liver tissue and cells caused by treatment and to record the degree of cancer trauma and prognosis of the treatments. From these study positive results, were obtained regarding the treatment of liver cancer using different extracts of herbs used in this study.

Experimental

In this study, 84 Male Wister Albino Rats, weighing 70-100 gm were maintained in clean cages. The rats were fed with commercial pelleted diet obtained from King Fahad Medical Research Center in Jeddah. The rats were divided into 4 groups, each group contained 21 rats. All groups except the first one were injected with 20 µl of (0.1ml/ 100 gm) B.W aflatoxin B_1 (**16**), the experiment was for 30 days. The first group acted as non tumor bearing control (NTB-C). The second group consisted of rats which were injected i/p with 20 µl (0.1 ml/100gm) B.W aflatoxin B_1 one time from the first day, and left for 10 days and served as tumor bearing rat control (TBR-C). After 10 days of aflatoxin B_1 injection (i.p) all the following groups from 11^{th} to 30^{th} day were treated by allowing the animals to drink plant extracts as following. Third group consisted of tumor bearing rat treated with cinnamon (TBRci). The fourth group consisted of tumor bearing rat treated with chinchona (TBRch).

After 10 and 20 days of treatment, the rats were anesthetized with ether and blood was collected from the heart and some biochemical parameters were determined including some enzymes such as aspartate aminotransferase (AST) (**17**), alanine aminotransferase (ALT) (**18**) and gama glutamyl aminotransferase (GGT) (**19**) and chemical parameters

which includes bilirubin (**20**), urea (**21**), uric acid (**22**), creatinine (**23**), cholesterol (**24**), triacylglycerols (**25**), glucose (**26**) which measured by Diminsion produced by DAD BEHRING company (Germany). Also, blood samples were used for the determination of hemoglobin (**27**) measured by Reflotron product by Boehringer company (Germany). The rats were killed by cervical decapitation and livers from each group were removed and divided into 2 parts, first part used for the determination of RNA, DNA (**28**) and total protein (**29**). The second part were put in formalin solution (10 %) and stained by Hematoxyline and Eosine (H & E) to be used for histological examination (**30**).

Rats in day 10 were treated (for third and fourth groups) by the 2 herbs, each one alone. Herbs extracts were prepared by heating distilled water (400 ml) to 80°C and soaking 20 gm of the herb material for about 60 min, then given through special drinking bottles daily (**31**).

Collected data were calculated by ANOVA using SPSS program version 11. Sigma plot program version 9 was also used.

Results and Discussion

The biochemical parameters in the group of tumor bearing rats (TBR-C) were compared to non tumor bearing control (NTB-C), which showed slightly change in the activity of AST by 6.8% (P=0.85), a decrease in the activity of ALT in (TBR-C) by 25.1% (P=0.377). Significant increase in the activity of GGT by 36% (P=0.007). A very highly significant increase in bilirubin level by 641.2% (P=0.000) and in glucose level by 25.3% (P=0.000). Slight decrease in urea level by 5.3% (P=0.316) and in hemoglobin level by 10.5% (P=0.151), an increase in uric acid by 41.4% (P=0.054) and in creatinine by 33.3% (P=0.091). A very highly significant decrease of cholesterol level by 43.5% (P=0.000) and triacylglycerol by 55.7% (P=0.000) (figure 1 to figure 11). From liver tissue, significant decrease in RNA level by 37.4% (P=0.012), a decrease in DNA by 37.3% (P=0.109) and total protein by 19.1% (P=0.338) (figure 12 to figure 14). Histological examination in the liver tissue showed that liver cells were seen without nucleus; degenerative, hepatoma focci and decrease in number of kupffer cells (figure 15-a, 15-b and figure 16-a, 16-b). There were significant increases in the level of serum bilirubin following aflatoxin B_1

administration due to degeneration of the hem of hemoglobin in red blood cells, which contracted the results obtained by (**32 and 33**). The lipids content in the liver and plasma showed a decrease in triacyglycerol, free fatty acids and cholesterol. These results agree with (**34 and 35**). They concluded that an increase of lipolysis in fat tissue and the metabolic alterations in the liver precedes catabolic reactions in peripheral tissues. From the results found here a decrease in the lipid content in tumor bearing rats, consider as one of cancer recognition. These results agree with (**35**), which they reported that the turnover rate of glucose was significantly greater in tumor bearing compared with non tumor bearing rats as with the rate of glucose recycling and the rate of gluconeogenesis energy increases which both demanding process. Also, the decrease in DNA level due to (AFB_1 DNA adduct) after short time from the administration might be due to a decrease in protein synthesis, and this agree with (**36**) which they declared that, significant changes in hepatic protein metabolism but not significantly changes in skeletal muscles. Tumor bearing rats have altered hepatic protein in a way similar to the previously reported (**37**) which they found a decrease in the level of total protein in the liver due to (AFB_1 DNA adduct) which may interrupt the transcription process of RNA to decrease the synthesis of protein. Histology, Hepatoma focci, degenerative and necrotic of hepatic cells, cells without nucleus, and decrease in the number of kupffer cells were shown which agree with (**38**).

Treatment with cinnamon and chinchona, each one alone, for10 and 20 days ($TBRci_{10}$), ($TBRci_{20}$), ($TBRch_{10}$) and ($TBRch_{20}$), respectively. In ($TBRci_{10}$), decreases in the activity of AST by 68.1% (P=0.162), this activity continue decreasing in ($TBRci_{20}$) by 14.6% (P=0.543) when compared with (TBR-C), this activity decreases by 20.3% compared with (NTB-C). In ($TBRch_{10}$), a decreases in the activity of AST by 15.4% (P=0.972), this activity increases in ($TBRch_{20}$) by 19.4% (P=0.239) compared with (TBR-C), an increase in this activity by 19.4% when compared with (NTB-C), (figure 1). In ($TBRci_{10}$), a decreases in the activity of ALT by 61.1% (P=0.203), and this activity increases in ($TBRci_{20}$) by 8.7% (P=0.879) when compared with (TBR-C), also this activity decreases by 18.6% when compared with the activity of (NTB-C). In ($TBRch_{10}$), an

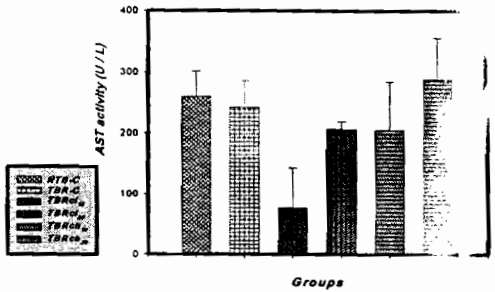
increases in the activity of ALT by 7.4% (P=0.645), this activity slightly increases in ($TBRch_{20}$) by 8.6% (P=0.939) compared with (TBR-C), but decreases by 18.7% when compared with (NTB-C), (figure 2). In ($TBRci_{10}$), significant decreases in the activity of GGT by 19.8% (P=0.032) was seen, but this activity slightly changed in ($TBRci_{20}$) by 1.5% (P=0.082) when compared with (TBR-C), also this activity increases by 34% compared with (NTB-C). In ($TBRch_{10}$), a decreases in the activity of GGT by 11.8% (P=0.052) was seen, this activity slightly decreases in ($TBRch_{20}$) by 6.6% (P=0.089) compared to (TBR-C), but increases by 27% when compared with (NTB-C) (figure 3). In ($TBRci_{10}$), a very highly significant decreases in the level of bilirubin by 50% (P=0.000) was seen, very highly significant decreases in ($TBRci_{20}$) by 88.9% (P=0.000) when compared with (TBR-C), also this level remain decreasing by 17.6% compared with (NTB-C). In ($TBRch_{10}$), a very highly significant decreases in the level of bilirubin by 64.3% (P=0.000) was seen, also very highly significant decreases in ($TBRch_{20}$) by 92.1% (P=0.000) compared with (TBR-C) were seen, also this level decreases by 41.2% compared with (NTB-C) (figure 4). In ($TBRci_{10}$), an increases in the level of urea by 4.4% (P=0.582) was seen. In ($TBRci_{20}$), slight decreases in this level by 21.3% (P=0.013) was shown compared with (TBR-C), also this level decreases by 26% compared with (NTB-C). In ($TBRch_{10}$), an increases in the level of urea by 6.8% (P=0.766) was seen, also this level increases in ($TBRch_{20}$) by 12.4% (P=0.066) when compared with (TBR-C), and this level increases by 6.5% compared with (NTB-C) (figure 5). In ($TBRci_{10}$), little increases in the level of uric acid by 0.3% (P=0.994) was seen, also this level decreases in ($TBRci_{20}$) by 16.4% (P=0.448) when compared with (TBR-C), but this level increases by 18.1% compared with level of (NTB-C). In ($TBRch_{10}$), a decrease in the level of uric acid by 6.1% (P=0.554) was shown, also this level decreases in ($TBRch_{20}$) by 45.3% (P=0.060) when compared with (TBR-C), this level decreases by 22.7% compared with (NTB-C) (figure 6). In ($TBRci_{10}$), significant decreases in the level of creatinine by 37.8% (P=0.013) was seen, also this level significantly decreases in ($TBRci_{20}$) by 5.4% (P=0.723) when compared with (TBR-C), but this level slightly increases by 16.7% compared with (NTB-C). In ($TBRch_{10}$), a decreases in the level of creatinine by 10.8% (P=0.357) was seen, this level decreases in ($TBRch_{20}$) by 13.5%

(P=0.654) compared with (TBR-C), but increases by 40% compared with (NTB-C) (figure 7). In ($TBRci_{10}$), a decreases in the level of cholesterol by 4% (P=0.667) was shown, very highly significant increases in ($TBRci_{20}$) by 63% (P=0.000) when compared with (TBR-C), but this level decreases by 7.8% when compared with (NTB-C). In ($TBRch_{10}$), an increases in the level of cholesterol by 13.9% (P=0.864) was seen, a very highly significant increases in ($TBRch_{20}$) by 59.3% (P=0.000) when compared with (TBR-C), but this level decreases by 2.3% compared with (NTB-C) (figure 8). In ($TBRci_{10}$), an increases in the level of triacylglycerol by 30.7% (P=0.145), this level significant increases in ($TBRci_{20}$) by 65.1% (P=0.011) when compared with (TBR-C), but this level decreases by 26.9% when compared with (NTB-C). In ($TBRch_{10}$), significant increases in the level of triacylglycerol by 53.6% (P=0.001) was seen, this level increases in ($TBRch_{20}$) by 75.3% (P=0.015) when compared with (TBR-C), but this level decreases by 22.3% when compared with (NTB-C) (figure 9). In ($TBRci_{10}$), an increases in the level of glucose by 2.9% (P=0.706) was seen, slightly increases of this level in ($TBRci_{20}$) by 3.6% (P=0.657) was seen when compared with (TBR-C), and this level increases by 29.8% compared with (NTB-C). In ($TBRch_{10}$), a very highly significant decreases in the level of glucose by 34.4% (P=0.000) was seen, this level slightly increases in ($TBRch_{20}$) by 0.3% (P=0.472) when compared with (TBR-C), and increases by 25.7% when compared with (NTB-C) (figure 10). In ($TBRci_{10}$), a decreases in the level of hemoglobin by 3.1% (P=0.621) was shown, this level slightly decreases in ($TBRci_{20}$) by 7.4% (P=0.152) when compared with (TBR-C), and decreases by 17.1% when compared with (NTB-C). In ($TBRch_{10}$), a decreases in the level of hemoglobin by 4.8% (P=0.324) was shown, this level decreases in ($TBRch_{20}$) by 5.6% (P=0.893) when compared with (TBR-C), and this level remains decreased by 11.1% compared with (NTB-C) (figure 11). From liver tissue, after treatment with cinnamon (TBRci), significant increases in the level of RNA by 73.6% (P=0.002) when compared to (TBR-C) was seen, this level increases by 7.8% compared with (NTB-C). After treatment with chinchona (TBRch), significant increases in the level of RNA by 55.8% (P=0.019) when compared with (TBR-C), but decreases by 2.4% when compared to (NTB-C) (figure 12). After treatment with cinnamon (TBRci), very highly

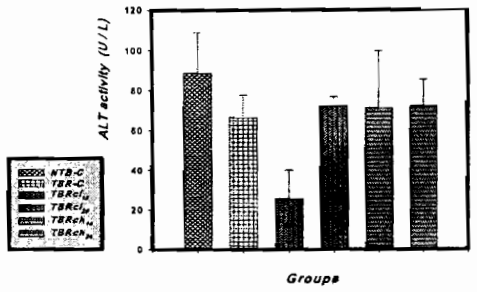
significant increases in the level of DNA by 196.3% (P=0.000) when compared with (TBR-C), an increases by 73.3% when compared with (NTB-C). After treatment with chinchona (TBRch), very highly significant increases in the level of DNA by 212.8% (P=0.000) when compared with (TBR-C), an increases by 96% when compared with (NTB-C) (figure 13). After treatment with cinnamon (TBRci), significant increases of total protein by 74.2% (P=0.004) was seen when compared with (TBR-C), also this level increases by 41% when compared with (NTB-C). After treatment with chinchona (TBRch), significant increase in the level of total protein by 77.1% (P=0.003) when compared with (TBR-C), an increases by 43% when compared with (NTB-C) (figure 14). Histological examination of liver tissue in the group of tumor bearing rats after treatment with cinnamon (TBRci), showed hepatomic focci with increasing numbers of kupffer cells in the liver (figure 17-a, 17-b). In tumor bearing rats treated by chinchona (TBRch), showed an increases in the number of kupffer cells and improvement in the healthy status of liver cells but the necrotic focci is still there (figure 18-a, 18-b).

The biochemical parameter in the group of tumor bearing rat treated with cinnamon (TBRci) compared with tumor bearing rat control (TBR-C), showed a significant increases in triacylglycerol, very highly significant increase in cholesterol, this results opposite with the results of other authors where they found that the dietary of cinnamon resulting in lower hepatic cholesterol content and suppresses lipid peroxidation via enhancement of hepatic antioxidant enzyme activities (**39**). Significant decreases in urea due to the content of cinnamon act as antioxidant (**5**). Effect of cinnamon bark on streptozotocin-induces tissue injury, causes decrease in urea level (**40**). Very highly significant decrease in bilirubin level may be existing due to presence of phenolic, flavonoids and oxygenic compounds in the cinnamon bark (**7**). Significant increase in RNA and total protein level and very highly significant increase in DNA were noticed in liver tissue, due to the antifungal role of cinnamon and anticancer (**41**). Histological examination,showed hepatomic focci with increasing the number of kupffer cells in the liver, may be due to the cinnamon protection the liver cells and inhibit free radicals (**5**).

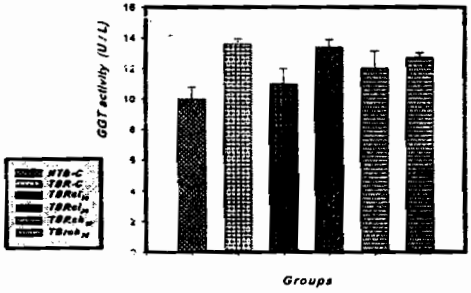
The biochemical parameters in the group of tumor bearing rat treated with chincona (TBRch) compared with tumor bearing rat control (TBR-C), showed a significantly increases in triacylglycerol level, a very highly significant increases in cholesterol level, may be due to anticancer activity (**42**). In addition, very highly significant decreases in bilirubin level was recorded due to the activity of glucoronoid transferase enzyme which then decrease the level of bilirubin which exit from the body as glucoronoid bilirubin (**43**). Significant increases in RNA, total protein level and very highly significant increases in DNA level were seen in liver tissue, may be due that the chincona contains qunovic acid which has weak cytotoxic activity and antitumor (**10**). Histological examination, showed an increases in the number of kupffer cells and improvement in the healthy status of liver cells but the necrotic focci is still there, due to the alkaloids content of chinchona bark, which inhibit the carcinogenic compounds cases the liver damage (**43**). In conclusion, this study demonstrated that cinnamon treatment gave best biochemical and histological results compared in chinchona.



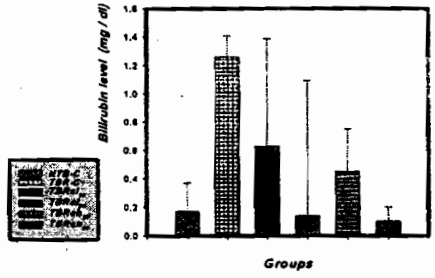
(Figure 1): The activity of serum AST in tumor bearing rat treated with cinnamon & chinchona (barks group).



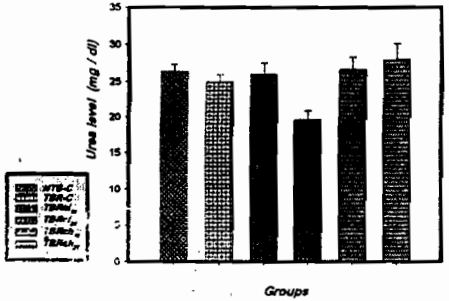
(Figure 2): The activity of serum ALT in tumor bearing rat treated with cinnamon & chinchona (barks group).



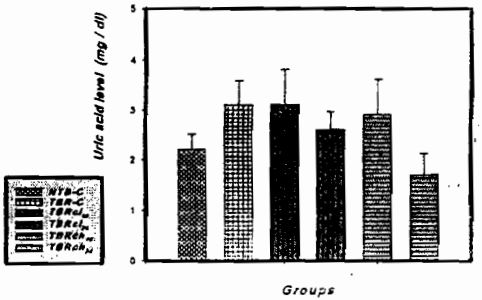
(Figure 3): The activity of serum GGT in tumor bearing rat treated with cinnamon & chinchona (barks group).



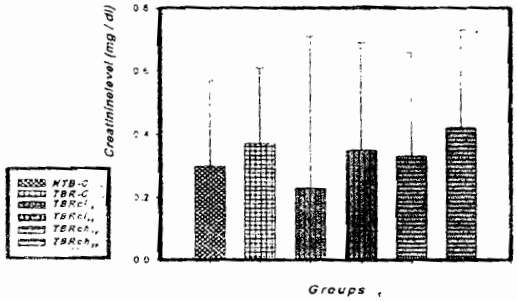
(Figure 4): The level of serum in bilirubine tumor bearing rat treated with cinnamon & chinchona (barks group).



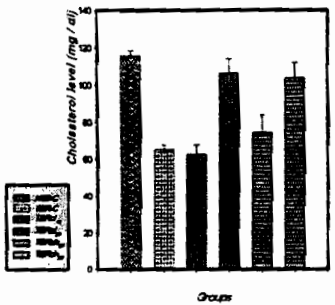
(Figure 5): The level of serum in urea tumor bearing rat treated with cinnamon & chinchona (barks group).



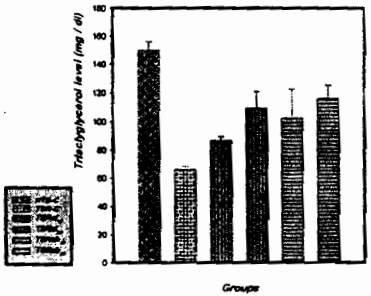
(Figure 6): The level of serum uric acid in tumor bearing ra treated with cinnamon & chinchona (barks group).



(Figure 7): The level of serum creatinine in tumor bearing rat treated with cinnamon & chinchona (barks group).

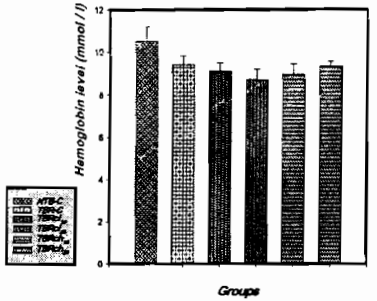


(Figure 8) The level of serum cholesterol in tumor bearing rat treated with cinnamon & chinchona (barks group).

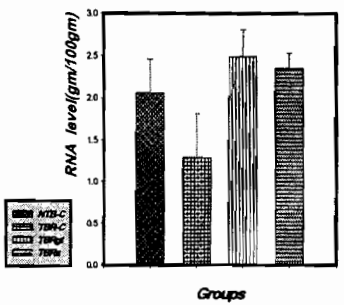


(Figure 9) The level of serum triacyglycerol in tumor bearing rat treated with cinnamon & chinchona (barks group).

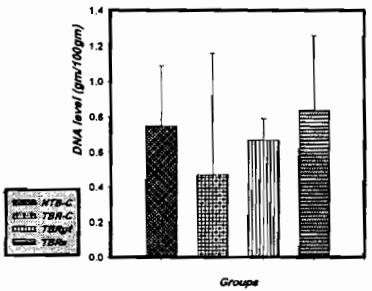
(Figure 10) The level of serum gl... in tumor bearing rat treated with cinnamon & chinch...na (barks group).



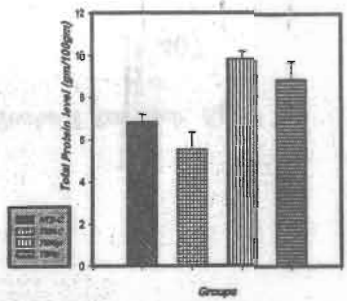
(Figure 11) The level of serum hemoglobine in tumor bearing rat treated with cinnamon & chinchona (barks group).



(Figure12) The liver content of RNA level in tumor bearing rat treated with cinnamon & chinchona (barks group).



(Figure13) The liver content of DNA level in tumor bearing rat treated with cinnamon & chinchona (barks group).



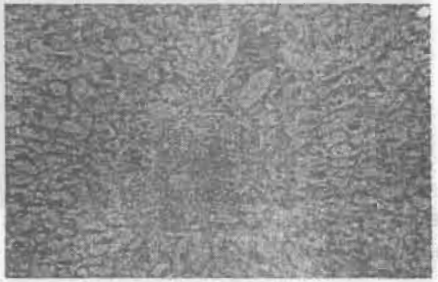
(Figure14) The liver content of total proteins level in tumor bearing rat treated with cinnamon & chinchona (barks group).

15-a

Fig (15-a). Part of liver from control group (NTB-C) showing hepatic cells (H.C) around the central vein (C.V), nucleus (N), and blood sinusoid (B.S). Hematoxyline & Eosine (H&E) (X 400)

Fig (15-b). Part of liver from control group (NTB-C) showing portal area (P.A), which contains portal vein (P.V), bile duct (B.D) inside the endothelial tissue (arrow) and laminal of hepatic cells (H.C). Hematoxyline & Eosine (H&E) (X 400)

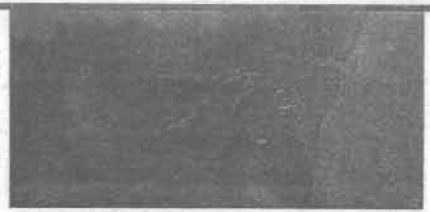
15-b



16-a

Fig (16-a). Part of liver from tumor group (TBR-C) showing degenerative, necrotic hepatic cells and hemorrhage in the portal area. Hematoxyline & Eosine (H&E) (X 400)

Fig (16-b). Part of liver from tumor group (TBR-C) showing hepatoma focci (arrow). Hematoxyline & Eosine (H&E) (X 400)



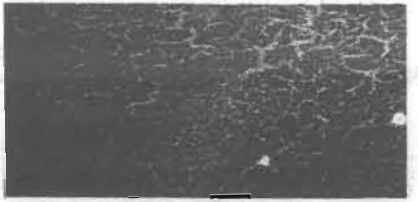
16-b

17-a

Fig (17-a). Part of liver from tumor group (TBRci) showing hepatoma focci (arrow). Hematoxyline & Eosine (H&E) (X 400)

Fig (17-b). Part of liver from tumor group (TBRci) showing dilatation in portal area, blood sinusoide (B.S) and congestion in portal area (arrow). Hematoxyline & Eosine (H&E) (X 100)

17-b



18-a

Fig (18-a). Part of liver from tumor group (TBRch) showing hepatoma focci (arrow), nicrosis in liver cells. Hematoxyline & Eosine (H&E) (X 100)

18-b

Fig (18-b). Part of liver from tumor group (TBRch) showing increase in the number of kupffer cels (K.C) and necrotic of the nucleus. Hematoxyline & Eosine (H&E) (X 200)

References

1. **Vimala,S.; Norhanom,A.W. and Yadav, M. Br. (1999):** J.Cancer., **80**, 110-6.
2. **Montalto, G.; Cervello, M.; Giannitrapani, L.; Dantona, F.; Terranova, A. and Castagnetta, L.A. (2002):** Ann. NY. Acad. Sci., **963**, 13-20.
3. **Uragoda, C.G. (1984):** Brit. J. Indust. Med., **41**, 224-227.
4. **Nair, S.; Nagar, R. and Gupta, R. (1998):** J. Assoc. Physicans India., **46**, 708-710.
5. **Dhuley, J.N. (1999):** Indian. J. Exp. Biol., **37**, 238-42.
6. **Nir, Y.; Potasman, I.; Stermer, E.; Tabak M. and Necman, I. (2000):** Helicobacterpylor. Helicobacter, **5**, 94-97.
7. **Jayaprakash, G.K.; Jagan Mohan Rao, L. and Sakariah, K.K. (2000):** J. Agric. Food Chem., **48**, 4294-5.
8. **Shobana S. and Naidu, K.A. (2000):** Prostaglandins Leukot. Essent. Fatty acids, **62**, 107-10.
9. **Lung, A. and Foster, S. (1996):** Encyclopedia of Common Natural Ingredients. Wiley Sons, New York.
10. **Raffauf, R.F.; Leoqewsne P.W. and Ghosh, P.C. (1978):** Lioydia., **41**, 432-434.
11. **White, N.J. (1985):** Clin. Pharmacokinet., **10**,187-215.
12. **Kirk, K.; Wong, H.Y.; Elford, B.C.; Newbold, C.I.; and Ellory, J.C. (1991):** Biochem. J., **278**, 521-5.
13. **Prinz, A. (1990):** Wien. Klin. Wochenschr., **102**, 721-723.
14. **Furusawa, S.; Nakano, S.; Wu, J.; Sakaguchi, S.; Takayanagi, M.; Sasaki, K.I. and Satoh, S. (2001):** J. Pharm. Pharmacol., **53**,1029-1039.
15. **Trepardoux, F. (2002):** Rv. Hist. Pharm., **336**, 401-426.
16. **Qin, G.; Gopalan-Kriczky, P.; Su, J.; Ning Y. and Lotlikar, D.P. (1997):**
17. Cancer Lett., **112**,149-154.
18. **Saris, N.E. (1978):** Clin. Chem., **24**, 720-721.
19. **Bergmeyer, H.U.; Scheibe P. and Wahlefeld, W.W. (1978):** Clin. Chem., **24**, 58-73.
20. **Shaw, L.M.; Stromme, J.L.; London, J.L. and Theodorsen, L. (1983):** Clinica Chemica Acta., **15**, 338.
21. **Jendrassik, L. and Grof, P. (1938):** Biochem., **297**, 81.
22. **Talke, H. and Schubert, G.E. (1965):** Klin Wschr, **41**,174.
23. **Bulgar, H.M. and Johns, H.E. (1941):** J. Biol. Chem., 140:427.
24. **Larsen, K. (1972):** Clin Chem Acta., **41**, 209-217.
25. **Stadtman, T.C. (1957):** Methods in Enzymology. Vol III, Colowick, S.P. and Caplan (Eds.), Academy Press, New York.
26. **Rautela, G.S. Hall, R.G. Bekiesz C.L. and Wermus, G.R. (1974):** Clin. Chem., **20**, 857.
27. **Henry, R.J. (1974):** Clinical Principles and Technics. Harper and Row, New York, NY.
28. **Van Assendelft, O.W.. (1970):** Spectrophotometry of hemoglobin derivatives, Royal van Gorem Ltd, The Netherlands.

29. **Bregman, A.A. (1983):** Laboratory Investigations and Cell Biology. New York, Wiley.
30. **Lowry, O.H.; Roesebrough, N.S.; Farr, A.L. and Randall, R. J. (1951):** J. Biol. Chem., **193**, 265-275.
31. **Bancroft, J.D. and Stevens, A. (1996):** Theory and Practice of Histological Technique. Churchill, Livingston, Edinburgh, London, Melbourne and New York.
32. **Zhou, R.; Zhou, Y.; Chen, D.; Li, S. and Hang, A. (2000):** Toxocology. Letters., **115**, 23-32.
33. **Guerre, P. Burgat, V. and Galtier, P. (1997):** Toxicol. Lett., **92**, 101-8.
34. **Rastogi, R. Srivastara A.K. and Rostog, A.K. (2001):** Pharmacol. Toxicol., **88**, 53-58.
35. **Singh, N. and Venkitasuburamanian, T.A. (1975):** Environ. Pysiol. Biochem., **5**, 147-57.
36. **Ekman, L.; Korlberg, I.; Edstrom, S.; Lindmark, L.; Scherston,T. and Lundholm, K. (1982):** J. Surg. Res., **33**, 23-31.
37. **Burt, M. E.; Lowry, S. f.; Gorschboth, C. and Brennan, M.F. (1981):** Cancer., **47**, 2138-2146.
38. **Raju, M.V. and Devegowada, G. (2000):** Br. Poult. Sci., **41**, 640-50.
39. **Baptista, A.S; Horii, J.; Calori-Domingues, M.A.; Glória, E.M.; Salgado J.M. and M.R. (2002):** Vizioli, Sci. agric. (Piracicaba, Braz.), (59) No. 2 Piracicaba.
40. **Lee, J.S.; Jeon, S.M.; Park, E.M.; Huh, T.L.; Kwon, O.S.; Lee, M.K. and Choi, M.S. (2003):** J. Med. Food., 6, 183-191.
41. **Onderoglu, S.; Sozer, S.; Erbil, K.M.; Ortac R. and Lermioglu, F. (1999):** J. Pharm. Pharmacol., **51**, 1305-1312.
42. **Lee, K.G. and Shibamoto, T. (2002):** J. Agric. Chem., 50, 4947-4952.
43. **Ziment, I. (1999):** Respiration, **58**, 37- 42.
44. **You, X. Mulchinski E.A. and Agarwal A.K. (1984):** Res. Commun. Chem. Pathol. Pharmacol., **84**, 223-232.

الملخص العربى

تعتبر القرفة عشبه طبية قديمة إلى جانب كونها أحد أهم التوابل في العالم، وهي من عائلة الغار، ويعود أصل القرفة إلى جنوب آسيا والهند. وتزرع اليوم في أنحاء أوروبا، وسيلان، وجاوة، وسومطرا. تعتبر الكينا من العائلة الفوية، وهي أشجار ضخمة دائمة الخضرة تكثر في غابات أمريكا الجنوبية وأوروبا وبلاد الهند. تهدف هذه الدراسة إلى معرفة التأثيرات العلاجية لهاتين النبتتين تحت مجموعة اللحاء، كلاً على حده، وذلك على سرطان الكبد. ولإجراء هذه الدراسة تم حقن ٠,١ مل/ جم من مادة الأفلاتوكسين ب١ في الغشاء البريتوني لذكور الفئران البيضاء وتركها لمدة ١٠ أيام لإصابتها بسرطان الكبد، وتمت معالجتها بإعطائها القرفة والكينا، كل على حده، لمدة ٢٠يوماً، وفي نهاية التجربة تم أخذ جزء من عينات الدم وتم اختبار تأثير النبتتين السابقتين على بعض المقاييس البيوكيميائية والتي شملت الجلوكوز، الجليسريدات الثلاثية، الكوليستيرول، البولينا، حامض البوليك، الكرياتينين، البليروبين، الهيموجلوبين، وبعض الإنزيمات مثل إنزيم جاما- جلوتاميل ترانسفيريز (GGT)، وإنزيم الأسبرتيت أمينو ترانسفيريز (AST) ، وإنزيم الانين أمينو ترانسفيريز (ALT). كما تم أخذ عينات من الكبد، وتم تقدير مستوى (الدنا DNA) ، و (الرنا RNA) والبروتين الكلي، والجزء الآخر تم وضعه في فورمالين للفحص النسيجي. اثبتت هذه الدراسة أن القرفة تساعد في التخفيف من حدة سرطان الكبد وذلك بوقف تأثير الأفلاتوكسين ب١ على الدنا كما يعمل على إعادة بناء الخلايا الكبدية مقارنة بالمجموعة الضابطة التي لم تعالج، وكذلك كان تأثير الكينا ولكنها أعطت نتائج أقل.