

## **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 19<sup>th</sup> week and 28<sup>th</sup> week to follow up the progress of hepatocarcinogenesis. At 28<sup>th</sup> 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 34<sup>th</sup> and 38<sup>th</sup> 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 3<sup>rd</sup> and 9<sup>th</sup> week followed by a significant decrease from the 14<sup>th</sup> week till the 25<sup>th</sup> week. Group G revealed a significant increase in body weight at 29<sup>th</sup> week whereas group H expressed a significant decrease at 29<sup>th</sup>, 34<sup>th</sup> and 35<sup>th</sup> week. Group I showed a significant decrease in body weight at 35<sup>th</sup> and 36<sup>th</sup> week and group J also exhibited a significant decrease at 30<sup>th</sup> week. A significant decrease in body weight in group K at 32<sup>nd</sup> week and in group L at 32<sup>nd</sup> and 35<sup>th</sup> week was recorded.

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

In the biochemical analysis, there was a significant decrease in serum albumin in group 2 and group K at 19<sup>th</sup> and 34<sup>th</sup> week respectively. Also at 34<sup>th</sup> 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 38<sup>th</sup> 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 34<sup>th</sup> week. At 38<sup>th</sup> 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 34<sup>th</sup> week and group 8 at 38<sup>th</sup> 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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## المخلص العربي

اجريت هذه الدراسة لتوضيح التأثير العلاجي للين الابل علي اورام الكبد المستحدثة في الجرذان .  
 اجريت هذه الدراسة 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 في 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  
 لين الابل, المجموعة رقم ٣ تم تجريعها لين الابل و مستخلص الكركم. المجموعة رقم ٤ تم تجريعها  
 مستخلص الكركم. المجموعة رقم ٥ تم حقنها بمادة السيسبلاتين و هو علاج كيميائي. المجموعة رقم  
 ٦ تم تجريعها بلين الابل و حقنها بالسيسبلاتين. المجاميع ٧ الي ١٢ تم علاجهم بنفس المواد  
 المستخدمة 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 الهيستوباثولوجي و فوق اوكسيد المناعي. العينات تم  
 تجميعها عند ١٩ و ٢٨ و ٣٤ و ٣٨ اسبوع عقب حقن مادة DENA .

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

التحليل الاحصائي للاوزان النسبيه للكبد اظهر وجود زياده في الاوزان في المجاميع ٧-١٢ عند  
 الاسبوع ١٩ و ٢٨. ايضا المجموعه ٧ و ١١ اظهرتا زياده 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 الاحصائي 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 ١٢ و في تركيز ال urea و ال creatinine في المجموعتين ١١ و ١٢ عند 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 ال urea في المجموعة رقم ١٢.

صورة الدم الكاملة عند الاسبوع ٣٤ اظهرت وجود انخفاضا في ال PCV و نسبة ال neutrophil في المجموعة رقم ١٢ و كذلك ارتفاعا في نسبة ال lymphocytes و total 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 نسبة ال lymphocytes و انخفاض في نسبة ال neutrophil في المجموعة ٦. اما بالنسبة لمؤشرات الاكسدة في انسجة الكبد فقد كان هناك ارتفاعا في تركيز MDA 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 بـ DENA 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 هستوباثولوجي كان في المجموعة رقم ١٢ 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 المجموعة 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 لظهار 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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قسم الباثولوجيا

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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 العربي

اجريت هذه الدراسة لتوضيح التاثير العلاجي للبن الابل مقارنة بمستخلص الكركم و السيسبلاتين  
(علاج كيميائي) علي اورام الكبد المستحدثة في الجرذان. تم احداث اورام الكبد باستخدام مادة  
دياثيل نيتروسامين و مادة الفينوباربيتون. تم تسجيل وزن الفئران اسبوعيا. تم تجميع دم و مصل من  
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الكرياتينين في الدم كان مرتفعا في المجاميع المعالجة بالسيسبلاتين. تاكسد الدهون سجل اعلي

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# دراسة باثولوجية مقارنة للتأثير العلاجي للبن الابل و مستخلص الكركم و السيسبلاتين علي اورام الكبد المستحدثة في الجرذان

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ط. ب / مروة محمد صلاح الدين ابراهيم خطاب  
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