荷葉專利報告、產學合作

報告人：王朝鐘 教授

開發荷葉黃酮為降低(1)酒精性及(2)非酒精性脂肪肝(3)體脂肪(減肥胖)形成(4)抗乳癌專利及輔助藥品之用途及技術

已研究並發表於國際SCI期刊證實具有
(1)調節血脂，抑制血管病變
(2)降低肝臟脂肪減少酒精性及非酒精性脂肪肝
(3)抑制體脂肪形成(減肥胖)之作用
(4)抗乳癌美國專利

荷葉可作癌症標靶藥物

中山醫大研究其萃取物，發現具抑制癌細胞等作用，值得商品化開發

■李淑慧

中山醫學大學研發抗癌獲新發現。日前中山醫學大學發表荷葉萃取物多項實驗成果，由動物試驗得知，荷葉萃取物具抑制乳癌細胞、尚具抑制血管病變、降體脂肪、排除脂肪肝等作用，未來將可開發成癌症標靶藥物。

中山醫學大學生化暨生物科技研究所研發長王朝鐘表示，荷葉萃取所得的荷葉萃取物，含逾50%類黃酮，利用化學物質NMU誘導及移植法，經過動物實驗研究，荷葉萃取物具抑制乳癌效果。該中心也進行多項機轉研究，抑制乳癌的研究，類似目前治療乳癌的標靶藥物，除了乳癌標靶—HER2，以及另一標靶　雌性激素接受體，大量表現所引起的癌症，荷葉萃取物均具抑制作用。

除此之外，亦可抑制FAS脂肪酸合成酶，進而抑制乳癌。王朝鐘表示，臨床藥物是針對標靶用標靶藥物，因此，該中心正進行其與臨床藥物比較，特別的是，該萃取物為多種標靶，希望將來更一步研發，讓多數乳癌患者皆能適用，目前該成果已於2009年8月取得美國抗乳癌專利。

荷葉有多項功能，可抑制血管病變的報告，中山醫學大學已發表在今（2010）年國際期刊。此外，亦具減脂肪作用，透過實驗得知，可降低腎臟、睪丸等器官周邊組織的脂肪，10周內可減約8%。第四項是可減低脂肪肝，脂肪肝為肝病變的起源，經由研究明顯地發現可排除肝臟的脂肪，該萃取物可抑制脂肪肝，進而達到護肝作用。

荷葉，不僅具保健功效，而且種植成本小、經濟效益高，對農業發展助益甚佳，有多項產品：蓮花、蓮子、蓮藕及荷葉等，經濟價值更高，極適合業者進行更深入研發及朝向健康食品商品化開發。

中華民國專利證書

發明第 I 406667 號

發明名稱：治療癌症之水萃荷葉萃取物

專利權人：中山醫學大學

發明人：王朝鐘、楊孟元

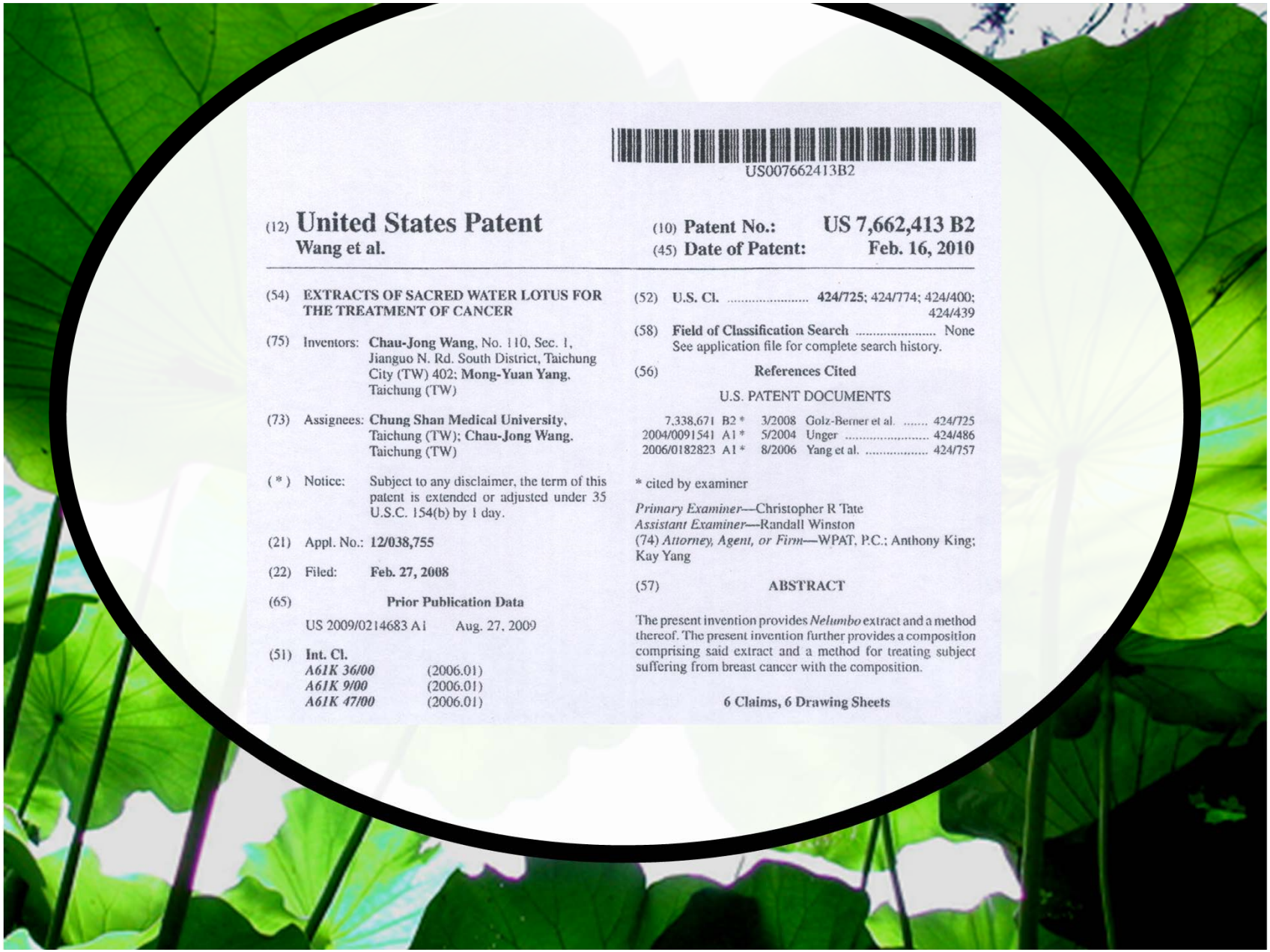
專利權期間：自 2013年 9 月 1 日至 2029年 2 月 9 日止

上開發明業經專利權人依專利法之規定取得專利權

經濟部智慧財產局
局長 王美花

中華民國 102 年 9 月 1 日

注意：專利權人未依法繳納年費者，其專利權自原繳費期限屆滿後消滅。



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(12) **United States Patent**
Wang et al.

(10) **Patent No.: US 7,662,413 B2**
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(54) **EXTRACTS OF SACRED WATER LOTUS FOR THE TREATMENT OF CANCER**

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A61K 47/00 (2006.01)

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(58) **Field of Classification Search** ..... None
See application file for complete search history.

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(57) **ABSTRACT**

The present invention provides *Nelumbo* extract and a method thereof. The present invention further provides a composition comprising said extract and a method for treating subject suffering from breast cancer with the composition.

6 Claims, 6 Drawing Sheets

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ARTICLE

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Improvement in High-Fat Diet-Induced Obesity and Body Fat Accumulation by a *Nelumbo nucifera* Leaf Flavonoid-Rich Extract in Mice

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Diets high in fat lead to excessive lipid accumulation in adipose tissue, which is a crucial factor in the development of obesity, hepatitis, and hyperlipidemia. In this study, we investigated the antiobesity effect of a flavonoid-enriched extract from *Nelumbo nucifera* leaf (NLFE) in vivo. C57BL/6 mice were fed with a high-fat diet (HFD) to induce obesity. NLFE reduced the body weight, body lipid accumulation, and activities of fatty acid synthase (FAS), glutamic oxaloacetic transaminase, and glutamic pyruvic transaminase. NLFE also suppressed the expression of FAS, acetyl-CoA carboxylase, and HMGCoA reductase and increased the phosphorylation of AMP-activated protein kinase in the liver. Taken together, we demonstrated that NLFE targets lipid-regulated enzymes and may be effective in attenuating body lipid accumulation and preventing obesity.

KEYWORDS: Obesity; *Nelumbo nucifera* leaf flavonoid-enriched extract; fatty acid synthase; AMPK

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Improvement for High Fat Diet-Induced Hepatic Injuries and Oxidative Stress by Flavonoid-Enriched Extract from *Nelumbo nucifera* Leaf

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Nelumbo nucifera Gaertn is widespread and a popular food in central and southern Taiwan. It has also been reported to possess different therapeutic effects, but the effects of *N. nucifera* leaf on lipid metabolism and liver function remain unclear. In this study, a high fat diet was used to induce hyperlipidemia, hypercholesterolemia, and fatty liver in hamster. The effects of flavonoid-enriched *N. nucifera* leaf extract supplement and two lipid-lowing drugs, silymarin and simvastatin, on the disorders induced by high fat diet were investigated. The results showed that a 10-week application of a high fat diet to hamsters led to significant increases of body weight, plasma lipid derivatives (triglyceride, total cholesterol, and lipoproteins), lipid peroxidation, and liver damage markers (plasma aspartate aminotransferase and alanine aminotransferase). Interestingly, flavonoid-enriched *N. nucifera* leaf extract supplement effectively ameliorated the high fat diet-induced lipid metabolic disorders as significantly as silymarin and simvastatin did. Moreover, the flavonoid-enriched supplement alleviated the high fat diet-induced accumulation of lipids in liver, the findings showing distinguishing mechanisms from the effects of silymarin and simvastatin. These results suggested that the flavonoid-enriched *N. nucifera* leaf extract supplement may significantly improve the high fat diet-induced abnormal blood lipids and liver damage as significantly as the common drugs. Consequently, it is suggested that the flavonoid-enriched *N. nucifera* leaf extract supplement is beneficial for the improvement of lipid metabolisms and the alleviation of liver damage in high fat diet treatment.

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Polyphenol-rich extract of *Nelumbo nucifera* leaves inhibits alcohol-induced steatohepatitis *via* reducing hepatic lipid accumulation and anti-inflammation in C57BL/6J mice†

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The present study was undertaken to evaluate the hepatoprotective effect mechanisms of *Nelumbo nucifera* leaves extract (NLE) in experimental alcoholic steatohepatitis animal models. We found that the NLE contained polyphenols (phenolic acids and flavonoids), and more than 70% of the main functional components in NLE could potentially provide benefits for alcoholic liver disease. The parameters of histopathology, immunohistochemistry, antioxidant defense, proinflammatory mediator and lipid synthesis-related proteins demonstrated the inhibitory effect of NLE on alcoholic steatohepatitis. Plasma and hepatic content analysis showed that NLE inhibited lipid accumulation by altering the levels of triglycerides (TG) and cholesterol (TC). Treatment with NLE increased the expression of the p-AMPK/AMPK ratio and PPAR-α. Furthermore, fatty acid oxidation and transport *via* carnitine palmitoyltransferase-1 (CPT1) and microsomal triglyceride transfer protein (MTP) were through the activation of the AMPK and PPAR-α signal. These results revealed that the polyphenol-rich component of NLE prevents alcoholic steatohepatitis by multiple pathways, including reduced lipid synthesis, enhanced fatty acid oxidation and transport responses, inhibited oxidative stress and facilitated anti-inflammation. Suggesting that NLE might be regarded as a beneficial food that has the potential to be developed as a natural agent for preventing alcoholic steatohepatitis.

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中山醫學大學執行食品領域項下「開發保健食品」科技計畫(計畫名稱: 開發荷葉黃酮原料及膠囊不易形成體脂肪及非酒精性與酒精性肝炎護肝作用之健康食品)研發成果擬申請技轉資料:

市場資料:

保健食品全球市場已經超過300億美金，以美國和日本為主，在2007年台灣保健食品產值為438億台幣，又美國、日本及台灣等開發國家具有脂肪肝及肥胖之人口比例相當高。荷葉黃酮原料或膠囊製品同時具多項用途，**市場潛力相當高，且目前排除非酒精性與酒精性肝炎脂肪肝之護肝作用尚未有健康食品字號之產品(衛署評估方法草案公佈中)，減體脂肪不易形成體脂肪(減體重)之產品亦不多。**

市場潛力:

(1)產品具有**高含量類黃酮(50%以上)較全世界保健市場第一名之銀杏葉(24.5%)兩倍以上。**

(2)目前**非酒精性與酒精性肝炎脂肪肝之護肝作用**高脂糧餵食動物之脂肪肝傷害尚未有產品申請健字號護肝作用，而台灣及世界且多數**脂肪肝之成人約佔60%以上，疾病尤其是代謝症候群疾病及肝硬化、肝癌多數因脂肪肝引起，因此本項用途有極大市場空間，尤其是國外市場。**

(3)許多代謝症候群等疾病，係因肥胖引起，而台灣及已開發國家均有多數肥胖人口，本產品用途具**不易形成體脂肪(減肥胖)**之作用，市場潛力大。

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