Summary and conclusion

This study was carried out in order to investigate the possible therapeutic effect of camel milk on induced hepatocarcinogenesis in rats and comparably with other antitumor agent either natural or chemical. Ninety six male rats were assigned into two groups (48 rats per group). Group 1 served as a non treated control. Group 2 was injected I/P with diethylnitrosamine (DENA) (200 mg/kg) as a single dose and after one week received 500 ppm phenobarbitone in drinking water for 28 weeks. Three rats from each group were euthanized at the 19th week and 28th week to follow up the progress of hepatocarcinogenesis. At 28th week, each group was subdivided into six groups. Group A served as a control negative group. Group B treated with camel milk. Group C treated with camel milk and turmeric extract. Group D treated with turmeric extract. Group E treated with cisplatin. Group F treated with cisplatin and camel milk. Group G was injected with DENA (control positive group). Group H was injected with DENA and treated with camel milk (5ml/day). Group I was injected with DENA and treated with camel milk and turmeric extract (250 mg/kg). Group J was injected with DENA and treated with turmeric extract. Group K was injected with DENA and treated with cisplatin (5mg/kg/3 weeks). Group L was injected with DENA and treated with cisplatin and camel milk. Body weight of rats was recorded weekly. Three and four rats from each group were euthanized at 34th and 38th week, respectively. Relative liver and kidneys weights were calculated for rats in all groups. Estimation of AST, ALT, Albumin, total protein and alpha fetoprotein (AFP) in the serum of euthanized rats was performed. Lipid peroxidation and superoxide dismutase activity was measured in liver tissue.

Histopathological examination and Immunohistochemical staining of placental glutathione-s-transferase of the liver were carried out.

Regarding the body weight result, group 2 recorded a significant increase at 3rd and 9th week followed by a significant decrease from the 14th week till the 25th week. Group G revealed a significant increase in body weight at 29th week whereas group H expressed a significant decrease at 29th, 34th and 35th week. Group I showed a significant decrease in body weight at 35th and 36th week and group J also exhibited a significant decrease at 30th week. A significant decrease in body weight in group K at 32nd week and in group L at 32nd and 35th week was recorded.

Group 2 showed a significant increase in relative liver weight at 19 and 28th weeks. Group G and K also expressed a significant increase at 38th week and 34th week respectively whereas group L showed a significant decrease at 38th week. Group H showed a significant increase in relative kidneys weight whereas group I and L expressed a significant decrease at 38th week.

In the biochemical analysis, there was a significant decrease in serum albumin in group 2 and group K at 19th and 34th week respectively. Also at 34th week there was a significant increase in AST activity and urea concentration in group L and group K, respectively. Moreover, both groups K and L expressed a significant increase in serum creatinine concentration. At 38th week there was a significant increase in total protein in group G and group K whereas the AST activity was significantly elevated in group J. Moreover, the urea concentration increased significantly in group L.

In the hematological parameters, there was a significant decrease in PCV and neutrophil percent in group L and a significant increase in percent of lymphocytes and total leukocytic count in group L and K, respectively at 34th week. At 38th week, there was a significant decrease in haemoglobin concentration in group G and a significant increase in lymphocyte percent and a significant decrease in neutrophil percent in group F.

In the oxidative stress parameters, there was a significant increase in MDA concentration in group J and a significant decrease in SOD activity in group K.

Gross lesions of the liver in the groups injected with DENA varied from abnormal focal discolored elevated areas to large rounded parenchymatous mass bulging from the liver surface.

Histopathological lesions observed in the groups injected with DENA were mainly altered hepatocellular foci, hepatocellular adenoma and hepatocellular carcinoma. Hepatocellular carcinoma developed only in group G and J. The mean area of hepatocellular altered foci and number of mitotic figures in all treated groups was lower than the control group, however the lowest mean area was recorded in group L at 34th week and group 8 at 38th week. Moreover, the area percent of preneoplastic P-GST positive foci in liver was the lowest in group L. Nephropathy and interstitial nephritis were mainly detected in groups E, F, K and L which were injected with cisplatin.

In conclusion:

1. Camel milk has a good therapeutic effect on hepatocarcinogenesis that increased with increase time of administration.
2. Turmeric extract posses the least therapeutic effect on hepatocarcinogenesis.
3. Camel milk and turmeric extract have synergism as therapeutic agents on hepatocarcinogenesis.
4. Camel milk and cisplatin have the best therapeutic effect on hepatocarcinogenesis in rats.
5. The camel milk ameliorated the side effect of cisplatin on the kidney.
6. Further investigations should be conducted to elucidate the exact mechanism and to clarify which constituent of camel milk is related to this positive therapeutic effect.

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الملخص العربي

اجريت هذه الدراسة لتوضيح التاثير العلاجي للبن الابل علي اورام الكبد المستحدثة في الجرذان . اجريت هذة الدراسه على عدد ٩٦ ذكر من الجرذان حيث قسمت الى مجموعتين رئيسيتين في كل مجموعة ٤٨ جرذ ثم بعد ٢٨ اسبوع قسمت المجموعتين الي ١٢ مجموعة فى كل مجموعة ٧ جرزان. المجاميع من ١ الي ٦ هي مجموعات ضابطة للمواد المستخدمة اما المجموعات من ٧ ال ١٢ تم حقنهم بمادة diethylnitrosamine (DENA) مرة واحد بجرعة ٢٠٠ مجم لكل كيلوجرام و بعد مرور اسبوع تم وضع لهم مادة phenobarbitone في مياه الشرب لمدة ٢٧ اسبوع. بعد مرور ٢٨ اسبوع بدأ العلاج حيث ان المجموعة رقم ١ لم يتم علاجها. المجموعة رقم ٢ تم تجريعها لبن الابل, المجموعة رقم ٣ تم تجريعها لبن الابل و مستخلص الكركم. المجموعة رقم ٤ تم تجريعها مستخلص الكركم. المجموعه رقم ٥ تم حقنها بمادة السيسبلاتين و هو علاج كيمائي. المجموعة رقم ٦ تم تجريعها بلبن الابل و حقنها بالسيسبلاتين. المجاميع ٧ الي ١٢ تم علاجهم بنفس المواد المستخدمه في المجاميع من ١ الي ٦ و استمر العلاج ٩ اسابيع.تم تسجيل اوزان الجرذان كل اسبوع من بداية الي نهاية التجربة. تم وزن الكبد و الكلي عند كل ذبحه و تم حساب الاوزان النسبيه للكبد و الكلي. تم تجميع مصل من مجموعات التجربة لعمل اختبارات وظائف الكبد ووظائف الكلي .تم تجميع العينات من الكبد و الكلي لعمل الفحص الهيستوباثولجي و فوق اوكسيد المناعى.العينات تم تجميعها عند ١٩و٢٨و٣٤و٣٨ اسبوع عقب حقن مادة DENA .

بالنسبة لاوزان الجسم الخاصة بالجرذان فقد سجلت ارتفاعا عند الاسبوع الثالث و التاسع في المجاميع المحقونة بال DENA تبعها انخفضا في الاوزان من الاسبوع ١٤ الي الاسبوع ٢٥. المجموعه ٧ سجلت زياده في الوزن عند ٢٩ اسبوع بينما المجموعه الثامنة سجلت انخفاضا في الوزن عند الاسبوع ٢٩و ٣٤ و ٣٥ . المجموعة ٩ ايضا سجلت انخفاضا في الوزن عند الاسبوع ال٣٥ و ٣٦و كذا المجموعه ١٠و ١١ عند الاسبوع ٣٠ و ٣٢ علي التوالي. المجموعة ١٢ ايضا سجلت انخفاضا عند الاسبوع ٣٢ و ٣٥.

التحليل الاحصاءي للاوزان النسبيه للكبد اظهر وجود زياده في الاوزان في المجاميع ٧-١٢ عند الاسبوع ١٩و ٢٨.ايضا المجموعه ٧ و ١١ اظهرتا زيادة في وزن الكبد النسبي عند الاسبوع ٣٨ و

٣٤ علي التوالي بينما المجموعة ١٢ اظهرت انخفاضا في الوزن النسبي للكبد عند الاسبوع ٣٨. اما بالنسبة للتحليل الاحصاءي لاوزان الكلي النسبي فقد اظهر وجود زياده ملحوظه في المجموعة ٨ بينما اظهر وجود انخفاضا في المجموعة ٩ و ١٢ عند الاسبوع ٣٨.

نتائج التحليل البيوكيميائي اظهر وجود انخفاضا في تركيز الالبومين في المجموعة ٧ و ١١ عند الاسبوع ١٩ و ٣٤ علي التوالي. بينما كان هناك زيادة في نشاط AST في المجموعة رقم ١٢و في تركيز ال urea و ال creatinine في المجموعتين ١١ و ١٢عند الاسبوع ٣٤. عند الاسبوع ٣٨ كان هناك زيادة ملحوظة في total protein في المجموعتين ٧ و ١١ كذلك كان هناك زيادة في نشاط AST في المجموعة ١٠ و زياده في تركيز الurea في المجموعة رقم ١٢.

صورة الدم الكاملة عند الاسبوع ٣٤ اظهرت وجود انخفاضا في الPCV و نسبة ال neutrophil في المجموعة رقم ١٢ و كذلك ارتفاعا في نسبة ال lymphocytes وtotal leukocytic count في المجموعتين ١٢ و ١١ علي التوالي. عند الاسبوع ٣٨ كان هناك انخفاض في تركيز الهيموجلوبين في المجموعة رقم ٧ و ارتفاعا في نسبه الlymphocytes و انخفاض في نسبة الneutrophil في المجموعة ٦ . اما بالنسبة لمأشرات الاكسدة في انسجة الكبد فقد كان هناك ارتفاعا في تركيزMDA في المجموعه ١٠ و انخفاضا في نشاط SOD في المجموعه رقم ١١ عند الاسبوع ٣٤.

اختلفت التغيرات المرئية بالعين المجردة ما بين بؤر مختلفة اللون الي وجود زوائد في النسيج الكبدي في المجاميع المحقونة بال DENA. التغيرات الهستوباثولوجية التي سجلت في المجموعات المحقونة بـDENA هي ظهور بؤر خلايا الكبد المختلفة و الانواع المختلفة من اورام الكبد. التغيرات الهستوباثولوجية كانت اخف في المجاميع المعالجة بلبن الابل بالمقارنة بمجموعة رقم ٧ حيث ان تحليل الصور اظهر صغر حجم هذه البؤر بالمقارنة للمجموعة رقم ٧.افضل تحسن هستوباثلوجي كان في المجموعة رقم١٢ المعالجه بلبن الابل و السيسبلاتين عند الاسبوع ٣٤ و المجموعة رقم ٩ المعالجة بلبن الابل و الكركم عند الاسبوع ٣٨ . اقل تحسن كان في المجموعة رقم ١٠ تليها المجوعة رقم ١١ عند الاسبوع ٣٤ بينما اقل تحسن كان في المجموعة رقم ١١ تليها المجموعة رقم ١٠ عند الاسبوع ٣٨ . ايضا تم استخدام فوق الاكسيد المناعي لاظهار انزيم P-GST و الذي يتم ظهوره في بؤر الخلايا الكبدية المختلفة القابلة للتحور الي اورام. متوسط المساحة

و العدد الخاصيين بهذه البؤر المختلفة كانت اقل في المجاميع المعالجة بلبن الابل و خاصة في المجموعة رقم ١٢ عند الاسبوع ٣٨ . اقل تحسن كان في المجموعة رقم ١٠ عند الاسبوع ٣٤ و في المجموعة رقم ١١ عند الاسبوع ٣٨.

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عنوان الرسالة: دراسة باثولوجية مقارنة للتاثير العلاجي للبن الابل و مستخلص الكركم و السيسبلاتين علي اورام الكبد المستحدثة في الجرذان

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المستخلص العربى

اجريت هذه الدراسة لتوضيح التاثير العلاجي للبن الابل مقارنة بمستخلص الكركم و السيسبلاتين (علاج كيميائي) علي اورام الكبد المستحدثة في الجرزان .تم احداث اورام الكبد باستخدام مادة دياثيل نيتروسامين و مادة الفينوباربيتون. تم تسجيل وزن الفئران اسبوعيا. تم تجميع دم و مصل من مجموعات التجربة لعمل اختبرات وظائف الكبد ووظائف الكلي. تم قياس نسبة تاكسد الدهون الخلاوي وكذلك نشاط انزيم SOD في نسيج الكبد . تم تجميع العينات من الكبد و الكلي لعمل الفحص الهيستوباثولجي و فوق او اكسيد المناعى لاظهار انزيم P-GST و نتائج هذا الفحص تم قياسها بواسطة محلل الصور. تركيز الالبومين في الدم كان منخفض في المجاميع المحقونة دياثيلنيتروزامين و لكنه استعاد تركيزه في المجاميع المعالجة بلبن الابل. تركيز حمض البوليك و الكرياتنين في الدم كان مرتفعا في المجاميع المعالجة بالسيسبلاتينن. تاكسد الدهون سجل اعلي

جامعة القاهرة
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دراسة باثولوجية مقارنة للتاثير العلاجي للبن الابل و مستخلص الكركم و السيسبلاتين علي اورام الكبد المستحدثة في الجرذان

رسالة
مقدمة من

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تحت إشراف

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