山苦瓜(*Momordica charantia* Linn. var. *abbreviata* Ser.)果實萃取物之成分分析

林珏豪、黃啟瑞、楊繼江*

國立臺東大學生物醫學碩士學位學程

摘要

本研究使用臺東產地的山苦瓜(*Momordica charantia* Linn. var. *abbreviata* Ser.) 果實通過液相層析串聯質譜儀 (LC/MS/MS) 來分析其中成分，以二次過濾水、1:1 酒精與水混合、95 % 酒精三種萃取液來探討其中有效成分的差異，其中含酚類化合物及類黃酮化合物為主要的生物活性指標。結果得出山苦瓜水萃主要有 8 種化合物，山苦瓜酒水混合萃主要有 9 種化合物，而山苦瓜酒萃主要有 6 種化合物，總共有 2 種類黃酮及 8 種多酚類化合物。雖然酒萃中的化合物較少，但是對香豆酸只有在酒萃才能析出。山苦瓜水萃及酒水混合萃比起酒萃多了 5-咖啡醯奎尼酸、奎尼酸及總綠原酸，而鄰苯三酚只有酒水混合萃有析出，在水萃及酒萃皆無此化合物。這十種化合物中，大多都有抗氧化、抗糖尿病、抗癌、抗代謝症候群、降高血壓、抗肥胖、抗發炎及抗病毒等等的功效，這與之前研究所描述的功效相同。本研究後續會以糖尿病作為研究的目標，以胰臟 α-澱粉酶和腸道 α-葡萄糖苷酶酵素抑制及 GLP-1 激素的提升，減少糖尿病患者餐後高血糖及抑制食物的攝取量。

關鍵字：山柰酚、黃岑素、5-咖啡醯奎尼酸、沒食子酸、抗糖尿病

林珏豪，國立臺東大學生物醫學碩士學位學程研究生。E-mail : juhowlin0406@yahoo.com.tw。

黃啟瑞，國立臺東大學生物醫學碩士學位學程兼任助理教授、經濟部東部深層海水創新研發中心研究員。E-mail : crhuang.ksn@gmail.com。

楊繼江(通訊作者)，國立臺東大學生物醫學碩士學位學程教授、國立臺東大學生醫農食研究中心主任。E-mail : cyang@nttu.edu.tw 。

Composition analysis of wild bitter melon fruit (*Momordica charantia* Linn. var. *abbreviata* Ser.) extract

Jue-Hao Lin, Ci-Ruei Huang, Chi-Chiang Yang*

Abstract

In this study, wild bitter melon (*Momordica charantia* Linn. var. *abbreviata* Ser.) fruit from Taitung was used to analyze its components by liquid chromatography tandem mass spectrometry (LC/MS/MS). The differences of active ingredients were explored by three extraction solvents: distilled deionized water, 1:1 alcohol-water mixed, and 95 % alcohol, among which phenolic compounds and flavonoids were the main biological activity indicators. The results showed that there were mainly 8 compounds in the water extract of wild bitter melon, 9 compounds in the alcohol-water mixed extract, and 6 compounds in the alcohol extract, a total of 2 flavonoids and 8 polyphenolic compounds. Although there are fewer compounds in the alcohol extract, p-coumaric acid can only be found in the alcohol extract. Compared with alcohol extract, wild bitter melon water extract and alcohol-water mixed extract have more 5-O-caffeoylquinic acid, quinic acid and chlorogenic acid, while pyrogallol is only present in alcohol-water mixed extract, but not in water or alcohol extract. Most of these ten compounds have antioxidant, anti-diabetic, anti-cancer, anti-metabolic syndrome, lowering blood pressure, anti-obesity, anti-inflammatory and anti-viral effects, which are the same as those described in previous studies. In the follow-up of this study, diabetes will be the research goal, and the inhibition of pancreatic α-amylase and intestinal α-glucosidase enzymes and the increase of GLP-1 hormone will reduce postprandial hyperglycemia and inhibit food intake in diabetic patients.

Keywords: Kaempferol, Baicalein, 5-O-Caffeoylquinic acid, Gallic acid, Anti-diabetic

Jue-Hao Lin, Master's Student, Master's Program in Biomedicine, National Taitung University. Email: juhowlin0406@yahoo.com.tw.

Ci-Ruei Huang, Adjunct Assistant Professor, Master's Program in Biomedicine, National Taitung University; Researcher, Eastern Taiwan Deep Sea Water Innovation and Research Center, Ministry of Economic Affiars. E-mail: crhuang.ksn@gmail.com

Chi-Chiang Yang (Corresponding Author), Professor, Master's Program in Biomedicine; Director, Biomedicine, Agriculture and Food Science Research Center, College of Science and Engineering, National Taitung University. E-mail: cyang@nttu.edu.tw

壹、前言

苦瓜(*Momordica charantia*)，一種常被食用的植物，由於全株植物皆帶有苦味因而得名。近年來，苦瓜及其不同溶劑的萃取物已被研究其生物活性，包括抗氧化劑(Wei et al., 2013)，抗糖尿病(Zhu et al., 2013)，抗癌(Kwatra et al., 2013)，抗炎(Chao et al., 2013)，抗菌(Costa et al., 2013)，抗真菌(Santos et al., 2013)，抗病毒(Pongthanapisith et al., 2013)，抗愛滋病(Fang & Ng, 2011)，驅蟲藥(Lal et al., 1975)，抗結核桿菌(Frame et al., 1998)，降血壓(Ojewole et al., 2006)，抗肥胖(Shih et al., 2008)，免疫調節(Deng et al., 2014)、抗高血脂血症(Manik et al., 2013)和神經保護活性(Malik et al., 2011)。

山苦瓜(*Momordica charantia* Linn. var. *abbreviata* Ser.)，是一種在台灣常見的野生苦瓜，一樣作為常被食用的植物。最近的研究報告了野生苦瓜的某些生物活性，有助於改善代謝綜合症(Tsai et al., 2012)，對抗酒精性脂肪肝(Lu et al., 2014)和減少炎症(Hsu et al., 2012)。但關於其生物活性的功能性研究仍然有限。

本研究取用台灣山苦瓜的果實，以不同萃取方式分析其成分。期望得知山苦瓜進一步的化合物，從此推測其有關的生物活性，也瞭解不同萃取液是否會對山苦瓜的化合物比例有所不同，進而影響相關的生物活性。

貳、文獻探討

一、山苦瓜特徵

山苦瓜為葫蘆科（*Cucurbitaceae*）苦瓜屬（*Momordica*），為一年生蔓性攀緣草本植物，分枝繁茂，藤蔓具有捲鬚和毛茸，可攀緣，全株具有特殊氣味，比一般苦瓜矮小（行政院農業委員會〔農委會〕，2016）。

二、山苦瓜萃取成分

將山苦瓜在陰涼處風乾，然後用研磨機研磨成粉末。以乙醇萃取後，用分配層析法得到乙醇萃取物（ET）、石油醚（PE）、氯仿（CF）、乙酸乙酯（EA）、正丁醇（Bu）和水層樣品。結果顯示乙酸乙酯（EA）對 DPPH 有較高的清除活性，IC_{50} 值為 0.43 ± 0.04 mg/mL。而氯仿（CF）、乙酸乙酯（EA）和正丁醇（Bu）對 2,2-azinobis-3-ethyl benzothiazoline-6-sulfonic acid（ABTS）具有較強的清除能力，IC_{50} 值分別為 0.36 ± 0.04 mg/mL、0.35 ± 0.02 mg/mL 和 0.35 ± 0.05 mg/mL。此外，乙酸乙酯（EA）可有效抑制 α-澱粉酶（α-Amylase）活性，IC_{50} 值為 0.27 ± 0.029 mg/mL。最後乙醇萃取物（ET）及乙酸乙酯（EA）還能降低由 LPS 刺激的小鼠巨噬細胞 RAW 264.7 中促炎因子一氧化氮（NO）的產生(Pham et al., 2019)。

先前研究指出，用山苦瓜水萃及乙醇萃對於 DPPH 清除活性 IC_{50} 值分別為 129.94 µg/ml 和 156.78 µg/ml，優於維生素 E 的 172.21 µg/ml。總黃酮試驗顯示水萃(62.0 mg/g)的總黃酮濃度大於乙醇萃(44.0 mg/g)，而總多酚試驗的結果則是乙醇萃

(68.8 mg/g)的總多酚濃度大於水萃(51.6 mg/g) (Wu & Ng, 2008)。

另一篇研究則是提到使用山苦瓜乙酸乙酯萃在體外能有效抑制由 *Propionibacterium acnes* 誘導 THP-1 細胞中的促炎細胞因子和基質金屬蛋白酶(Matrix metalloproteinase, MMP)-9 的表現量。不僅如此，在小鼠中注射山苦瓜乙酸乙酯萃能有效減輕由 *P. acnes* 誘導的耳朵腫脹(Ear swelling)及肉芽腫性炎症(Granulomatous inflammation)。作者為了瞭解其生物活性，從山苦瓜乙酸乙酯萃中發現了可皂物（Saponifiable, S）與非皂物（Nonsaponifiable, NS），這兩者部分有能抑制促炎細胞因子和 MMP-9 的表現量，在 NS 中鑒定的植物醇和葉黃素也抑制細胞因子的產生。最後結果顯示，PPARα 或 PPARγ 的信號傳導可能有助於山苦瓜的抗炎活性(Hsu et al., 2012)。

山苦瓜乙醇萃取物（Ethanol extract of wild bitter gourd, WBGE）的總多酚（TPC）、總多醣（TPSC）、總黃酮（TFC）和總皂苷（TSC）的值分別為 139.35±3.77 mg GAE/g DW、25.07±1.04 mg Glc/g DW、13.96±0.89 mg RE /g DW，6.04 ± 0.32 mg OA/g DW。另一方面使用 LC-MS 分析鑑定出 27 種化學成分。實驗比較了苦瓜的水萃（WBGW）、乙醇萃（WBGE）及山苦瓜的水萃（BGW）、乙醇萃（BGE），得出 WBGE 對 α-葡萄糖苷酶（α-Glucosidase）、PTP1B 和脂肪酶（Lipase）抑制活性效果最好，WBGE 在體外也有明顯地降血糖降脂的效果。作者進一步做口服 WBGE 對 SD 大鼠高脂飲食（High-fat diet, HFD）和鏈脲佐菌素（Streptozotocin, STZ）誘導的第二型糖尿病的抗糖尿病作用，得出 WBGE 有效地降低血糖和血脂濃度，緩解葡萄糖耐受不良和胰島素抗性的症狀。此外，WBGE 的消耗還可以抑制氧化反應和發炎損傷。機制研究顯示，WBGE 可能通過調節 AMPK / PI3K 路徑發揮作用(Fu et al., 2022)。

除了山苦瓜的果實之外，在葉子也表現出抗炎活性，針對山苦瓜葉子總酚萃取物（Total phenolic extract, TPE）進行 HPLC 得到含有沒食子酸（Gallic acids）、總綠原酸（Chlorogenic acids）、咖啡酸（Caffeic acids）、阿魏酸（Ferulic acids）、肉桂酸（Cinnamic acids）、楊梅素（Myricetin）、槲皮素（Quercetin）、木犀草素（Luteolin）、芹菜素（Apigenin）和百里酚（Thymol）化合物，能抑制由 *P. acnes* 所誘導體內和體外炎症反應的活性，還能減輕了由 *P. acnes* 所誘導的小鼠耳朵腫脹以及微膿腫（Microabscess）。流式細胞分析顯示經由 TPE 處理能顯著降低體內嗜中性球（Neutrophils）和介白素（Interleukin, IL）-1β 群體的遷移。TPE 在體外抑制 *P. acnes* 誘導 THP-1 細胞中的 mRNA 表現量及 IL-8，IL-1β 和腫瘤壞死因子（Tumor necrosis factor, TNF）-α 的產生。此外，TPE 抑制 *P. acnes* 誘導的 MMP-9 的水平，阻斷 nuclear factor-κB（NF-κB）活化和絲裂原活化蛋白激酶（MAPK）的失活;這些作用可能部分解釋了 TPE 對細胞因子產生的抑制作用(Huang et al., 2015)。

根據上述文獻顯示山苦瓜果實具有抗氧化、抗發炎、抑制 α-amylase 活性、抑制 α-glucosidase、PTP1B 和 lipase 的活性、降低血糖和血脂表現量、緩解葡萄糖耐受不良和胰島素抵抗的症狀、抑制氧化反應和發炎損傷、抑制促炎細胞因子和 MMP-9 的

表現量、減輕由 *P. acnes* 誘導的耳朵腫脹及肉芽腫性炎症和降低由 LPS 刺激的小鼠巨噬細胞 RAW 264.7 中 NO 的產生等等功能。而葉子也表現出抗炎活性、降低體內嗜中性球和 IL-1β 群體的遷移、抑制 *P. acnes* 誘導 THP-1 細胞中的 mRNA 表現量及 IL-8，IL-1β 和 TNF-α 的產生和抑制 *P. acnes* 誘導的 MMP-9 的表現量，阻斷 NF-κB 活化和 MAPK 的失活。

參、研究方法

一、樣品來源及處理

此研究使用的品種為山苦瓜，其果實來自臺東當地廠商御心頻有限公司(臺東，臺灣)購買，已先將山苦瓜果實風乾裁剪，樣品抵達後放置於 -20℃ 冰箱中進行保存，接著將樣品先放置乾燥箱 (40℃) 進行烘乾 (5 天) ，隨後用電動粉碎機將其磨成碎粉狀(研磨 20 秒休息 10 秒為一個循環，進行三個循環)，磨粉後儲存於乾燥箱（溫度 25℃、濕度 40%）備用。

二、樣品製備

山苦瓜果實萃取物樣品分為為水萃取（Water extract, WE）、酒精萃取（Alcohol extract, AE）、酒精水混合萃取（Mixed water and alcohol extract, ME）。水萃溶劑為二次水，酒萃溶劑為 95% 酒精，酒水萃溶劑為二次水與 95% 酒精以 1:1 的比例混合。山苦瓜乾燥粉末與溶劑以 1:10 的比例混合後使用磁石攪拌器震盪 24 小時。取上清液以 0.45 μm 過濾膜過濾，置於 40℃ 烘箱乾燥，待樣品成為固體，秤重後以二次水回溶，0.22 μm 過濾膜過濾，製成濃度 1 g/mL 之樣品，於 -20℃ 冰箱冷凍備用。

三、成分分析方法

由東部深層海水創新研發中心提供 AB SCIEX QTRAP® 4500 LC/MS/MS System 以高效能液相層析串聯質譜儀(LC/MS/MS)，先進行 HPLC 以高效層析系統分離，再以熱電子撞擊分子，使其產生碎片及離子，再經由磁場分離分子碎片，依據質荷比之測量，來決定分子質量，通過資料的比對來確定最終化合物。山苦瓜果實萃取物之功效成分分析，包含多酚類非揮發性功能性成分檢測，將以 0.45 μm 過濾膜過濾之原液稀釋 100 至 10,000 倍並以 0.2 μm 過濾膜過濾，使用 C18 管柱進行梯度分析試驗，移動相為乙腈與 2.5% 甲酸溶液，並以梯度形式洗滌，有效分離出萃取物中的多酚與類黃酮物質，並以相對應的標準品進行標準曲線的繪製，測定化合物之含量。

四、儀器設備

粉碎機(探月, J-150A)、數位恆溫乾燥箱(YIH DER, DFO-150)、震盪儀(YIH DER, TS-500D)、磁石攪拌儀(SUNTEX, SH-301)、液相層析串聯質譜儀(LC/MS/MS) 含 Shimadzu LC-30A 與 Ab SCIEX Triple Quad 4500 System 設備、層析管 Dikma tech HPLC、C18(2)，5 μm，內徑 4.6 mm X 150 mm。

肆、結果與討論

通過 LC/MS/MS 一共獲得了 2 種類黃酮及 8 種多酚類化合物，其中山柰酚(Kaempferol)及黃岑素(Baicalein)在 3 種萃取方式皆有發現。山柰酚(3,5,7-Trihydroxy-2-(4-hydroxyphenyl)-4H-1-benzopyran-4-one) 是一種黃酮類化合物，存在於許多可食用植物（例如茶、西蘭花、捲心菜、羽衣甘藍、豆類、菊苣、韭菜、番茄、草莓和葡萄）和植物中或傳統醫學中常用的植物產品（如銀杏、紫椴屬、木賊屬、辣木油橄欖、槐花和蜂膠）。一些流行病學研究發現食用含有山柰酚的食物會降低罹患多種疾病的風險，例如癌症和心血管疾病(Calderon-Montano et al., 2011)。大量臨床前研究顯示，山柰酚和山柰酚的某些苷具有廣泛的藥理活性，包括抗氧化(Kampkötter et al., 2007)、抗炎(Park et al., 2009)、抗菌(Kataoka et al., 2001)、抗癌(Yasukawa et al., 1990)、心臟保護(Hertog et al., 1993)、神經保護(Samhan-Arias et al., 2004)、抗糖尿病(Chen et al., 2010)、抗骨質疏鬆(Wattel et al., 2003)、雌激素/抗雌激素(Oh et al., 2006)、抗焦慮(Aguirre-Hernández et al., 2010)、鎮痛(De Melo et al., 2009)和抗過敏活性(Medeiros et al., 2009)。

黃芩素(5,6,7-Trihydroxyflavone)是存在於黃芩中一種重要的藥用類黃酮，具有抗氧化(Shao et al., 2002)、抗病毒(Song et al., 2021)、抗細菌(Yun et al., 2012)、抗炎(Wei et al., 2017)、抗肝毒性、抗癌(Hwang et al., 2005)和抗過敏治療(Bae et al., 2016)等多種生物學益處。黃芩素通過其對細胞增殖、轉移、凋亡和自噬等多種生物學過程的作用而具有抗癌活性(Chao et al., 2007，Gao et al., 2016)。最近的研究顯示，黃芩素是一種有效的抗肝癌藥物(Tian et al., 2021)，還對於膀胱癌細胞系和前列腺癌細胞中細胞週期進程具有強烈的抗增殖作用(Jiang et al., 2018; Guo et al., 2015)。這種天然物質具有很高的商業價值，因為它可以增強心臟和腦血管(Pan et al., 2021)，保護神經系統(Li et al., 2017)，還可以減少糖尿病和糖尿病並發症(Fang et al., 2020)。此外，已知黃芩素可降低炎症標誌物，如 IL-1β、IL-6 和 TNF-α(Jin et al., 2019)。

本研究中，8 種多酚類化合物中，5-咖啡醯奎尼酸(5-O-Caffeoylquinic acid, 5-CQA)、奎尼酸(Quinic acid)及總綠原酸(CGA)只存在水萃及酒水混合萃中，對香豆酸(p-Coumaric acid)只存在酒萃中，而鄰苯三酚 (Pyrogallol)只存在於酒水混合萃取中。綠原酸又稱 5-咖啡醯奎尼酸，是人類飲食中最豐富、功能最強大的多酚化合物之一。大量研究顯示，5-CQA 是一種有效的膳食保護性酚類化合物，它與各種危害呈負相關，例如氧化壓力、炎症壓力(Liang & Kitts, 2016)、代謝綜合症 (Roshan et al., 2018)、脂肪肝（Salomone et al., 2017）、急性肺損傷 (Zhang et al., 2010)、神經退行性疾病(NDDs) (Larsson et al., 2011)、精神障礙 (Nabavi et al., 2017)、心血管疾病 (CVDs)（Mubarak et al., 2012; Onakpoya et al., 2015)、胃腸功能障礙(Ruan et al., 2014; Shimoyama et al., 2013)和癌症(Meng et al., 2013)。

沒食子酸（GA-3,4,5-trihydroxybenzoic acid）是一種酚類植物化學物質，是一種普遍存在於大多數植物中的次級代謝物，在葡萄籽、玫瑰花、漆樹、橡樹和金縷梅中具有可觀的濃度。沒食子酸通常由萜烯和多酚單寧酸的水解產生（Khan et al., 2018）。沒

食子酸苯酚環的羥基苯甲酸上具有很多游離-OH 基團對人類免疫缺陷病毒 (Human immunodeficiency virus, HIV) 和 C 型肝炎病毒 (Hepatitis C virus, HCV) 具有強烈的抵抗力(Nutan et al., 2013，Rivero-Buceta et al., 2015)。從機制的角度來看，沒食子酸可以抑制銅綠假單胞菌(*Pseudomonas aeruginosa*)、金黃色葡萄球菌(*Staphylococcus aureus*)、變形鏈球菌(*Streptococcus mutans*)、紫色色桿菌(*Chromobacterium violaceumand*)和李斯特菌(*Listeria monocytogenes*)的運動、附著和形成生物膜（Shao et al., 2015; Borges et al., 2012; Kang et al., 2008）。該化合物還可以破壞革蘭氏陽性和革蘭氏陰性細菌中細胞膜的完整性，並改變膜表面的電荷、疏水性和滲透性（Teodoro et al., 2015）。接著沒食子酸可以干擾空腸彎曲菌(*Campylobacter jejuni*)的膜通透性並提高微生物中的抗生素積累（Oh et al., 2015）。此外，它可以通過螯合二價陽離子來分解革蘭氏陰性菌的外膜（Nohynek et al., 2006）。最後，沒食子酸能通過調節抗氧化劑/促氧化劑的平衡發揮細胞毒殺和抗腫瘤作用（Giftson et al., 2010; Liao et al., 2012）。

總綠原酸(3-CQA)是 5-咖啡醯奎尼酸(5-CQA)中含量最豐富的異構體。它是酚酸化合物中最常見的酸之一，天然存在於生咖啡提取物和茶中（Huang & Chang, 2008）。CGA 是一種重要且具有生物活性的膳食多酚，具有抗氧化、抗炎（Yun et al., 2012）、抗菌（Fiamegos et al., 2011）、傷口癒合（Bagdas et al., 2014）、保護神經（Les et al., 2017）、抗肥胖（Cho et al., 2010）、抗病毒（Tamura et al., 2006）、抗真菌（Sung & Lee, 2010）、抗高血壓（Zhao et al., 2012）等多種重要的治療作用。此外，已經發現 CGA 可以調節遺傳和健康代謝相關疾病中的脂質代謝和葡萄糖（Yukawa et al., 2004，Johnston et al., 2003）。據推測，CGA 可以在脂質和葡萄糖代謝調節中發揮關鍵作用，因此有助於治療許多疾病，例如脂肪肝、心血管疾病、糖尿病和肥胖症（Wan et al., 2013; Jin et al., 2015）。此外，這種 CGA 酚酸通過保護動物免受化學或脂多醣引起的傷害而產生保肝作用（Shi et al., 2016）。

奎尼酸是一種環己烷羧酸，存在於多種藥用植物的提取物中，包括紅果(*Haematocarpus validus*)、金絲桃(*Hypericum empetrifolium*)、蓍草(*Achillea pseudoaleppica*)、尼泊爾酸模(*Rumex nepalensis*)、*Phagnalon saxatile* subsp. *saxatile*、小果咖啡(*Coffea Arabica*)、紅棗(*Ziziphus lotus* L)和黃花蒿(*Artemisia annua* L) 等等。目前，體外和體內藥理研究顯示，奎尼酸具有多種生物活性，如抗氧化(Karaman et al., 2021)、抗糖尿病(Aras et al., 2019)、抗癌(Murugesan et al., 2020)、抗菌(Pires et al., 2018)、抗病毒(Gamaleldin et al., 2016)、抗衰老、保護、抗傷害(Pero et al., 2009)和鎮痛作用(Toghyani Khorasgani et al., 2021)。

對-羥基苯甲酸 (p-Hydroxybenzoic acid, PHBA) 是苯甲酸的單羥基酚衍生物，廣泛用作食品、飲料、藥品和化妝品中的抗氧化劑、防腐劑和殺菌劑(Manuja et al., 2013，Merkl et al., 2010，Oksana et al., 2012，Pulido et al., 2000)，對-羥基苯甲酸還能夠通過參與鏈引發的促氧化副反應來保護魚油免受氧化(Farhoosh et al., 2016)，最後觀察到對-羥基苯甲酸比間羥基苯甲酸(3-Hydroxybenzoic acid)具有更好的抗氧化活性，因為對-

羥基苯甲酸上的對羥基與間羥基苯甲酸上的間羥基相比具有更好的供氫能力來抑制自由基的產生(Velika & Kron, 2012)。

香豆酸是肉桂酸的羥基衍生物，天然存在三種異構體（鄰位、間位和對位），而對香豆酸(4-Hydroxy-cinnamic acid)是自然界中最常見的異構體。對香豆酸被歸類為植物化學和營養保健品，存在於各種可食用植物中，例如胡蘿蔔、番茄和穀物。對香豆酸廣泛存在於禾本科植物的細胞壁中。它在籽粒的胚乳中含量有限，然而外周組織中對香豆酸的含量顯著增加。就穀物類型而言，大麥、小麥、燕麥和玉米的果皮部分似乎是對香豆酸含量最高的部分。對香豆酸是水果、蔬菜和穀物中最重要的抗炎成分之一(Kannan et al., 2013)，在人類惡性腫瘤中具有抗腫瘤作用，此外，在 1-4.5 mmol L^{-1} 的濃度下細胞增殖表現量降低了 50 % (Garrait et al., 2006，Gani et al., 2012)。此外，對香豆酸可通過減少致癌亞硝胺的形成來治療胃癌(Navaneethan & Rasool, 2014)。尤其是過去研究顯示，對香豆酸具有化學保護和抗氧化特性(Mussatto et al., 2007)。還觀察到對香豆酸對哺乳動物細胞的結腸癌具有保護作用(Ferguson et al., 2005)。口服香豆酸（每天 317 毫克）在 30 天有顯著抑制低密度脂蛋白(LDL)的氧化(Zang et al., 2000)。根據研究，對香豆酸具有保護及抗心臟病作用，因為它降低了脂質過氧化、膽固醇氧化和低密度脂蛋白抗性 (Garrait et al., 2006，Zilic et al., 2011)。

連苯三酚(Pyrogallol)又名鄰苯三酚，是一種普遍存在的酚類物質，存在於多種可食用植物（如可可、堅果、果皮、蔬菜和藥用植物）中的類黃酮和多酚中。鄰苯三酚類化合物的舊名稱是"植物單寧"，這是因為它們在皮革製造的"鞣製"過程中得到的稱呼。鄰苯三酚化合物有抗氧化活性和抗癌作用(Ramos, 2008)。此外鄰苯三酚也被評估為乙醯膽鹼酯酶的潛在抑制劑。研究顯示，鄰苯三酚對乙醯膽鹼甾體具有有效的抑制活性。IC_{50} 和 K_i 值分別為 10.2 和 8.6 μM (Ozturk Sarikaya, 2015)。抗膽鹼酯酶藥可與乙醯膽鹼酯酶結合，使乙醯膽鹼酯酶活性受抑，導致膽鹼能神經末梢釋放的乙醯膽鹼堆積，產生擬膽鹼作用。低劑量可逆的抗膽鹼酯酶藥可治療重症肌無力和阿爾茨海默病。除此之外，鄰苯三酚的化合物可能是抑制 α-glucosidase 潛在藥物，通過靶 α-glucosidase 活性位點關鍵殘基，IC_{50} 和 K_i 值分別為 7.2 和 0.37 mM(Zheng et al., 2018)。

肉桂酸 (Cinnamic acid) 食品中常見的苯丙烯酸在化學結構方面是肉桂酸的羥基和甲氧基衍生物。許多苯基丙烯酸，包括肉桂酸的甲氧基衍生物:阿魏酸、對甲氧基肉桂酸(p-Methoxycinnamic acid)和 3,4-二甲氧基肉桂酸(3,4-Dimethoxycinnamic acid)，這些也是藥用植物的活性化合物，例如：當歸 (*Angelica sinensis*)、耬鬥菜(*Aquilegia vulgaris*)、大三葉升麻(*Cimicifuga heracleifolia*)、北玄参 (*Scrophularia buergeriana*) 或山柰 (*Kaempferia galanga*)。幾個世紀以來，這些植物在東方醫學中被用作預防和治療許多與消化、呼吸、神經和免疫系統功能相關的疾病的自然療法(Pei et al., 2016，He et al., 2012)。此外阿魏酸在日本作為抗氧化食品添加劑(Itagaki et al., 2009)。接著在體外試驗中證實了它的抗菌(Shi et al., 2016)和抗癌（抗肺癌(Fong et al., 2016)、乳腺癌(Zhang et al., 2016)、子宮頸癌(Hemaiswarya & Doble, 2013)、前列腺癌(Eroğlu et al., 2015)、甲狀腺癌(Dodurga et al., 2016)和胃腸道癌(Kawabata et al., 2000)等癌症）。此外，在動物模型的體內試驗中也證實了抗糖尿病(Vinayagam et al., 2016)、肝臟(Rukkumani et al., 2004)、心臟 (Kwon et al., 2010)和神經保護(Ojha et al., 2015)等有益活性。

現在的研究中較少有山苦瓜的成分分析研究，而不同地區及氣候也會造成山苦瓜中的成分有所改變，本篇研究使用了台灣台東的山苦瓜作為成分分析，得出山苦瓜水萃主要有 8 種化合物，山苦瓜酒水混合萃有 9 種化合物，最後山苦瓜酒萃僅有 6 種化合物。雖然酒萃中的化合物較少，但是對香豆酸只有在酒萃才能析出。山苦瓜水萃及酒水混合萃比起酒萃多了 5-咖啡醯奎尼酸、奎尼酸及總綠原酸，而鄰苯三酚只有在酒水混合萃有析出，在水萃及酒萃皆無此化合物。

這十種化合物中，大多都有抗氧化、抗糖尿病、抗癌、抗代謝症候群、降高血壓、抗肥胖、抗發炎及抗病毒等等的功效，這與之前研究所描述的功效相同，雖然山苦瓜對於這些功效的現象還未有明確的機制路徑，但是得出了山苦瓜其中的化合物成分或許可以幫助我們盡早得出功效機制，或許能讓山苦瓜作為一種保健食品或是從中萃取功效成分作為藥品的開發。

伍、結論

本實驗使用了臺東山苦瓜果實當作研究材料，以不同溶劑萃取來進行功效成分的比較，得出山苦瓜水萃主要有 8 種化合物，酒水混合萃有 9 種化合物，而酒萃有 6 種化合物，山苦瓜總共主要有 2 種類黃酮及 8 種多酚類化合物。雖然有越多化合物代表其萃取的功效成分越佳，但是也會被萃取化合物的含量所影響。不過若以化合物總量來確認其萃取溶劑的好壞，最好的就是酒水混合萃，其次是水萃，最後則是酒萃。但是實際的生物活性及山苦瓜功效路徑，則要經由後續實驗來證實。

表 1 類黃酮化合物

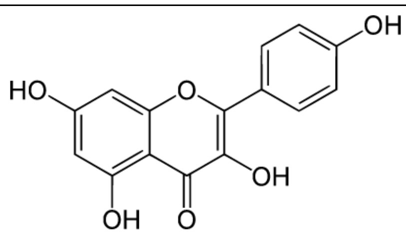
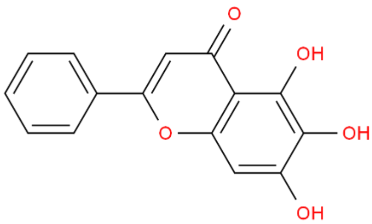
編號	化合物名稱	化學結構
1.	山柰酚 (Kaempferol)	
2.	黃岑素 (Baicalein)	

表2 酚類化合物

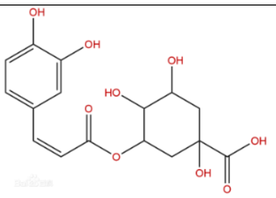
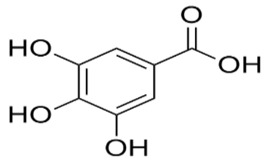
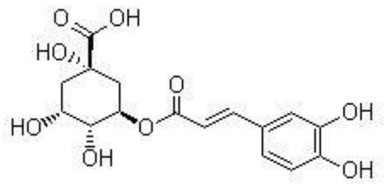
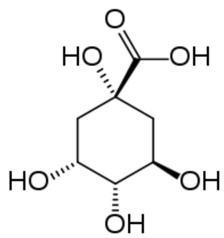
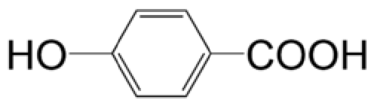
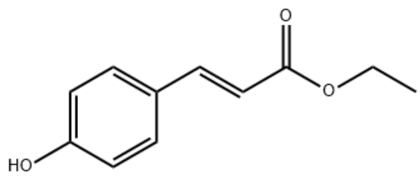
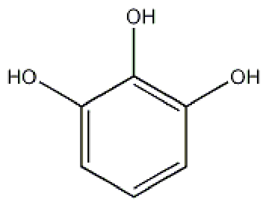
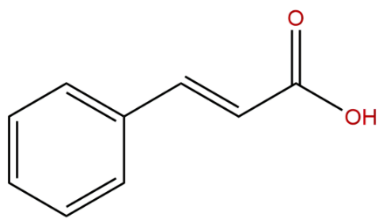
編號	化合物名稱	化學結構
1	5-咖啡醯奎尼酸 (5-O-Caffeoylquinic acid, 5-CQA)	
2	沒食子酸 (Gallic acid)	
3	綠原酸 (Chlorogenic acid, CGA)	
4	奎尼酸 (Quinic acid)	
5	對-羥基苯甲酸 (p-Hydroxybenzoic acid)	
6	對香豆酸 (p-Coumaric acid)	
7	鄰苯三酚 (Pyrogallol)	
8	肉桂酸 (Cinnamic acid)	

表 3 山苦瓜果實三種萃取物之主要成分比較

	化合物	水萃取物	酒水混合萃取物	酒萃取物
1[a]	奎尼酸(Quinic acid)	✓	✓	
2	5-咖啡醯奎尼酸 (5-O-Caffeoylquinic acid, 5-CQA)	✓	✓	
3	總綠原酸 (Chlorogenic acid, CGA)	✓	✓	
4	沒食子酸 (Gallic acid)	✓	✓	✓
5	黃芩素 (Baicalein)	✓	✓	✓
6	山柰酚 (Kaempferol)	✓	✓	✓
7	鄰苯三酚 (Pyrogallol)		✓	
8	對-羥基苯甲酸 (p-Hydroxybenzoic acid)	✓	✓	✓
9	對香豆酸 (p-Coumaric acid)			✓
10	肉桂酸 (Cinnamic acid)	✓	✓	✓

a：依其含量多寡排序

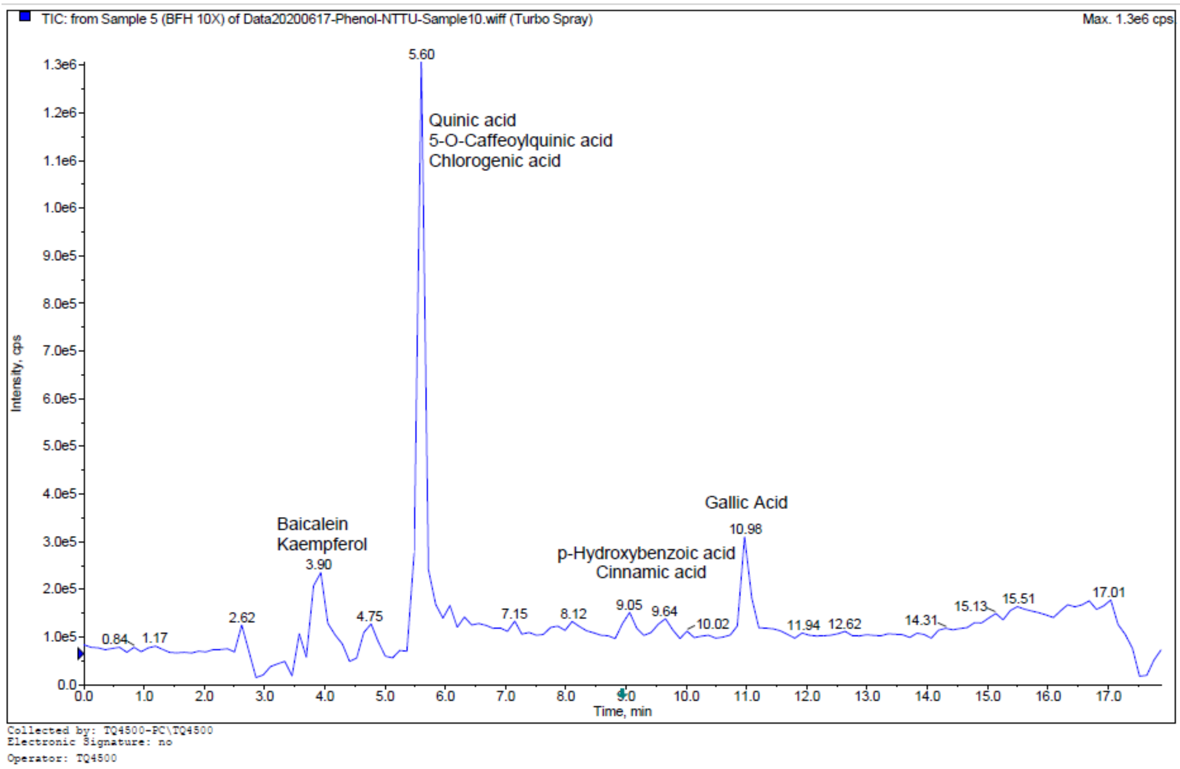


圖 1 山苦瓜水萃取物（WE）LC-MS/MS 成分分析之結果

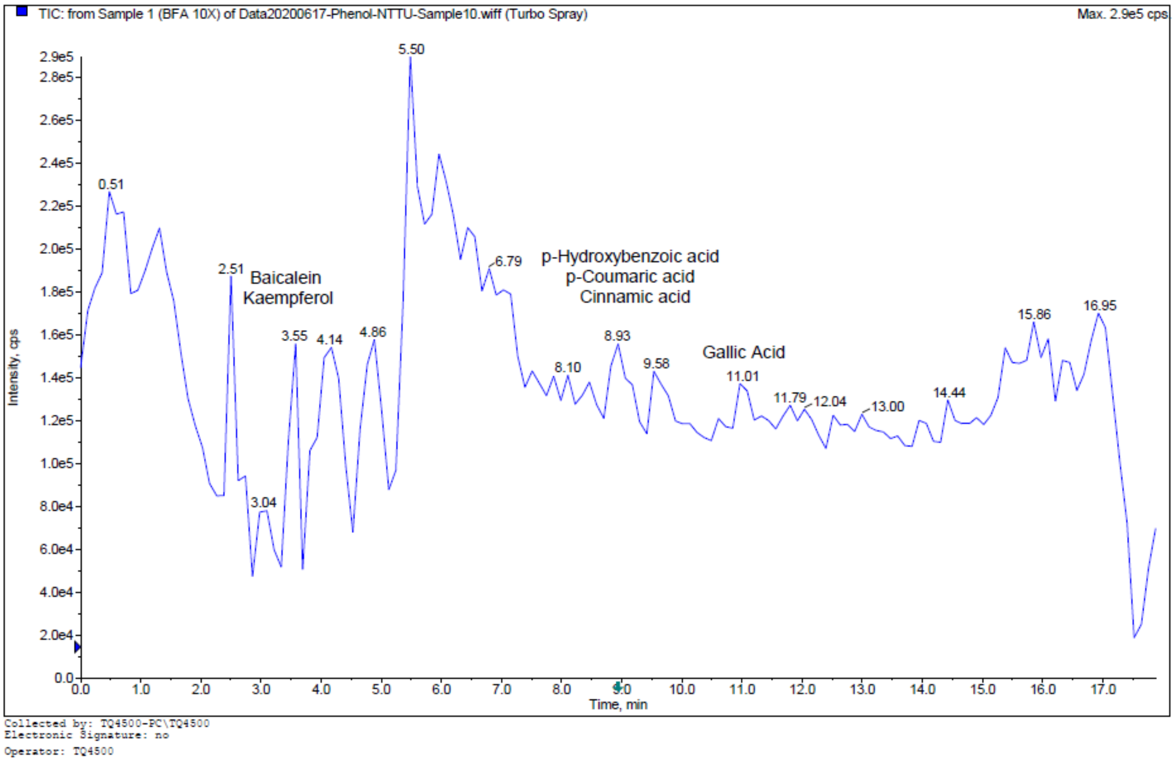


圖 2 山苦瓜酒萃取物（AE）LC-MS/MS 成分分析之結果

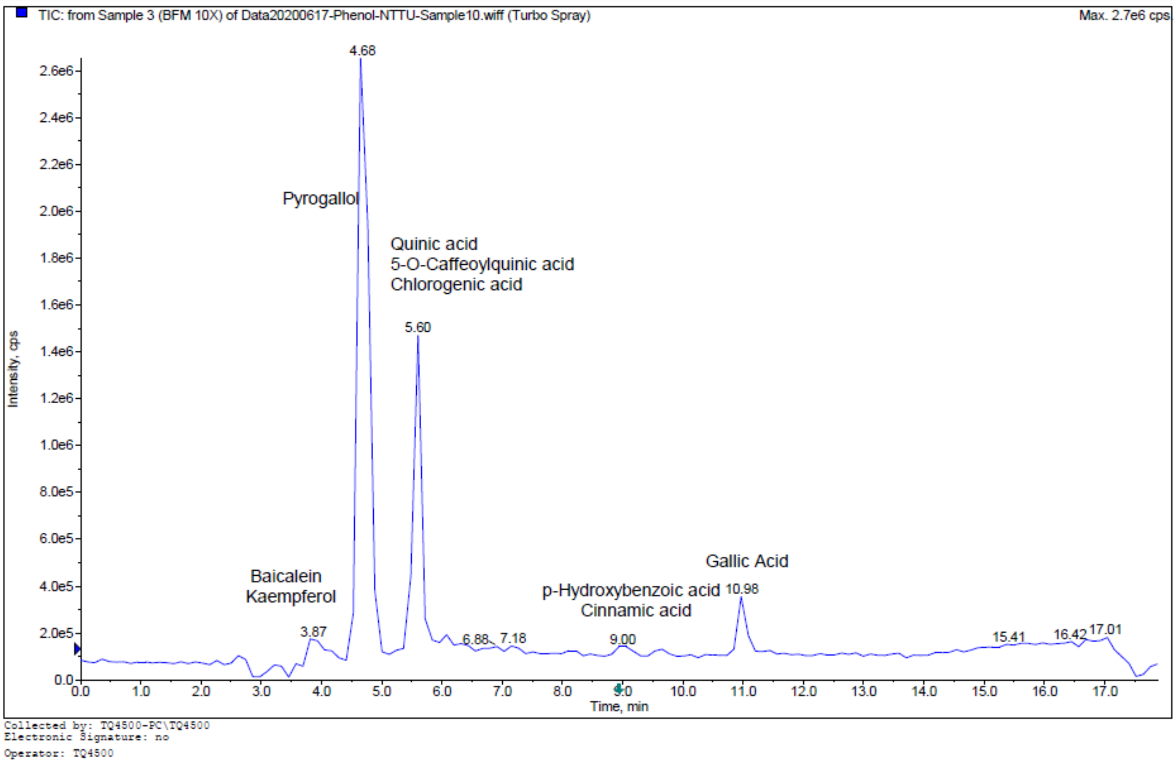


圖 3 山苦瓜酒水萃取物（ME）LC-MS/MS 成分分析之結果

引用文獻

一、中文部分

行政院農業委員會 (2016)。
https://kmweb.coa.gov.tw/theme_data.php?theme=production_map&id=44

二、外文部分

Aguirre-Hernández, E., González-Trujano, M. E., Martínez, A. L., Moreno, J., Kite, G., Terrazas, T., & Soto-Hernández, M. (2010). HPLC/MS analysis and anxiolytic-like effect of quercetin and kaempferol flavonoids from Tilia americana var. mexicana. *Journal of ethnopharmacology*, *127*(1), 91–97. https://doi.org/10.1016/j.jep.2009.09.044

Aras, A., Bursal, E., Türkan, F., Tohma, H., Kılıç, Ö., Gülçin, İ., & Köksal, E. (2019). Phytochemical Content, Antidiabetic, Anticholinergic, and Antioxidant Activities of Endemic Lecokia cretica Extracts. *Chemistry & biodiversity*, *16*(10), e1900341. https://doi.org/10.1002/cbdv.201900341

Bae, M. J., Shin, H., See, H. J., Jung, S. Y., Kwon, D. A., & Shon, D. H.(2016). Baicalein induces CD4+Foxp3+ T cells and enhances intestinal barrier function in a mouse model of food allergy. *Sci Rep, 6*, 32225. https://doi.org/10.1038/srep32225

Bagdas, D., Gul, N. Y., Topal, A., Tas, S., Ozyigit, M. O., Cinkilic, N., Gul, Z., Etoz, B. C., Ziyanok, S., Inan, S., Turacozen, O., & Gurun, M. S. (2014). Pharmacologic overview of systemic chlorogenic acid therapy on experimental wound healing. *Naunyn-Schmiedeberg's archives of pharmacology*, *387*(11), 1101–1116. https://doi.org/10.1007/s00210-014-1034-9

Borges, A., Saavedra, M. J., & Simões, M. (2012). The activity of ferulic and gallic acids in biofilm prevention and control of pathogenic bacteria. *Biofouling*, *28*(7), 755–767. https://doi.org/10.1080/08927014.2012.706751

Calderon-Montano, J. M., Burgos-Moron, E., Perez-Guerrero, C., & Lopez-Lazaro, M.(2011). A Review on the Dietary Flavonoid Kaempferol. *Mini Reviews in Medicinal Chemistry*, 11 (4), 298-344. https://doi.org/10.2174/138955711795305335

Chao, C. Y., Sung, P. J., Wang, W. H., & Kuo, Y. H. (2014). Anti-inflammatory effect of *Momordica charantia* in sepsis mice. *Molecules (Basel, Switzerland)*, *19*(8), 12777–12788. https://doi.org/10.3390/molecules190812777

Chao, J. I., Su, W. C., & Liu, H. F.(2007). Baicalein induces cancer cell death and proliferation retardation by the inhibition of CDC2 kinase and survivin associated with opposite role of p38 mitogen-activated protein kinase and AKT. *Mol Cancer Ther*, *6* (11), 3039–3048. https://doi.org/10.1158/1535-7163.MCT-07-0281

Chen, Q. C., Zhang, W. Y., Jin, W., Lee, I. S., Min, B. S., Jung, H. J., Na, M., Lee, S., & Bae, K. (2010). Flavonoids and isoflavonoids from Sophorae Flos improve glucose uptake *in vitro*. *Planta medica*, *76*(1), 79–81. https://doi.org/10.1055/s-0029-1185944

Cho, A. S., Jeon, S. M., Kim, M. J., Yeo, J., Seo, K. I., Choi, M. S., & Lee, M. K. (2010). Chlorogenic acid exhibits anti-obesity property and improves lipid metabolism in high-fat diet-induced-obese mice. *Food and chemical toxicology : an international journal published for the British Industrial Biological Research Association*, *48*(3), 937–943. https://doi.org/10.1016/j.fct.2010.01.003

Costa, J. G., Nascimento, E. M., Campos, A. R., & Rodrigues, F. F. (2010). Antibacterial activity of *Momordica charantia* (Curcubitaceae) extracts and fractions. *Journal of basic and clinical pharmacy*, *2*(1), 45–51. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3979203/

De Melo, G. O., Malvar, D., Vanderlinde, F. A., Rocha, F. F., Pires, P. A., Costa, E. A., de Matos, L. G., Kaiser, C. R., & Costa, S. S. (2009). Antinociceptive and anti-inflammatory kaempferol glycosides from Sedum dendroideum. *Journal of ethnopharmacology*, *124*(2), 228–232. https://doi.org/10.1016/j.jep.2009.04.024

Deng, Y. Y., Yi, Y., Zhang, L. F., Zhang, R. F., Zhang, Y., Wei, Z. C., Tang, X. J., & Zhang, M. W. (2014). Immunomodulatory activity and partial characterisation of polysaccharides from *Momordica charantia*. *Molecules (Basel, Switzerland)*, *19*(9), 13432–13447. https://doi.org/10.3390/molecules190913432

Dodurga, Y., Eroğlu, C., Seçme, M., Elmas, L., Avcı, Ç. B., & Şatıroğlu-Tufan, N. L. (2016). Anti-proliferative and anti-invasive effects of ferulic acid in TT medullary thyroid cancer cells interacting with URG4/URGCP. *Tumour biology : the journal of the International Society for Oncodevelopmental Biology and Medicine*, *37*(2), 1933–1940. https://doi.org/10.1007/s13277-015-3984-z

Eroğlu, C., Seçme, M., Bağcı, G., & Dodurga, Y. (2015). Assessment of the anticancer mechanism of ferulic acid via cell cycle and apoptotic pathways in human prostate cancer cell lines. *Tumour biology : the journal of the International Society for Oncodevelopmental Biology and Medicine*, *36*(12), 9437–9446. https://doi.org/10.1007/s13277-015-3689-3

Fang, F. E., & Ng, B. T.(2011). Bitter Gourd (*Momordica charantia*) is a Cornucopia of Health: A Review of its Credited Antidiabetic, Anti-HIV, and Antitumor Properties. *Current Molecular Medicine, 11*(5), 417-436. https://doi.org/10.2174/156652411795976583

Fang, P., Yu, M., Shi, M., Bo, P., Gu, X., & Zhang, Z. (2020). Baicalin and its aglycone: a novel approach for treatment of metabolic disorders. *Pharmacological reports : PR*, *72*(1), 13–23. https://doi.org/10.1007/s43440-019-00024-x

Farhoosh, R., Sharif, A., Asnaashari, M., Johnny, S., & Molaahmadibahraseman, N. (2016) Temperature-dependent mechanism of antioxidant activity of *o*-hydroxyl, *o*-methoxy, and alkyl ester derivatives of *p*-hydroxybenzoic acid in fish oil. *Journal of the American Oil Chemists' Society*, *93*, 555– 567. https://doi.org/10.1007/s11746-016-2790-0

Ferguson, L.R., Zhu, S.T. & Harris, P.J. (2005). Antioxidant and antigenotoxic effects of plant cell wall hydroxycinnamic acids in cultured HT-29 cells. *Molecular Nutrition & Food Research*, *49*, 585–593. DOI: 10.1002/mnfr.200500014

Fiamegos, Y. C., Kastritis, P. L., Exarchou, V., Han, H., Bonvin, A. M., Vervoort, J., Lewis, K., Hamblin, M. R., & Tegos, G. P. (2011). Antimicrobial and efflux pump inhibitory activity of caffeoylquinic acids from Artemisia absinthium against gram-positive pathogenic bacteria. *PloS one*, *6*(4), e18127. https://doi.org/10.1371/journal.pone.0018127

Fong, Y., Tang, C. C., Hu, H. T., Fang, H. Y., Chen, B. H., & Wu, C.Y.(2015). Inhibitory effect of *trans*-ferulic acid on proliferation and migration of human lung cancer cells accompanied with increased endogenous reactive oxygen species and β-catenin instability. *Chin Med, 11*(45). https://doi.org/10.1186/s13020-016-0116-7

Frame, A. D., Ríos-Olivares, E., De Jesús, L., Ortiz, D., Pagán, J., & Méndez, S. (1998). Plants from Puerto Rico with anti-*Mycobacterium tuberculosis* properties. *Puerto Rico health sciences journal*, *17*(3), 243–252. https://pubmed.ncbi.nlm.nih.gov/9883470/

Fu, S. K., Li, C., Li, P., Fang, T., Xu, L., & Yuqing, J. Z.(2022). Effects of Dietary Wild Bitter Melon (*Momordica Charantia* var. *Abbreviate* Ser.) Extract on Glucose and Lipid Metabolism in HFD/STZ-Induced Type 2 Diabetic Rats. Available at SSRN: https://ssrn.com/abstract=4142030 or http://dx.doi.org/10.2139/ssrn.4142030

Gamaleldin Elsadig Karar, M., Matei, M. F., Jaiswal, R., Illenberger, S., & Kuhnert, N. (2016). Neuraminidase inhibition of Dietary chlorogenic acids and derivatives - potential antivirals from dietary sources. *Food & function*, *7*(4), 2052–2059. https://doi.org/10.1039/c5fo01412c

Gani, A., Wani, S.M., Masoodi, F.A. & Hameed, G. (2012). Wholegrain cereal bioactive compounds and their health benefits: a review. *Journal of Food Process and Technology*, *3*, 146. DOI:10.4172/2157-7110.1000146

Gao, Y., Snyder, S.A., Smith, J.N., & Chen, Y. C. (2016). Anticancer properties of baicalein: a review. *Med Chem Res, 25*, 1515–1523. https://doi.org/10.1007/s00044-016-1607-x

Garrait, G., Jarrige, J.F., Blanquet, S., Beyssac, E., Cardot, J.M. & Alric, M. (2006). Gastrointestinal absorption and urinary excretion of trans-cinnamic and p-coumaric acids in rats. *Journal of Agriculture and Food Chemistry*, *54*, 2944–2950. DOI: 10.1021/jf053169a

Giftson, J. S., Jayanthi, S., & Nalini, N. (2010). Chemopreventive efficacy of gallic acid, an antioxidant and anticarcinogenic polyphenol, against 1,2-dimethyl hydrazine induced rat colon carcinogenesis. *Investigational new drugs*, *28*(3), 251–259. https://doi.org/10.1007/s10637-009-9241-9

Guo, Z., Hu, X., Xing, Z., Xing, R., Lv, R., Cheng, X., Su, J., Zhou, Z., Xu, Z., Nilsson, S., & Liu, Z. (2015). Baicalein inhibits prostate cancer cell growth and metastasis via the caveolin-1/AKT/mTOR pathway. *Molecular and cellular biochemistry*, *406*(1-2), 111–119. https://doi.org/10.1007/s11010-015-2429-8

He, Z. H., Yue, G. G., Lau, C. B., Ge, W., & But, P. P. (2012). Antiangiogenic effects and mechanisms of trans-ethyl p-methoxycinnamate from *Kaempferia galanga* L. *Journal of agricultural and food chemistry*, *60*(45), 11309–11317. https://doi.org/10.1021/jf304169j

Hemaiswarya, S., & Doble, M. (2013). Combination of phenylpropanoids with 5-fluorouracil as anti-cancer agents against human cervical cancer (HeLa) cell line. *Phytomedicine*, *20*(2), 151-158. https://doi.org/10.1016/j.phymed.2012.10.009

Hertog, M. G., Feskens, E. J., Hollman, P. C., Katan, M. B., & Kromhout, D. (1993). Dietary antioxidant flavonoids and risk of coronary heart disease: the Zutphen Elderly Study. *Lancet*, *342*(8878), 1007–1011. https://doi.org/10.1016/0140-6736(93)92876-u

Hsu, C., Tsai, T. H., Li, Y. Y., Wu, W. H., Huang, C. J., & Tsai, P. J.(2012).Wild bitter melon (*Momordica charantia* Linn. var. *abbreviata* Ser.) extract and its bioactive components suppress Propionibacterium acnes-induced inflammation. *Food Chemistry*, *135*(3), 976-984. https://doi.org/10.1016/j.foodchem.2012.05.045

Huang, W. C., Tsai, T. H., Huang, C. J., Li, Y. Y., Chyuan, J. H., Chuang, L. T., & Tsai, P. J.(2015). Inhibitory effects of wild bitter melon leaf extract on *Propionibacterium acnes*-induced skin inflammation in mice and cytokine production *in vitro*. *Food Function*, *6*(8), 2550-2560.http://dx.doi.org/10.1039/C5FO00550G

Huang, Z., & Chang, C. (2008). *Wei sheng yan jiu = Journal of hygiene research*, *37*(5), 637–639. https://downloads.hindawi.com/journals/ecam/2013/801457.pdf?crsi=662496674&cicada_org_src=healthwebmagazine.com&cicada_org_mdm=direct

Hwang, J.M., Tseng, T.H., Tsai, Y.Y., Lee, H.J., Chou, F.P., Wang, C.J., & Chu, C.Y. (2005). Protective effects of baicalein on tert-butyl hydroperoxide-induced hepatic toxicity in rat hepatocytes. *J. Biomed. Sci*, 12, 389-397 https://doi.org/10.1007/s11373-005-1572-8

Itagaki, S., Kurokawa, T., Nakata, C., Saito, Y., Oikawa, S., Kobayashi, M., Hirano, T., & Iseki, K.(2009). *In vitro* and *in vivo* antioxidant properties of ferulic acid: A comparative study with other natural oxidation inhibitors. *Food Chem*, *114*, 466–471. https://doi.org/10.1016/j.foodchem.2008.09.073

Jiang, L., Song, H., Guo, H., Wang, C., & Lu, Z. (2018). RETRACTED: Baicalein inhibits proliferation and migration of bladder cancer cell line T24 by down-regulation of microRNA-106. *Biomedicine & pharmacotherapy = Biomedecine & pharmacotherapie*, *107*, 1583–1590. https://doi.org/10.1016/j.biopha.2018.08.107

Jin, H., Wang, Q., Wu, J., Han, X., Qian, T., Zhang, Z., Wang, J., Pan, X., Wu, A., & Wang, X. (2019). Baicalein Inhibits the IL-1β-Induced Inflammatory Response in Nucleus Pulposus Cells and Attenuates Disc Degeneration *In vivo*. *Inflammation*, *42*(3), 1032–1044. https://doi.org/10.1007/s10753-019-00965-8

Jin, S., Chang, C., Zhang, L., Liu, Y., Huang, X., & Chen, Z. (2015). Chlorogenic acid improves late diabetes through adiponectin receptor signaling pathways in db/db mice. *PloS one*, *10*(4), e0120842. https://doi.org/10.1371/journal.pone.0120842

Johnston, K. L., Clifford, M. N., Morgan, L. M.(2003). Coffee acutely modifies gastrointestinal hormone secretion and glucose tolerance in humans: glycemic effects of chlorogenic acid and caffeine. *The American Journal of Clinical Nutrition*, *78*(4), 728-733. DOI:10.1093/ajcn/78.4.728

Kampkötter A., Gombitang N. C., Zurawski R. F., Timpel C., Chovolou Y., Wätjen W., & Kahl R.(2007). Effects of the flavonoids kaempferol and fisetin on thermotolerance, oxidative stress and FoxO transcription factor DAF-16 in the model organism *Caenorhabditis elegans*. *Archives of Toxicology*, *81*(12), 849-858. DOI: 10.1007/s00204-007-0215-4.

Kang, M. S., Oh, J. S., Kang, I. C., Hong, S. J., & Choi, C. H. (2008). Inhibitory effect of methyl gallate and gallic acid on oral bacteria. *Journal of microbiology (Seoul, Korea)*, *46*(6), 744–750. https://doi.org/10.1007/s12275-008-0235-7

Kannan, R.R.R., Arumugam, R., Thangaradjou, T. & Anantharaman, P. (2013). Phytochemical constituents, antioxidant properties and p-coumaric acid analysis in some seagrasses. *Food Research International*, *54*, 1229–1236. https://doi.org/10.1016/j.foodres.2013.01.027

Karaman, M., Tesanovic, K., Gorjanovic, S., Pastor, F. T., Simonovic, M., Glumac, M., & Pejin, B. (2021). Polarography as a technique of choice for the evaluation of total antioxidant activity: The case study of selected Coprinus Comatus extracts and quinic acid, their antidiabetic ingredient. *Natural product research*, *35*(10), 1711–1716. https://doi.org/10.1080/14786419.2019.1628753

Kataoka, M., Hirata, K., Kunikata, T., Ushio, S., Iwaki, K., Ohashi, K., Ikeda, M., & Kurimoto, M. (2001). Antibacterial action of tryptanthrin and kaempferol, isolated from the indigo plant (*Polygonum tinctorium* Lour.), against Helicobacter pylori-infected Mongolian gerbils. *Journal of gastroenterology*, *36*(1), 5–9. https://doi.org/10.1007/s005350170147

Kawabata, K., Yamamoto, T., Hara, A., Shimizu, M., Yamada, Y., Matsunaga, K., ... & Mori, H. (2000). Modifying effects of ferulic acid on azoxymethane-induced colon carcinogenesis in F344 rats. *Cancer letters*, *157*(1), 15-21. https://doi.org/10.1016/S0304-3835(00)00461-4

Khan, B. A., Mahmood, T., Menaa, F., Shahzad, Y., Yousaf, A. M., Hussain, T., & Ray, S. D. (2018). New Perspectives on the Efficacy of Gallic Acid in Cosmetics & Nanocosmeceuticals. *Current pharmaceutical design*, *24*(43), 5181–5187. https://doi.org/10.2174/1381612825666190118150614

Kwatra, D., Subramaniam, D., Ramamoorthy, P., Standing, D., Moran, E., Velayutham, R., Mitra, A., Umar, S., & Anant, S. (2013). Methanolic extracts of bitter melon inhibit colon cancer stem cells by affecting energy homeostasis and autophagy. Evidence-based complementary and alternative medicine : eCAM, 2013, 702869. https://doi.org/10.1155/2013/702869

Kwon, E. Y., Do, G. M., Cho, Y. Y., Park, Y. B., Jeon, S. M., & Choi, M. S. (2010). Anti-atherogenic property of ferulic acid in apolipoprotein E-deficient mice fed Western diet: comparison with clofibrate. *Food and Chemical Toxicology*, *48*(8-9), 2298-2303. https://doi.org/10.1016/j.fct.2010.05.063

Lal, J., Chandra, S., Raviprakash, V.,　&　Sabir, M.(1975). *In vitro* anthelmintic action of some indigenous medicinal plants on *Ascardia galli* worms. *Indian Journal of Physiology and Pharmacology*, *20*(2), 64-68. https://europepmc.org/article/med/965077

Larsson, S. C., Virtamo, J., & Wolk, A. (2011). Coffee consumption and risk of stroke in women. *Stroke, 42*(4), 908–912. https://doi.org/10.1161/strokeaha.110.603787

Les, F., Venditti, A., Cásedas, G., Frezza, C., Guiso, M., Sciubba, F., Serafini, M., Bianco, A., Valero, M. S., & López, V.(2017).Everlasting flower (Helichrysum stoechas Moench) as a potential source of bioactive molecules with antiproliferative, antioxidant, antidiabetic and neuroprotective properties.*Industrial Crops and Products*, *108*, 295-302. https://doi.org/10.1016/j.indcrop.2017.06.043.

Li, Y., Zhao, J., & Hölscher, C. (2017). Therapeutic Potential of Baicalein in Alzheimer's Disease and Parkinson's Disease. *CNS drugs, 31*(8), 639–652. https://doi.org/10.1007/s40263-017-0451-y

Liang, N., & Kitts, D. D. (2016). Role of Chlorogenic acids in controlling oxidative and inflammatory stress conditions. *Nutrients, 8*(1),16. https://doi.org/10.3390/nu8010016

Liao, C. L., Lai, K. C., Huang, A. C., Yang, J. S., Lin, J. J., Wu, S. H., Gibson Wood, W., Lin, J. G., & Chung, J. G. (2012). Gallic acid inhibits migration and invasion in human osteosarcoma U-2 OS cells through suppressing the matrix metalloproteinase-2/-9, protein kinase B (PKB) and PKC signaling pathways. *Food and chemical toxicology : an international journal published for the British Industrial Biological Research Association, 50*(5), 1734–1740. https://doi.org/10.1016/j.fct.2012.02.033

Lu, K. H., Tseng, H. C., Liu, C. T., Huang, C. J., Chyuan, J. H., & Sheen, L. Y.(2014). Wild bitter gourd protects against alcoholic fatty liver in mice by attenuating oxidative stress and inflammatory responses. *Food Function, 5,* 1027-1037. http://dx.doi.org/10.1039/C3FO60449G

Malik, Z. A., Singh, M., & Sharma, P. L. (2011). Neuroprotective effect of *Momordica charantia* in global cerebral ischemia and reperfusion induced neuronal damage in diabetic mice. *Journal of ethnopharmacology*, *133*(2), 729–734. https://doi.org/10.1016/j.jep.2010.10.061

Manik, S., Gauttam, V., & Kalia, A. N. (2013). Anti-diabetic and antihyperlipidemic effect of allopolyherbal formulation in OGTT and STZ-induced diabetic rat model. *Indian journal of experimental biology*, *51*(9), 702–708.

Manuja, R., Sachdeva, S., Jain, A., & Chaudhary, J. (2013) A comprehensive review on biological activities of p-hydroxy benzoic acid and its derivatives. *International Journal of Pharmaceutical Sciences Review & Research*, *22*, 109– 115. https://www.researchgate.net/profile/Jasmine-Chaudhary/publication/264420140_A_Comprehensive_Review_on_Biological_activities_of_p-hydroxy_benzoic_acid_and_its_derivatives/links/5bbc806792851c7fde371acb/A-Comprehensive-Review-on-Biological-activities-of-p-hydroxy-benzoic-acid-and-its-derivatives.pdf

Medeiros, K. C., Faustino, L., Borduchi, E., Nascimento, R. J., Silva, T. M., Gomes, E., Piuvezam, M. R., & Russo, M. (2009). Preventive and curative glycoside kaempferol treatments attenuate the TH2-driven allergic airway disease. *International immunopharmacology*, *9*(13-14), 1540–1548. https://doi.org/10.1016/j.intimp.2009.09.005

Merkl, R., Hradkova, I., Filip, V., & Smidrkal, J. (2010) Antimicrobial and antioxidant properties of phenolic acids alkyl esters. *Czech Journal of Food Sciences*, *28*, 275– 279. https://www.agriculturejournals.cz/publicFiles/132_2010-CJFS.pdf

Mubarak, A., Bondonno, C. P., Liu, A. H., Considine, M. J., Rich, L., Mas, E., Croft, K. D., & Hodgson, J. M. (2012). Acute effects of chlorogenic acid on nitric oxide status, endothelial function, and blood pressure in healthy volunteers: A randomized trial. *Journal of Agricultural and Food Chemistry*, *60*(36), 9130–9136. https://doi.org/10.1021/jf303440j

Murugesan, A., Holmstedt, S., Brown, K., Koivuporras, A., Macedo, A., Nguyen, N., Fonte, P., Rijo, P., Yli-Harja, O., Candeias, N., & Kandhavelu, M. (2020). Design and synthesis of novel quinic acid derivatives: *In vitro* cytotoxicity and anticancer effect on glioblastoma. *Future medicinal chemistry*, *12*, 1891-1910. 10.4155/fmc-2020-0194.

Mussatto, S.I., Dragone, G. & Roberto, I.C. (2007). Ferulic and pcoumaric acids extraction by alkaline hydrolysis of brewer's spent grain. *Industrial Crops and Products*, *25*, 231–237. https://doi.org/10.1016/j.indcrop.2006.11.001

Nabavi, S. F., Tejada, S., Setzer, W. N., Gortzi, O., Sureda, A., Braidy, N., Daglia, M., Manayi, A., & Nabavi, S. M. (2017). Chlorogenic acid and mental diseases:From chemistry to medicine. *Current neuropharmacology*, *15*(4), 471–479. https://doi.org/10.2174/1570159X14666160325120625

Navaneethan, D. & Rasool, M. (2014). p-Coumaric acid, a common dietary polyphenol, protects cadmium chloride-induced nephrotoxicity in rats. *Renal Failure*, *36*, 244–251. DOI: 10.3109/0886022X.2013.835268

Nohynek, L. J., Alakomi, H. L., Kähkönen, M. P., Heinonen, M., Helander, I. M., Oksman-Caldentey, K. M., & Puupponen-Pimiä, R. H. (2006). Berry phenolics: antimicrobial properties and mechanisms of action against severe human pathogens. *Nutrition and cancer*, *54*(1), 18–32. https://doi.org/10.1207/s15327914nc5401_4

Nutan, Modi, M., Goel, T., Das, T., Malik, S., Suri, S., Rawat, A. K., Srivastava, S. K., Tuli, R., Malhotra, S., & Gupta, S. K. (2013). Ellagic acid & gallic acid from Lagerstroemia speciosa L. inhibit HIV-1 infection through inhibition of HIV-1 protease & reverse transcriptase activity. *The Indian journal of medical research*, *137*(3), 540–548.

Oh, E., & Jeon, B. (2015). Synergistic anti-*Campylobacter jejuni* activity of fluoroquinolone and macrolide antibiotics with phenolic compounds. *Frontiers in microbiology*, *6*, 1129. https://doi.org/10.3389/fmicb.2015.01129

Oh, S. M., Kim, Y. P., & Chung, K. H. (2006). Biphasic effects of kaempferol on the estrogenicity in human breast cancer cells. *Archives of pharmacal research*, *29*(5), 354–362. https://doi.org/10.1007/BF02968584

Ojewole J. A.O., Adewole S. O., & Olayiwola G.(2006).Hypoglycaemic and hypotensive effects of *Momordica charantia* Linn (Cucurbitaceae) whole-plant aqueous extract in rats : cardiovascular topics. *Cardiovascular Journal of South Africa*, *17*, 227-232. doi: 10.10520/EJC24147

Ojha, S., Javed, H., Azimullah, S., Khair, S. B. A., & Haque, M. E. (2015). Neuroprotective potential of ferulic acid in the rotenone model of Parkinson's disease. *Drug design, development and therapy, 9*, 5499. doi: 10.2147/DDDT.S90616

Oksana, S., Marian, B., Mahendra, R., & Bo, S. H. (2012) Plant phenolic compounds for food, pharmaceutical and cosmetics production. *Journal of Medicinal Plants Research*, *6*, 2526– 2539. https://www.researchgate.net/profile/Jasmine-Chaudhary/publication/264420140_A_Comprehensive_Review_on_Biological_activities_of_p-hydroxy_benzoic_acid_and_its_derivatives/links/5bbc806792851c7fde371acb/A-Comprehensive-Review-on-Biological-activities-of-p-hydroxy-benzoic-acid-and-its-derivatives.pdf

Onakpoya, I. J., Spencer, E. A., Thompson, M. J., & Heneghan, C. J. (2015). The effect of chlorogenic acid on blood pressure: A systematic review and meta-analysis of randomized clinical trials. *Journal of Human Hypertension*, *29*, 77. https://doi.org/10.1038/jhh.2014.46

Ozturk Sarikaya, S. B. (2015). Acethylcholinesterase inhibitory potential and antioxidant properties of pyrogallol. *J Enzyme Inhib Med Chem*, *30*(5), 761-766. https://doi.org/10.3109/14756366.2014.965700

Pan, L., Cho, K. S., Yi, I., To, C. H., Chen, D. F., & Do, C. W. (2021). Baicalein, Baicalin, and Wogonin: Protective Effects against Ischemia-Induced Neurodegeneration in the Brain and Retina. *Oxidative medicine and cellular longevity*, 2021, 8377362. https://doi.org/10.1155/2021/8377362

Park, M. J., Lee, E. K., Heo, H. S., Kim, M. S., Sung, B., Kim, M. K., Lee, J., Kim, N. D., Anton, S., Choi, J. S., Yu, B. P., & Chung, H. Y. (2009). The anti-inflammatory effect of kaempferol in aged kidney tissues: the involvement of nuclear factor-kappaB via nuclear factor-inducing kinase/IkappaB kinase and mitogen-activated protein kinase pathways. *Journal of medicinal food*, *12*(2), 351–358. https://doi.org/10.1089/jmf.2008.0006

Pei, K., Ou, J., Huang, J., & Ou, S. (2016). p-Coumaric acid and its conjugates: dietary sources, pharmacokinetic properties and biological activities. *Journal of the science of food and agriculture*, *96*(9), 2952–2962. https://doi.org/10.1002/jsfa.7578

Pero, R. W., & Lund, H. (2009). *In vivo* treatment of humans with quinic acid enhances DNA repair and reduces the influence of lifestyle factors on risk to disease. *International Journal of Biotechnology & Biochemistry*, 5(3), 293+. https://link.gale.com/apps/doc/A215925274/AONE?u=anon~32494ea1&sid=googleScholar&xid=504924c0

Pham, T.M.H., Ngo, D.-H., Ngo, D.-N., & Vo, T.S. (2019). "Investigation of Biological Activities of Wild Bitter Melon (*Momordica charantia* Linn. Var. *Abbreviata* Ser.)" *Biomolecules 9*, no. 6, 211. https://doi.org/10.3390/biom9060211

Pires, T., Dias, M. I., Barros, L., Alves, M. J., Oliveira, M., Santos-Buelga, C., & Ferreira, I. (2018). Antioxidant and antimicrobial properties of dried Portuguese apple variety (*Malus domestica* Borkh. cv Bravo de Esmolfe). *Food chemistry*, *240*, 701–706. https://doi.org/10.1016/j.foodchem.2017.08.010

Pongthanapisith, V., Ikuta, K., Puthavathana, P., & Leelamanit, W. (2013). Antiviral Protein of *Momordica charantia* L. Inhibits Different Subtypes of Influenza A. *Evidence-based complementary and alternative medicine : eCAM*, *2013*, 729081. https://doi.org/10.1155/2013/729081

Pulido, R., Bravo, L., & Saura-Calixto, F. (2000) Antioxidant activity of dietary polyphenols as determined by a modified ferric reducing/antioxidant power assay. *Journal of Agricultural and Food Chemistry*, *48*, 3396– 3402. https://doi.org/10.1021/jf9913458

Ramos S. (2008). Cancer chemoprevention and chemotherapy: dietary polyphenols and signalling pathways. *Molecular nutrition & food research*, *52*(5), 507–526. https://doi.org/10.1002/mnfr.200700326

Rivero-Buceta, E., Carrero, P., Doyagüez, E. G., Madrona, A., Quesada, E., Camarasa, M. J., Peréz-Pérez, M. J., Leyssen, P., Paeshuyse, J., Balzarini, J., Neyts, J., & San-Félix, A. (2015). Linear and branched alkyl-esters and amides of gallic acid and other (mono-, di- and tri-) hydroxy benzoyl derivatives as promising anti-HCV inhibitors. *European journal of medicinal chemistry, 92*, 656–671. https://doi.org/10.1016/j.ejmech.2015.01.033

Roshan, H., Nikpayam, O., Sedaghat, M., & Sohrab, G. (2018).Effects of green coffee extract supplementation on anthropometric indices, glycaemic control, blood pressure, lipid profile, insulin resistance and appetite in patients with the metabolic syndrome: A randomised clinical trial. *British Journal of Nutrition*, *119*(3), 250–258. https://doi.org/10.1017/S0007114517003439

Ruan, Z., Liu, S., Zhou, Y., Mi, S., Liu, G., Wu, X., Yao, K., Assaad, H., Deng, Z., Hou, Y., Wu, G., & Yin, Y.　(2014). Chlorogenic acid decreases intestinal permeability and increases expression of intestinal tight junction proteins in weaned rats challenged with LPS. *PLOS ONE*, *9*(6), e97815. https://doi.org/10.1371/journal.pone.0097815

Rukkumani, R., Aruna, K., Suresh Varma, P., & Padmanabhan Menon, V. (2004). Hepatoprotective role of ferulic acid: a dose-dependent study. *Journal of medicinal food*, *7*(4), 456-461. https://doi.org/10.1089/jmf.2004.7.456

Salomone, F., Galvano, F., & Li Volti, G. (2017). Molecular bases underlying the hepatoprotective effects of coffee. *Nutrients*, *9*(1), 85. https://doi.org/10.3390/nu9010085

Samhan-Arias, A. K., Martín-Romero, F. J., & Gutiérrez-Merino, C. (2004). Kaempferol blocks oxidative stress in cerebellar granule cells and reveals a key role for reactive oxygen species production at the plasma membrane in the commitment to apoptosis. *Free radical biology & medicine, 37*(1), 48–61. https://doi.org/10.1016/j.freeradbiomed.2004.04.002

Santos, K. K., Matias, E. F., Sobral-Souza, C. E., Tintino, S. R., Morais-Braga, M. F., Guedes, G. M., Santos, F. A., Sousa, A. C., Rolón, M., Vega, C., de Arias, A. R., Costa, J. G., Menezes, I. R., & Coutinho, H. D. (2012). Trypanocide, cytotoxic, and antifungal activities of *Momordica charantia*. *Pharmaceutical biology*, *50*(2), 162–166. https://doi.org/10.3109/13880209.2011.581672

Shao, D., Li, J., Li, J., Tang, R., Liu, L., Shi, J., Huang, Q., & Yang, H. (2015). Inhibition of Gallic Acid on the Growth and Biofilm Formation of Escherichia coli and Streptococcus mutans. *Journal of food science*, *80*(6), M1299–M1305. https://doi.org/10.1111/1750-3841.12902

Shao, Z. H.,Vanden Hoek, T. L.,Qin, Y., Becker, L. B.,Schumacker, P. T.,Li, C. Q.,Dey, L.,Barth, E., Halpern, H., Rosen, G. M., & Yuan, C. S.(2002). Baicalein attenuates oxidant stress in cardiomyocytes. *American Journal of Physiology-Heart and Circulatory Physiology*, *282*(3). doi: 10.1152/ajpheart.00163.2001

Shi, C., Zhang, X., Sun, Y., Yang, M., Song, K., Zheng, Z., Chen, Y., Liu, X., Jia, Z., Dong, R., Cui, L., & Xia, X. (2016). Antimicrobial Activity of Ferulic Acid Against Cronobacter sakazakii and Possible Mechanism of Action. *Foodborne pathogens and disease*, *13*(4), 196–204. https://doi.org/10.1089/fpd.2015.1992

Shi, H., Shi, A., Dong, L., Lu, X., Wang, Y., Zhao, J., Dai, F., & Guo, X. (2016). Chlorogenic acid protects against liver fibrosis in vivo and in vitro through inhibition of oxidative stress. *Clinical nutrition (Edinburgh, Scotland)*, *35*(6), 1366–1373. https://doi.org/10.1016/j.clnu.2016.03.002

Shih, C. C., Lin, C. H., & Lin, W. L. (2008). Effects of *Momordica charantia* on insulin resistance and visceral obesity in mice on high-fat diet. *Diabetes research and clinical practice*, *81*(2), 134–143. https://doi.org/10.1016/j.diabres.2008.04.023

Shimoyama, A. T., Santin, J. R., Machado, I. D., de Oliveira e Silva, A. M., de Melo, I. L., Mancini-Filho, J., & Farsky, S. H. (2013). Antiulcerogenic activity of chlorogenic acid in different models of gastric ulcer. *Naunyn-Schmiedeberg's archives of pharmacology*, *386*(1), 5–14. https://doi.org/10.1007/s00210-012-0807-2

Song J., Zhang L., Xu Y., Yang D., Zhang L., Yang S., Zhang W., Wang J., Tian S., Yang S., Yuan T., Liu A., Lv Q., Li F., Liu H., Hou B., Peng X., Lu Y., & Du G.(2021). The comprehensive study on the therapeutic effects of baicalein for the treatment of COVID-19 *in vivo* and *in vitro*. *Biochemical Pharmacology*, *183*, 114302. https://doi.org/10.1016/j.bcp.2020.114302.

Sung, W. & Lee, D. (2010). Antifungal action of chlorogenic acid against pathogenic fungi, mediated by membrane disruption. *Pure and Applied Chemistry*, *82*(1), 219-226. https://doi.org/10.1351/PAC-CON-09-01-08

Tamura, H., Akioka, T., Ueno, K., Chujyo, T., Okazaki, K., King, P. J., & Robinson, W. E., Jr (2006). Anti-human immunodeficiency virus activity of 3,4,5-tricaffeoylquinic acid in cultured cells of lettuce leaves. *Molecular nutrition & food research*, *50*(4-5), 396–400. https://doi.org/10.1002/mnfr.200500216

Teodoro, G. R., Ellepola, K., Seneviratne, C. J., & Koga-Ito, C. Y. (2015). Potential Use of Phenolic Acids as Anti-Candida Agents: A Review. *Frontiers in microbiology*, *6*, 1420. https://doi.org/10.3389/fmicb.2015.01420

Tian, J., Li, J., Bie, B., Sun, J., Mu, Y., Shi, M., Zhang, S., Kong, G., Li, Z., & Guo, Y.(2021). MiR-3663-3p participates in the anti-hepatocellular carcinoma proliferation activity of baicalein by targeting SH3GL1 and negatively regulating EGFR/ERK/NF-κB signaling. *Toxicology and Applied Pharmacology*, *420*, 115522. https://doi.org/10.1016/j.taap.2021.115522

Toghyani Khorasgani, A., Amini-Khoei, H., Shadkhast, M., Salimian, S., Majidian, M., Habibian Dehkordi, S. (2021). Quinic acid through mitigation of oxidative stress in the hippocampus exerts analgesic effect in male mice. *Future Natural Products*, *7*(2), 1-11. http://futurenatprod.skums.ac.ir/article_248390.html

Tsai, C. H., Chen, E. C., Tsay, H. S., & Huang, C. J. (2012). Wild bitter gourd improves metabolic syndrome: a preliminary dietary supplementation trial. *Nutrition journal*, *11*, 4. https://doi.org/10.1186/1475-2891-11-4

Velika, B., & Kron, I. (2012) Antioxidant properties of benzoic acid derivatives against superoxide radical. *Free Radicals & Antioxidants*, **2**: 62– 67. DOI: https://doi.org/10.5530/ax.2012.4.11

Vinayagam, R., Jayachandran, M., & Xu, B. (2016). Antidiabetic Effects of Simple Phenolic Acids: A Comprehensive Review. *Phytotherapy research : PTR*, *30*(2), 184–199. https://doi.org/10.1002/ptr.5528

Wan, C. W., Wong, C. N., Pin, W. K., Wong, M. H., Kwok, C. Y., Chan, R. Y., Yu, P. H., & Chan, S. W. (2013). Chlorogenic acid exhibits cholesterol lowering and fatty liver attenuating properties by up-regulating the gene expression of PPAR-α in hypercholesterolemic rats induced with a high-cholesterol diet. *Phytotherapy research : PTR*, *27*(4), 545–551. https://doi.org/10.1002/ptr.4751

Wattel, A., Kamel, S., Mentaverri, R., Lorget, F., Prouillet, C., Petit, J. P., Fardelonne, P., & Brazier, M. (2003). Potent inhibitory effect of naturally occurring flavonoids quercetin and kaempferol on *in vitro* osteoclastic bone resorption. *Biochemical pharmacology*, *65*(1), 35–42. https://doi.org/10.1016/s0006-2952(02)01445-4

Wei, L., Shaoyun, W., Shutao, L., Jianwu, Z., Lijing, K., & Pingfan, R.(2013). Increase in the free radical scavenging capability of bitter gourd by a heat-drying process. *Food Function, 4*, 1850-1855.http://dx.doi.org/10.1039/C3FO60169B

Wei, N., Wei, Y., Li, B., & Pang, L. (2017). Baicalein Promotes Neuronal and Behavioral Recovery After Intracerebral Hemorrhage Via Suppressing Apoptosis, Oxidative Stress and Neuroinflammation. *Neurochem Res, 42,* 1345–1353. https://doi.org/10.1007/s11064-017-2179-y

Wu S. J., & Ng, L. T.(2008).Antioxidant and free radical scavenging activities of wild bitter melon (*Momordica charantia* Linn. var. *abbreviata* Ser.) in Taiwan. *Food Science and Technology*, *41*(2), 323-330.https://doi.org/10.1016/j.lwt.2007.03.003.

Yang, Y. Q., Yan, C., Branford-White, C. J., & Hou, X. Y. (2014). Biological values of acupuncture and chinese herbal medicine: impact on the life science. *Evidence-based complementary and alternative medicine : eCAM*, *2014*, 593921. https://doi.org/10.1155/2014/593921

Yasukawa, K., Takido, M., Takeuchi, M., Sato, Y., Nitta, K., & Nakagawa, S. (1990). Inhibitory effects of flavonol glycosides on 12-O-tetradecanoylphorbol-13-acetate-induced tumor promotion. *Chemical & pharmaceutical bulletin*, *38*(3), 774–776. https://doi.org/10.1248/cpb.38.774

Yukawa, G. S., Mune, M., Otani, H., Tone, Y., Liang, X. M., Iwahashi, H., & Sakamoto, W. (2004). Effects of coffee consumption on oxidative susceptibility of low-density lipoproteins and serum lipid levels in humans. *Biochemistry. Biokhimiia*, *69*(1), 70–74. https://doi.org/10.1023/b:biry.0000016354.05438.0f

Yun, B. Y., Zhou, L., Xie, K. P.,Wang, Y. J., & Xie, M. J.(2012). Antibacterial activity and mechanism of baicalein. *Yao xue xue bao = Acta pharmaceutica Sinica*, *47*(12), 1587-1592. http://europepmc.org/abstract/MED/23460962

Yun, N., Kang, J. W., & Lee, S. M. (2012). Protective effects of chlorogenic acid against ischemia/reperfusion injury in rat liver: molecular evidence of its antioxidant and anti-inflammatory properties. *The Journal of nutritional biochemistry*, *23*(10), 1249–1255. https://doi.org/10.1016/j.jnutbio.2011.06.018

Zhang, X., Huang, H., Yang, T., Ye, Y., Shan, J., Yin, Z., & Luo, L. (2010). Chlorogenic acid protects mice against lipopolysaccharideinduced acute lung injury. *Injury*, *41*(7), 746–752. https://doi.org/10.1016/j.injury.2010.02.029

Zhang, X., Lin, D., Jiang, R., Li, H., Wan, J., & Li, H. (2016). Ferulic acid exerts antitumor activity and inhibits metastasis in breast cancer cells by regulating epithelial to mesenchymal transition. *Oncology Reports*, *36*(1), 271-278. https://doi.org/10.3892/or.2016.4804

Zhao, Y., Wang, J., Ballevre, O., Luo, H., & Zhang, W. (2012). Antihypertensive effects and mechanisms of chlorogenic acids. *Hypertension research : official journal of the Japanese Society of Hypertension*, *35*(4), 370–374. https://doi.org/10.1038/hr.2011.195

Zheng, L., Lee, J., Yue, L. M., Lim, G. T., Yang, J. M., Ye, Z. M., & Park, Y. D. (2018). Inhibitory effect of pyrogallol on α-glucosidase: Integrating docking simulations with inhibition kinetics. *Int J Biol Macromol*, *112*, 686-693. https://doi.org/10.1016/j.ijbiomac.2018.02.026

Zhu, Y., Ying, D., Xiwen Q., Fengjie, C., Qin, G., Xinghua, Z., Yun, W., Yi, Z., & Zhiyu, X.(2012). "Effect of Superfine Grinding on Antidiabetic Activity of Bitter Melon Powder" *International Journal of Molecular Sciences, 13,* 14203-14218. https://doi.org/10.3390/ijms131114203

Zilic, S., Sukalovic, V.H.-T., Dodig, D., Maksimovic, V., Maksimovic, M. & Basic, Z. (2011). Antioxidant activity of small grain cereals caused by phenolics and lipid soluble antioxidants. *Journal of Cereal Science*, *54*, 417–424. https://doi.org/10.1016/j.jcs.2011.08.006