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Effects of camel thorn extract on patients suffering from Hepatitis B Virus: a preliminary human study

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Abstract

Hepatitis B virus infection is a major challenge health problem worldwide. Camel thorn is used in Libyan folk medicine for hepatitis**.** The aim of this study is to investigate the effect of camel thorn on hepatitis B virus. After pharmacological and toxicological screening of camel thorn on experimental animals in our laboratories. By using open labeled study, 15 patients were randomly chosen with their agreement.

The patient were given a very low safe dose of camel thorn powder (2.6 gm soaked in boiling water for 10 min), TID for six months. The viral load was measured before treatment, three and six months after the beginning of experiment by polymerase chain reaction (PCR). The level of transaminases, bilirubin, creatinine, blood glucose, lipid profile, thyroid function, prothrombin were assessed before and after three months of beginning of experiment. Our data showed no significant changes in creatinine, blood urea, glucose level, bilirubin, alkaline phosphatase, lipid profile, prothrombin and thyroid function. The level of viral load before and three and six months after the beginning of our study were 1689 ± 289, 558 ± 160 and 271 ± 26 IU/ml, respectively. From this study, we may conclude that the camel thorn is safe and showed activity against viral hepatitis B. Further investigations are needed by increasing the number of patients and using higher doses of plant extract to explore its mechanism of action.

عدوى فيروس التهاب الكبد B هي مشكلة صحية رئيسية في جميع أنحاء العالم. يستخدم شوكة الجمل في الطب الشعبي الليبي لالتهاب الكبد. الهدف من هذه الدراسة هو معرفة تأثير شوكة الجمل على فيروس التهاب الكبد .B بعد الفحص الدوائي والسموم لشوكة الجمل على حيوانات التجارب في مختبراتنا. باستخدام دراسة مفتوحة المسمى ، تم اختيار 15 مريضًا بشكل عشوائي بموافقتهم. أخذ المرضى جرعة منخفضة جداً وآمنة من مسحوق شوكة الجمل (2.6 جم غارقة في الماء المغلي لمدة 10 دقائق) لمدة ستة أشهر. تم قياس الحمل الفيروسي قبل العلاج ، و بعد ثلاثة و ستة أشهر من بداية التجربة بواسطة تفاعل البلمرة المتسلسل .(PCR) تم تقييم مستوى الترانساميناز ، والبيليروبين ، والكرياتينين ، وجلوكوز الدم ، ومستوى الدهون ، ووظيفة الغدة الدرقية ، والبروثرومبين قبل وبعد ثلاثة أشهر من بداية التجربة. أظهرت بياناتنا عدم وجود تغيرات كبيرة في الكرياتينين ، واليوريا في الدم ، ومستوى الجلوكوز ، والبيليروبين ، والفوسفاتيز القلوي ، وملف الدهون ، والبروثرومبين ، ووظيفة الغدة الدرقية. كان مستوى الحمل الفيروسي قبل وبعد ثلاثة و ستة أشهر من بداية دراستنا 1689 ± 289 ، 558 ± 160 و 271 ± 26 وحدة دولية / مل ، على التوالي. من هذه الدراسة ، قد نستنتج أن شوكة الجمل آمنة وأظهرت نشاطًا ضد التهاب الكبد الفيروسي .B هناك حاجة إلى مزيد من التحقيقات عن طريق زيادة عدد المرضى واستخدام جرعات أعلى من مستخلصات النبات لاستكشاف آلية عملها.

Keywords: Camel thorn, Transaminase, Alkaline phosphatase, Creatinine.

Introduction

Viral hepatitis is a public health problem worldwide as well as a therapeutic challenge. Many recent used drugs may have a high toxicity. Additionally, the development of resistant mutants during the period of the treatments is another issue

with these medicines. Although the interferon (PEG-IFN) and nucleotide analog therapy are currently considered as the standard therapy for treatment of chronic hepatitis B, they are not totally effective and have several side effects (Bruix, Fonseca, & Reig, 2019; Sonneveld & Janssen, 2010). Because the reverse transcriptase of HBV lacks proof-reading function, the virus has rapid mutagenesis. Thus the virus may develop a resistance to antiviral drugs rapidly (Locarnini & Warner, 2007; Mauss & Wedemeyer, 2008). Therefore, the replacement of these drugs with medicinal plants that have lower toxicity can be useful (Govind & Pandey, 2011; Thomas, Leoutsakas, Zabransky, & Kumar, 2011).

Alhagi maurorum (Camel thorn) is a very common woody perennial shrub, rich in phenolic and flavonoid compounds(Al-Jaber, Awaad, & Moses, 2011). Camel thorn is used traditionally as a remedy for rheumatic pains, bilharziasis, liver disorders, urinary tract infection and for various types of gastrointestinal discomfort with both peripheral and central anti-nociceptive activity(Atta & El-Sooud, 2004). It has been also reported that the camel thorn shows Antioxidants, anti-diarrheal and anti-ulcerogenic activities(Awaad, Maitland, & Soliman, 2006). Based on previous studies that showed the hepatoprotective activity of this herb (Abdellatif et al., 2014; Huda, S, et al., 2013), our aim in this study is to investigate the effect of camel thorn on the load of hepatitis B virus.

Material and methods

Preliminary human studies:

The significant relative safety of camel thorn extract (CTE) (LD_{50}= 5.4 g/kg) in mice and its significant hepato-protective effect of our previous experimental studies on animals stimulated the use of small doses of camel thorn powder (CTP) as hepato-protective agent (Huda, El-Naser, et al., 2013). The dose selected was 1.5-2 g three times a day (TID) for 6 months. This dose is extremely small compared with the LD_{50} in mice.

By open labeled study 15 patients with Hepatitis B virus but not with Hepatitis C virus were randomly chosen, with their agreements and consent forms were signed. An ethical approval was also obtained from the University Research Ethics Committee.

The patients were of either sexes and of different ages (20 to 50 yrs.). They had no liver cirrhosis or co-morbid diseases. They were not alcoholics.

All patients underwent basic investigations, including checking their body weight and blood pressure before and after CTP use. The patients used the herb orally in a dose 4.5 gm divided for 6 months.

The investigations included polymerase chain reaction test (PCR), liver function test (LFT) (includes: bilirubin, alanine transaminase (ALT), aspartate aminotransferase (AST), Alkaline, and Albumin); renal function test (RFT) (includes: Urea (Ur), creatinine (Cr)); thyroid function tests (TFT) (incudes: tri-iodothyronine (T3), Tetra-iodothyronine or thyroxine (T4), thyroid stimulating hormone (TSH)); blood glucose levels; total lipid profile (including total cholesterol, triglyceride (TG), high density lipoprotein (HDL), low density lipoprotein (LDL)); complete blood count (CBC); prothrombin time (PT) and international normalized ratio (INR) were measured before and three months after receiving the CTP. PCR test was also repeated at the end of examination (after 6 months).

Thyroid function was determined in Immunoassay analyzer, Elecsys 2010 and Cobas, Roche, Austria. By use of Electrochemiluminescence immunoassay (ECLIA). Complete blood count was determined by a coulter counter, a hematology analyzer, Sysmex KX-21N, Roche, Austria. And prothrombin time determined by coagulation analyzer, Catron. All other biochemical parameters were determined using COBAS Integra 400 plus, biochemical autoanalyzer, Roche, Austria. Polymerase chain reaction for hepatitis B fragments was carried in Cobas Amplicor Analyzer, Roche, Austria, by use of Cobas Amplicor HBV Moniter Test, for HBV.

Results

The potential role of CTP as an alternative treatment of the hepatitis:

Figure (1) shows the change in the mean of the level of viremia before and after use of CTP in patients infected with HBV. The data in the table (1) revealed that there was a significant reduction ($P = 0.02$, $P = 0.01$) of PCR 3 and 6 months respectively, in patients with HBV infection treated with CTP.

As presented in the figure (2A), there was no significant change in the bilirubin (P= 0.2), AST (P= 0.4), ALT (P= 0.1), ALK (P= 0.06) and albumin (P= 0.3) levels in post CTP treated patients with HBV infection as compared with pre CTP patients. As compared with pre CTP treated HBV patients, the P values of blood urea (P= 0.6), creatinine levels (P= 0.08), were insignificant in HBV patients in HBV treated with CTP for three months figure (2B).

As shown in the figure (2C), in both situations when HBV infected patients treated or not with CTP, there was no significant change in the lipid profiles levels. The P value of cholesterol, TG, HDL, LDL were 0.64, 0.88, 0.9, 0.59 respectively. Although the blood level of T4 decreased in pre CTP treated patients from 94.78± 4.43 to 78.77± 15.88 in post CTE treated patients and the blood level of TSH elevated in pre CTP treated patients from 2.55± 0.64 to 3.56± 0.92 in post CTP treated patients, comparatively, there were no significant changes in the P values (P = 0.39, P = 0.16) of these level in pre and post CTE treated patients. The change in T3 blood level was also insignificant (Figure 2 D).

The blood glucose concentration ranged in normal level between 80 and 95 mg % in all pre and post CTP treated patients (Figure 2 E). There also was no significant difference between all parameters of the blood picture, (P values of RBC, WBC and Platelet = 0.88, 0.86, 0.66 respectively) (Figure 2F). The figure 2G reveals that prothrombin time and INR were slightly decreased in post CTP treated patients as compared to pre CTP treated patients. However, these variations were not significant (P= 0.076 and 0.08 respectively).

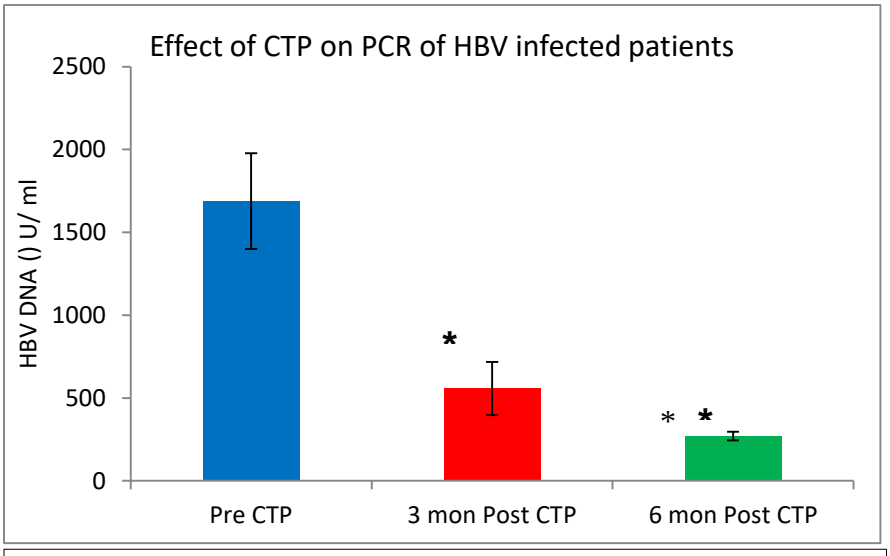

Figure 1: Effect of CTP on PCR of HBV infected patients.
* =Significantly decreased as compared to pretreated patients (P < 0.05).
** =Significantly decreased as compared to pretreated patients (P < 0.01).

	Pre CTP	3 months. Post CTP	6 months. Post CTP
PCR U/ml	1689 ± 289	557 ± 160	271 ± 26

Table1: Effect of CTP on PCR in HBV infected patients

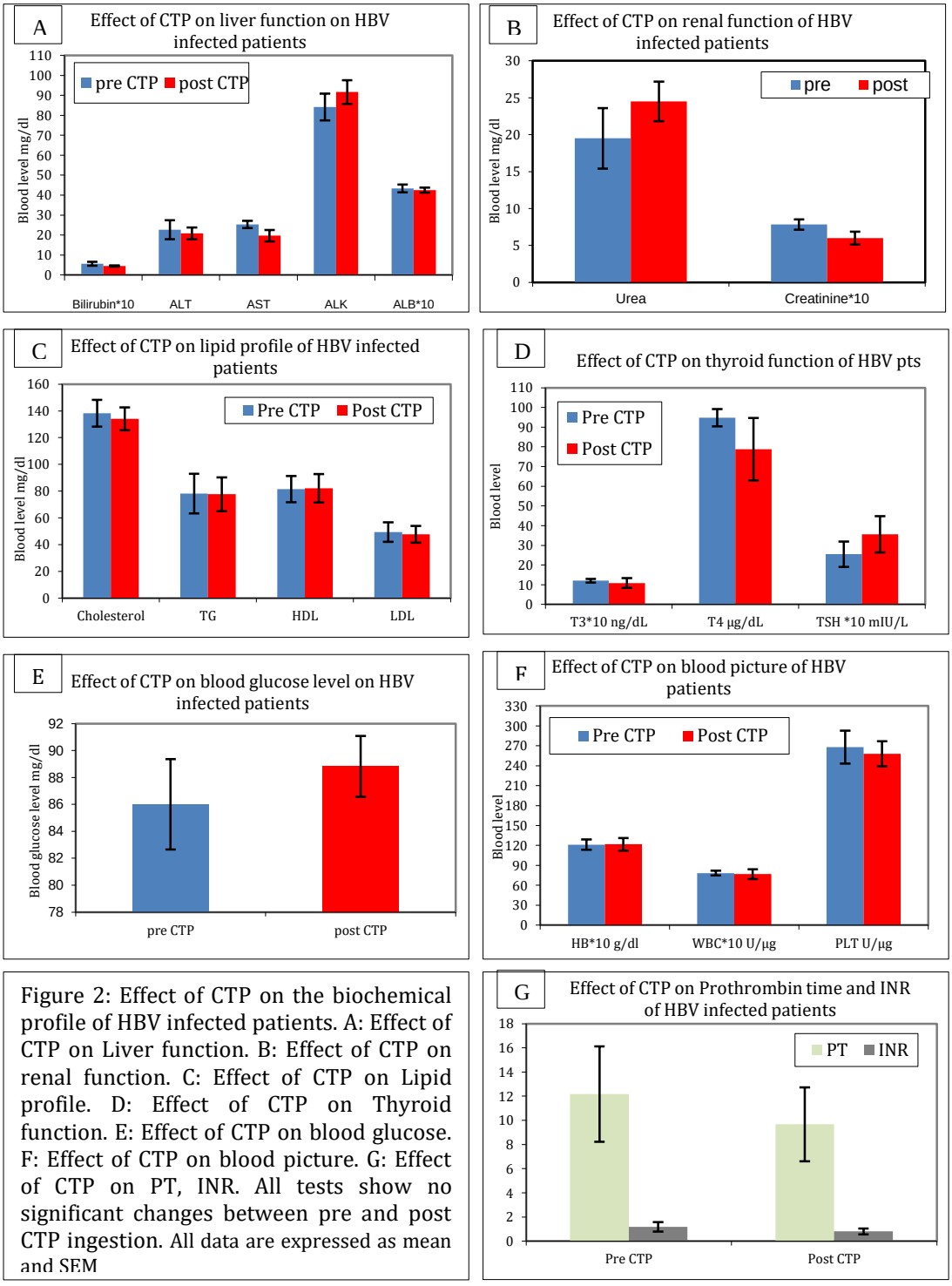

Figure 2: Effect of CTP on the biochemical profile of HBV infected patients. A: Effect of CTP on Liver function. B: Effect of CTP on renal function. C: Effect of CTP on Lipid profile. D: Effect of CTP on Thyroid function. E: Effect of CTP on blood glucose. F: Effect of CTP on blood picture. G: Effect of CTP on PT, INR. All tests show no significant changes between pre and post CTP ingestion. All data are expressed as mean and SEM

Discussion

Many herbs are used traditionally to treat viral infected patients (Solati, Heidari-Soureshjani, & Pocock, 2017; Thyagarajan, Jayaram, & Valliammai, 1990; Venkateswaran, Millman, & Blumberg, 1987) and several studies have revealed that camel thorn improves the transaminase enzymes in experimental animals (Abdellatif et al., 2014; Al-Saleem, Al-Wahaib, Abdel-Mageed, Gouda, & Sayed, 2019; Alqasoumi, Al-Rehaily, AlSheikh, & Abdel-Kader, 2008; Jalil et al., 2015; Maysa, 2016).

It has been shown that some herbs have several phytochemicals with potent antioxidant properties such as alkaloids, carotenoids, flavonoids (isoflavones, flavonones, and quercetin), terpenoids, polyphenols (ellagic acid, gallic acid and tannins), carotenoids,, polysaccharides (Ghasemi & Lorigooini, 2016; Govind, 2011). In our previous preliminary phytochemical screening of camel thorn, as well as in other studies, we had a clear evidence for the presence of phenolics, flavonoids, tannins and alkaloids in addition to carbohydrates and sterols (Ahmad et al., 2010; Huda, S, et al., 2013). Antioxidants treat various diseases by protecting cells against free radical-induced damage (Govind, 2011). Therefore, The mechanism of such hepatoprotective activity may be related to the flavonoids and other phytochemicals compounds of CTE (Al-Saleem et al., 2019).

In the current study, we found the viral load of HBV DNA is significantly reduced after receiving camel thorn powder, Indicating that this plant is effective against HBV. The present finding also suggests the camel thorn is not toxic since no marked change on the biochemical, hematological, and thyroid parameters were observed. Therefore the camel thorn may be considered as an alternative treatment option that exhibits minimal side effects for subjects suffering from viral infections.

The molecular mechanism behind the anti-HBV activity of the camel thorn has not been studied well. However, other studies showed that the anti-oxidant compounds in many medicinal plants have antiviral effects. Some studies reveal that phenolic acids showed antiviral effects. 3,4-*O*-dicaffeoylquinic acid and 3,5-*O*-dicaffeoylquinic acid isolated from *Laggera alata* significantly suppressed the HBsAg and HBeAg production (Hao et al., 2012; Kim, Kim, & Lee, 2007; Wu et al., 2012). In addition,

curcumin (a natural polyphenol) exhibited an inhibitory effect on HBV gene expression and replication in HBV-expressing cells by down-regulation of peroxisome proliferator-activated receptor-γ co-activator 1α (PGC-1α), a co-activator of HBV transcription (Rechtman et al., 2010). Phenols from *Swertia mussotii* inhibited the secretion of HBsAg and HBeAg and HBV DNA replication (Cao et al., 2015).

Oxymatrine (an alkaloids) from the plant Kushen (*Sophora japonica*) often is used to substitute the nucleoside analogues to lower the emergence of treatment-resistant HBV mutants(Chen, Mao, & Jiang, 2002). It has been also shown that the flavonoids have antiviral activity. Epigallocatechin-3-gallate (EGCG) from green tea inhibited HBV entry into immortalized human primary hepatocytes (Huang et al., 2014). EGCG effectively suppressed the HBsAg and HBeAg secretion in HepG2 2.2.15 cells and reduced the extracellular HBV DNA level. Interestingly, its effect was stronger than that of lamivudine (Pang, Zhao, Wang, Ma, & Xiao, 2014).

In conclusion, we found that the Camel Thorn significantly lowered the Hepatitis B viral load with no significant side effects. we suggest this may related to its anti-oxidant property of the plant. further studies are required to explore the mechanism of the antiviral effect of the Camel Thorn.

Competing interests

The authors declare that they have no competing interests.

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