Journal of Taibah University Medical Sciences (2018) ■(■), 1–10

Taibah University

Journal of Taibah University Medical Sciences

www.sciencedirect.com

Original Article

Hepatoprotective and antioxidant activities of *Spondias mombin* leaf and stem extracts against carbon tetrachloride-induced hepatotoxicity

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Received 24 November 2017; revised 11 March 2018; accepted 14 March 2018; Available online ■ ■ ■

الملخص

أهداف البحث: تستخدم ورقة نبات سبونديلس مومبين (بطمية) في الطب الشعبي في نيجيريا لعلاج التهاب الكبد. هذه الدراسة تقيم نسبيا تأثيرات الحماية الكبدية ومضادات الأكسدة في الجسم الحي لورقة نبات سبونديلس مومبين ومستخلصات الميثانول في جذع النبات في نموذج الفئران لتسمم الكبد.

طرق البحث: تم تقسيم اثنين وأربعين فأرا إلى سبع مجموعات. أعطيت المجموعة أ الماء، وأعطيت المجموعة ب الماء، كما أعطيت المجموعتين س و د ورقة نبات سبونديلس مومبين بجرعة ٥٠٠ و١٠٠٠ مجم/كجم من وزن الجسم، على التوالي، وأعطيت المجموعتين إ و ف جذع نبات سبونديلس مومبين ٥٠٠ و ١٠٠٠ مجم /كجم من وزن الجسم، على التوالي، و أعطيت المجموعة ج سيليمارين بجرعة ١٠٠ مجم/كجم. أعطيت جميع المستخلصات والأدوية يوميا بواسطة غشاء فموي لمدة سبعة أيام، ثم تم حث تسمم الكبد الحاد للمجموعتين ب و ج بإعطاء CCl_4. بعد ٤٨ ساعة تم ذبح الفئران وفحص المؤشرات النسيجية والكيميائية الحيوية لتسمم الكبد.

الاستنتاجات: أحدث CCl_4 إصابة بالكبد بزيادة كبيرة في مستويات علامات الإصابة الكبدية: ALT,AST, TBIL,CBIL, بالإضافة إلى خفض كبير في البروتين الكلي في الدم. حسنت المستخلصات النباتية لورقة نبات سبونديلس مومبين وجذع نبات سبونديلس مومبين عند ٥٠٠ و١٠٠٠ مجم/كجم قبل العلاج ب CCl_4 بشكل ملحوظ إصابة الكبد، وخفضت مستويات ALT,AST,TBIL, CBIL. مستخلصات ورقة نبات سبونديلس مومبين أو جذع نبات سبونديلس مومبين زاد كثيرا المستويات الخلوية للجلوتاثيون، ونشاطات الكتالاز وديسموتاز الفائق، وخفض كثيرا المواد المتفاعلة لحمض ثيوباربيتوريك.

النتائج: تقدم هذه الدراسة أدلة أولية تدعم الفوائد المحتملة لنبات سبونديلس مومبين لعلاج تسمم الكبد -الناجم عن الاكسيوبيوتيك.

الكلمات المفتاحية: ورقة نبات سبونديلس مومبين؛ تسمم الكبد؛ حماية الكبد؛ الأكسدة

Abstract

Objective: *Spondias mombin* L. is a tree used in folk medicine in Nigeria for the treatment of hepatitis. This study was carried out to comparatively evaluate the hepatoprotective and antioxidant effects of *S. mombin* leaf and stem (SML and SMS) methanolic extracts in a rat model of carbon tetrachloride (CCl_4)-induced hepatotoxicity.

Methods: Forty-two rats were distributed into seven groups. Groups A and B received water; groups C and D received 500 and 1000 mg/kg SML extract, respectively; groups E and F received 500 and 1000 mg/kg SMS extract, respectively; and group G received 100 mg/kg silymarin. Water, the two extracts, and silymarin were administered daily by oral gavage for 7 days. Hepatotoxicity was induced in groups B to G by the administration of CCl_4 once on the seventh day. After 48 h, rats were sacrificed, and tissues and serum samples were examined for histological and biochemical indices of hepatotoxicity.

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Peer review under responsibility of Taibah University.

ELSEVIER Production and hosting by Elsevier

1658-3612 https://doi.org/10.1016/j.jtumed.2018.03.006

Please cite this article in press as: Nwidu LL, et al., Hepatoprotective and antioxidant activities of *Spondias mombin* leaf and stem extracts against carbon tetrachloride-induced hepatotoxicity, Journal of Taibah University Medical Sciences (2018), https://doi.org/10.1016/j.jtumed.2018.03.006

Results: Administration of CCl_4 resulted in liver injury with significant elevation in the hepatocellular injury markers alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), total bilirubin (TBIL), and conjugated bilirubin (CBIL), associated with a significant reduction in total circulatory protein. Pretreatment with SML and SMS extracts at both doses significantly ameliorated liver injury; lowered ALT, AST, ALP, TBIL, and CBIL levels; elevated cellular glutathione levels as well as catalase and superoxide dismutase activities; and decreased the levels of thiobarbituric acid reactive substances.

Conclusion: This study provides preliminary evidence supporting the potential therapeutic benefit of *S. mombin* in xenobiotic-induced hepatotoxicity.

Keywords: Hepatoprotection; Hepatotoxicity; Oxidative stress; *Spondias mombin* L.

Introduction

Liver diseases are major causes of illness and death worldwide,[1–4] and constitute a public health challenge that requires the development of new therapeutic options. Investigating the hepatoprotective effects of medicinal plants in laboratory animals is an important initial step in evaluating the safety of new biomolecules.[5–9] Natural products from ethnomedicine have provided safe and effective alternatives for the treatment of hepatotoxicity. Many previous reports have demonstrated the hepatoprotective effects of local phytoextracts rich in natural antioxidants,[5–15] and several bioactive compounds and plant extracts have been investigated for their hepatoprotective and antioxidant effects.[16,17]

Phenolic compounds found in several plants are usually associated with multiple biological activities such as free radical scavenging activities.[18–20] It has been suggested that natural antioxidants found in food, such as phenolic compounds or flavonoids, might play an important role in the prevention of oxidative stress-related disorders and in the reduction of premature mortality.[21,22] Flavonoids are certainly ubiquitous in the epidermal cells of many plant parts and exist in both glycosidic and non-glycosidic forms.[23]

Spondias mombin L. (Anacardiaceae) is commonly known as hog plum (English), akika (Yoruba), ijikara (Igbo), tsadarmaser (Hausa), chabbuh (Fulani), nsukakara (Efik), and atoa (Ashanti).[24] It is a deciduous erect tree, which grows up to 15–20 m high, with a trunk that is 60–75 cm wide.[25,26] *S. mombin* is commonly found in the tropical Americas, including the West Indies, and has also been naturalized in parts of Africa, including Ghana, and some parts of Asia.[26] In ethnomedicine, *S. mombin* parts, including the stem bark, leaves, and roots, have been used for the treatment of various conditions. *S. mombin* possesses antimicrobial[27,28] and antiviral activities.[29] Its leaves show anti-inflammatory,[30] anthelmintic,[31] hematinic,[32] and sedative[33] activities, while its stem bark possesses anti-mycobacterial activity.[34] In a previous study, phytochemical screening indicated that *S. mombin* leaf (SML) contains tannins, saponins, alkaloids, flavonoids, and phenols.[35] It is also rich in ascorbic acid and niacin, and contains riboflavin and thiamine.[35]

The hepatoprotective effects of *Ocimum gratissimum* and SML have been previously evaluated in rats after intoxication with dimethylnitrosamine.[36] However, the effects of SML and *S. mombin* stem (SMS) on carbon tetrachloride (CCl_4)-induced hepatotoxicity have not yet been assessed. Thus, the aim of this study was to establish whether SML and SMS methanolic extracts show hepatoprotective effects against CCl_4-induced hepatotoxicity in rats.

Materials and Methods

Chemicals and reagents

CCl_4, silymarin, diethyl ether, and methanol were purchased from Sigma–Aldrich, St. Louis, Missouri, USA. Diagnostic kits for serum alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), conjugated bilirubin (CBIL), and total bilirubin (TBIL) were purchased from Randox Laboratories Ltd., London, UK. All other chemicals and solvents were of the highest commercially available grade (analytical grade) and were obtained either from Sigma–Aldrich or Merck, UK.

Plant collection and validation

Fresh leaves and stems of *S. mombin* L. were collected from Obafemi Awolowo University campus in January 2015. The plant was identified and authenticated by Dr. Oladele Adekunle, a Taxonomist at the Forestry Department, University of Port Harcourt, Nigeria, where specimens of SML (20015) and SMS (20016) were deposited.

Preparation of S. mombin leaf and stem methanolic extracts

Three hundred grams of *S. mombin* L. fresh leaves and stem barks were weighed, air dried, and powdered. Then, powdered leaves and stems were extracted by the cold extraction method (maceration) using methanol as a solvent; SML and SMS powders were soaked in one liter of 50% methanol for 3 days, during which the mixture was shaken twice daily to promote extraction. The solvent was filtered over a layer of gauge and the filtrate was evaporated to dryness *in vacuo* at 55 °C. The weights of the dried extracts were 21.3 g and 9.4 g, and the obtained yields were 7.1% and 3.1% for SML and SMS extracts, respectively. The extracts were stored in a refrigerator for up to 4 weeks for subsequent use in assays.

Phytochemical screening

The methanolic extracts of SML and SMS were quantitatively assayed for the presence of phytochemicals such as saponins, tannins, alkaloids, terpenoids, cardiac glycosides, and flavonoids using standard procedures.[36]