行政院國家科學委員會專題研究計畫成果報告

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※膽固醇對糙薏仁降低STZ所引起的糖尿病大白鼠血脂質的影響※

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一、中文摘要

本研究目的在於探討薏仁在添加或不添加膽固醇飲食條件下對糖尿病大白鼠血脂質及血糖濃度的影響。以 Sprague-Dawley (S.D)系統之雄性大白鼠為實驗動物，經皮下注射 streptozotocin (STZ) (60mg/kg B.W.)以誘發糖尿病。實驗共分為四組，分別是(1) Corn starch (2) Dehulled adlay (3) Corn starch + 0.5% Cholesterol (4) Dehulled adlay + 0.5% Cholesterol，實驗共進行六週。實驗結果發現，在不添加膽固醇條件下，薏仁飲食會明顯降低血漿總膽固醇、葡萄糖、果糖胺、三酸甘油酯、磷脂質、游離脂肪酸、apolipoprotein B 與 β-羥基丁酸的含量。此外，薏仁飲食亦會降低血漿極低密度脂蛋白膽固醇及低密度脂蛋白膽固醇含量，而無論飲食中有無膽固醇的添加，攝食薏仁飲食後皆有明顯較高的脂肪組織。另一方面，膽固醇的添加會顯著提高血漿總膽固醇、極低密度脂蛋白膽固醇及低密度脂蛋白膽固醇含量，且降低糖尿病大白鼠的體重，但並不影響血糖及三酸甘油酯含量。在添加膽固醇條件下，薏仁亦會顯著性降低血漿總膽固醇、極低密度脂蛋白膽固醇、低密度脂蛋白膽固醇、葡萄糖、果糖胺、β-羥基丁酸及游離脂肪酸含量，提高脂肪組織重量。

由本研究結果顯示(1)膽固醇的添加可能促進糖尿病大白鼠的脂肪組織分解作用(2)無論膽固醇添加與否，薏仁可能具有降低糖尿病血脂質及血糖濃度的作用。

Abstract

To investigate the effect of dietary adlay on plasma lipids and glucose concentrations in diabetic rats fed on a diet with or without cholesterol supplementation, Spraque-Dawley (SD) rats were used as animal model. The diabetic status was induced by subcutaneous injection of streptozotocin (60 mg/kg). All the rats were divided into 4 groups, there are (1) corn starch (CS), (2) Dehulled adlay (DA), (3) corn starch + 0.5% cholesterol (CSC) and (4) Dehulled adlay + 0.5% cholesterol (DAC). The experiment was done for 6 weeks. Lower plasma total cholesterol, triglyceride, phospholipids, glucose, fructosamine, free fatty acid and β-HBA concentrations were observed in rats fed DA diet when compared with those fed the CS diet. Significantly decreased VLDL-cholesterol and LDL-cholesterol was observed in DA group. Cholesterol supplementation significantly dramatically increased plasma total cholesterol, LDL-cholesterol and VLDL-cholesterol but decreased adipose tissue weight in diabetic rats. Adlay supplementation significantly increased adipose tissue weight in diabetic rats fed on a diet with or without cholesterol supplementation. No significant difference in plasma TG and glucose was observed in rats after cholesterol supplementation. In cholesterol supplement groups, lower plasma total cholesterol, LDL-cholesterol, VLDL-cholesterol, glucose, fructosamine, β-HBA, free fatty acid concentration and higher adipose tissue weight were observed in rats after adlay treatment. Results from the present study suggest that (1) cholesterol supplement may promote the lipolysis in diabetic rats. (2) adlay treatment may decrease plasma lipids and glucose

concentration in diabetic rats fed on a diet with or without cholesterol supplementation.

二、緣由與目的

薏苡為禾本科一年生之草本植物，學名為 *Coix lachryma-job* L. var. *mayuen* Stapf，日文名為鳩麥(ハトムギ)，英文名為 adlay 或 job's tears，薏苡種實經過脫殼後為糙薏仁，糙薏仁再經過碾白後的種仁為精白薏仁，俗稱薏仁或薏米。薏仁自古以來為我國傳統的食療材料，根據神農本草經和本草綱目等漢藥書籍記載，具有健胃、利尿、消炎、止痛與抗癌學等功能。在近代科學的研究中初步發現薏仁也具有提昇免疫能力、抗腫瘤、降血糖及降血脂等功效。然而，有關薏仁會降低血糖與血脂質的機制尚未明瞭。

近幾年來，隨著人們生活型態的改變及西方文化的入侵，國人的飲食型態日趨於高油脂、高蛋白質、低纖維與低碳水化合物的飲食，相對地罹患心血管疾病與糖尿病等慢性疾病有逐年增加的趨勢。目前糖尿病的罹患率高居國人十大死因之一，其死亡原因常常是因為併發腦中風、冠狀動脈疾病與高血脂症等疾病所引起的。去年，我們曾經提出報告指出，在膽固醇的添加之下，糙薏仁會明顯下降糖尿病大白鼠血脂質及血糖濃度，其原因可能與糙薏仁會抑制脂肪分解有關。由於飲食膽固醇會明顯影響肝臟脂質代謝及脂蛋白的分泌與合成，因此我們推測飲食膽固醇可能在薏仁降低糖尿病大白鼠血脂質上扮演著重要的角色。

有鑑於此，為了進一步了解膽固醇在糙薏仁影響糖尿病大白鼠血糖及血脂質中所扮演的角色，以 S.D. 系統之雄性大白鼠為實驗動物，於六週齡時經由皮下注射 streptozotocin(60mg/kg B.W.) 的方式，以誘發糖尿病。實驗為期六週，分為四組，分別為 (1) Corn starch (CS) ; (2) Adlay (AD) ; (3) Corn starch +0.5% Cholesterol (CSC) ; (4) Adlay +0.5% Cholesterol (ADC)，主要探討重點在於飲食中有無膽固醇的添加之下，糖尿病大白鼠在攝食糙薏仁之後，對脂質代謝及糖代謝的變化情形。

三、結果與討論

由實驗結果發現，無論飲食中有無膽固醇的添加，在實驗六週後，糙薏仁飲食組皆有明顯的增加糖尿病大白鼠的體重(圖一)，顯示攝食糙薏仁有改善糖尿病病情的現象，而且膽固醇的添加並不會降低糖尿病大白鼠的生長。在肝臟及脂肪組織重量的變化上(表二)，不論在有無膽固醇的添加情形之下，糙薏仁飲食會明顯增加肝臟組織的重量，但膽固醇的添加則會更加顯著性的增加肝臟重量，這在我們之前的報告中亦有此類似現象，其原因與肝臟中含有較多的脂質有關。此外，由於糖尿病大白鼠對於醣類的利用不佳，容易導致脂肪動員的現象產生，而膽固醇的添加會明顯降低玉米澱粉組之脂肪組織含量，但攝食糙薏仁的糖尿病大白鼠的脂肪組織重量則不受飲食膽固醇添加與否的影響，相對於玉米澱粉組，不論在有無膽固醇的添加情形之下，攝食糙薏仁皆有較高的脂肪組織重量及有較低的血漿游離脂肪酸與 β-hydroxybutric acid 的含量(表五)，顯示糙薏仁具有抑制糖尿病大白鼠脂肪動員的作用，同時又能顯著降低肝臟酮體的產生。

研究指出糖尿病患者通常合併血脂質異常的現象，容易產生心血管方面的併發症(Howard., 1987a)，本實驗結果顯示膽固醇的攝取會明顯提升糖尿病大白鼠血膽固醇含量，而無論有無膽固醇的添加，糙薏仁皆能顯著降

低血膽固醇及磷脂質的含量，但並不改變三酸甘油酯含量(表三)。進一步比較時發現，當飲食中不含膽固醇時，糙薏仁降低膽固醇的效果約 22%左右，但一旦添加膽固醇之後，降低血膽固醇的效果竟高達 72%左右。另一方面，糙薏仁能明顯降低血漿中葡萄糖、果糖胺及乳酸濃度(表四)，而膽固醇的添加有無並沒有造成任何影響。由於乳酸葡萄糖不完全氧化的產物，而果糖胺的增加則是血糖控制不佳的表現，因此糙薏仁能降低糖尿病大白鼠血糖、果糖胺及乳酸濃度，顯示糙薏仁能改善糖尿病大白鼠之糖代謝。

在脂蛋白膽固醇含量方面(表六)，膽固醇的添加會使糖尿病大白鼠血漿極低密度脂蛋白膽固醇(VLDL-C)以極低密度脂蛋白膽固醇(LDL-C)的含量明顯上升，同時測定血漿中 apolipoprotein B 的含量也有相同的表現(圖二)。許多研究指出，膽固醇具有促進肝臟中 VLDL 及 apo B 之分泌的能力(Khan et al., 1990; Fungwe et al., 1993)，本研究結果顯示糙薏仁會明顯增加糞便膽固醇及三酸肝由酯的排泄(表七)，且顯著性降低血液中 VLDL 膽固醇及 apo B 的含量，但肝臟膽固醇含量卻明顯較高，推測糙薏仁可能藉由降低飲食膽固醇的吸收及降低肝臟 VLDL 的分泌，因此能顯著性降低血液中 VLDL 膽固醇及 apo B 的含量。

在盲腸內容物方面(表八)，由實驗結果發現膽固醇的添加較不添加膽固醇時會明顯增加盲腸中 Acetate 的含量，減少 Propionate 和 Butyrate 的含量，但糙薏仁飲食組皆有顯著增加 Acetate、Propionate 的含量，而 Butyrate 含量只有在不添加膽固醇組裡才有顯著增加。許多實驗發現 Propionate 會降低肝臟膽固醇合成（Chen 等人(1984)，而 Butyrate 則是會降低腸道 pH 值，降低腸癌的發生，因此由本研究結果顯示，膽固醇的添加與否會影響糖尿病大白鼠腸內細菌代謝，而糙薏仁增加盲腸中 Propionate 和 Butyrate 的含量可能亦有利於糖尿病大白鼠之脂質代謝與腸道生理。

四、自評

本研究結果再一次確認糙薏仁具有降低糖尿病大白鼠血糖及血脂質的作用，特別是在膽固醇的添加下，糙薏仁會較顯著的下降血膽固醇濃度及抑制脂肪組織分解。

五、參考文獻

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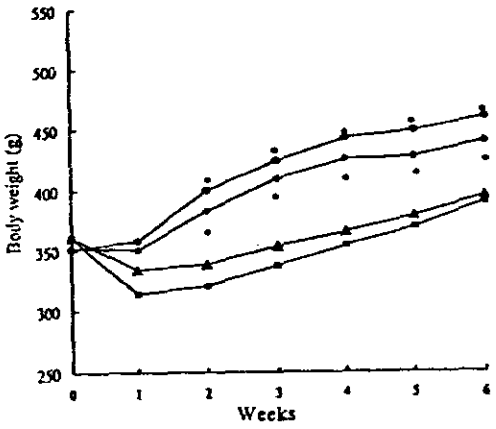
Table 1. Composition of the experimental diet (%)

Ingredient(%)	Corn starch	Dehulled adlay	Corn starch +Cholesterol	Dehulled adlay +Cholesterol
Lard	10	10	10	10
Casein	20	20	20	20
Vitamin mixture[1]	1	1	1	1
Salt mixture[2]	5	5	5	5
Cellulose	5	5	5	5
Cholesterol	—	—	0.5	0.5
Cholic acid	—	—	0.3	0.3
Choline chloride	0.2	0.2	0.2	0.2
Corn starch	58.8	—	58	—
Dehulled dlay	—	58.8	—	58

[1] Based on AIN-76 formula
[2] AIN-76 mixture



圖一. 糖尿病大白鼠餵食不同實驗飼料六週後體重的變化情形
Fig.1. Changes of body weight in diabetic rats fed experimental diets for six weeks.[1]

[1]Result are expressed as mean± SD.for 7~9 rats in each dietary group.
*Values are significantly different from corn starch dietary group($p<0.05$).

表四、糖尿病大白鼠餵食不同實驗飼料六週後血漿中葡萄糖、果糖胺和乳酸含量的變化
Table 4. Changes of plasma glucose, fructosamine and lactate levels in diabetic rats fed different experimental diets for 6 weeks.[1]

Diet[2]	Glucose (mg/dL)	Fructosamine (mmol/L)	Lactate (mg/dL)
Corn starch	590.8 ± 79.8[a]	3.4 ± 0.5[a]	27.6±7.3[a]
Dehulled adlay	329.1 ± 44.1[b]	2.0 ± 0.5[b]	21.6±3.7[b]
Corn starch+Cholesterol	544.3 ± 112.6[a]	3.4 ± 0.4[a]	28.6±3.9[a]
Dehulled adlay+Cholesterol	307.1 ± 75.0[b]	1.8 ± 0.7[b]	22.7±3.6[b]

[1]Results are expressed as mean±SD. for n=7~9 rats per each dietary group. Values in the same column with the superscript letter are significantly different ($p<0.05$).
[2]See Table 1-1.

表五、糖尿病大白鼠餵食不同實驗飼料六週後血漿中游離脂肪酸和β-羥基丁酸含量的變化。
Table 5. Changes of plasma free fatty acid and β-hydroxybutyric acid (β-HBA) levels in diabetic rats fed different experimental diets for 6 weeks.[1]

Diet[2]	Free fatty acid (m Eq/L)	β-HBA (mg/dL)
Corn starch	1.0 ±0.3[a]	9.9±1.6[a]
Dehulled adlay	0.6 ±0.2[b]	7.5±1.4[b]
Corn starch +Cholesterol	0.8±0.3[a]	9.2 ± 1.6[a]
Dehulled adlay +Cholesterol	0.5±0.1[b]	7.2 ± 1.1[b]

[1]Results are expressed as mean ± SD. for n=7~9 rats per each dietary group. Values in the same column with the superscript letter are significantly different ($p<0.05$).
[2]See Table 1-1.

表二、糖尿病大白鼠餵食不同實驗飼料六週後組織臟器重量的變化。
Table 2. Changes of tissues weight in diabetic rats fed different experimental diets for 6 weeks.[1]

Diet[2]	Liver (g)	Kidney (g)	Adipose tissue (g)	Liver (g/100g B.W)	Kidney (g/100g B.W)
Corn starch	13.6± 1.2[a]	3.8± 0.4	7.4± 2.5[b]	3.7± 0.3[b]	1.1± 0.1
Dehulled adlay	14.6± 1.0[a]	4.3± 0.4	14.6± 4.4[a]	3.5± 0.2[b]	1.1± 0.1
Corn starch+Cholesterol	25.2± 4.3[b]	3.9± 0.8	5.4± 2.2[a]	7.0± 0.8[a]	1.1± 0.1
Dehulled adlay+ Cholesterol	29.6± 1.8[a]	4.2± 0.6	14.5± 4.6[a]	6.8± 0.7[a]	1.0± 0.2

[1] Results are expressed as mean ±S.D. for n=7~9 rats per each dietary group. Values in the same column with the different superscript letter are significant ($p<0.05$).
[2] See Table 1-1.

表三、糖尿病大白鼠餵食不同實驗飼料六週後血漿中總膽固醇、三酸甘油脂和磷脂質含量的變化。
Table 3. Change of plasma total cholesterol, triglyceride and phospholipid levels in diabetic rats fed different experimental diets for 6 weeks.[1]

Diet[2]	Total cholesterol (mg/dL)	Triglyceride (mg/dL)	Phospholipid (mg/dL)
Corn starch	147 ± 21[a]	141 ± 26[a]	181 ± 42[b]
Dehulled adlay	114 ± 6[d]	84 ± 21[b]	136 ± 15[a]
Corn starch + Cholesterol	767 ± 234[b]	152 ± 30[a]	373 ± 98[a]
Dehulled adlay + Cholesterol	214 ± 71[b]	76 ± 23[b]	173 ± 25[b]

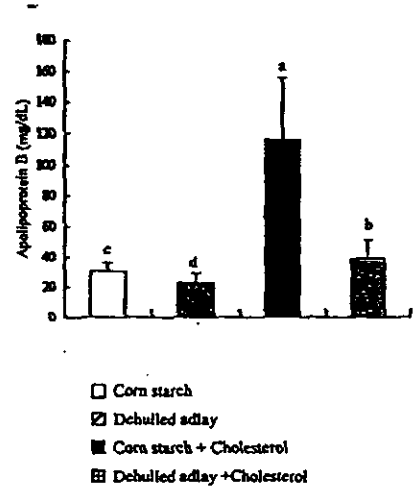
[1]Results are expressed as mean ± SD. for n=7~9 rats in each dietary group. Value in the same column with the different superscript letter are significantly different ($p<0.05$).
[2]See Table 1-1.

表六、糖尿病大白鼠餵食不同實驗飼料六週後，血漿中脂蛋白膽固醇含量以及高密度脂蛋白膽固醇與總膽固醇比值的變化。

Table 6. Changes of plasma lipoprotein-cholesterol and the ratios of HDL-cholesterol to total cholesterol in diabetic rats fed different experimental diets for 6 weeks.[1]

Diet[2]	VLDL-cholesterol	LDL- cholesterol	HDL-cholesterol	HDL-C/TC
	(mg/dL)			
Corn starch	69.7± 14.2[a]	40.2± 6.7[a]	37.0± 5.2[a]	0.25± 0.06[b]
Dehulled adlay	45.9± 2.7[d]	29.6± 0.8[d]	38.6± 3.5[a]	0.34± 0.03[a]
Corn starch + Cholesterol	475.3± 149.9[a]	254.3± 76.1[a]	32.8± 4.0[b]	0.04± 0.02[d]
Dehulled adlay + Cholesterol	113.4± 43.2[b]	69.8± 27.0[b]	30.5± 2.9[b]	0.16± 0.06[c]

[1]Result are expressed as mean± SD. for n=7~9 rats in each dietary group. Values in the same column with the different superscript letter are significantly different ($p<0.05$).
[2]See composition of the experimental diet.



圖二、糖尿病大白鼠餵食不同實驗飼料六週後血漿中主脂蛋白 B 含量的變化

Fig. 2. Changes of plasma apolipoprotein B levels in diabetic rats fed experimental diets for 6 weeks.[1]

[1]Result are expressed as mean± SD. for 7~9 rats in each dietary group. Values in the same column with the different superscript letter are significantly different ($p<0.05$).

表七、糖尿病大白鼠餵食不同實驗飼料六週後，糞便中總膽固醇和三酸甘油酯含量的變化。

Table 7. Changes of fecal total cholesterol and triglyceride levels in diabetic rats fed different experimental diets for 6 weeks.[1]

Diet[2]	Total cholesterol		Triglyceride	
	(mg/g)	(mg/total feces)	(mg/g)	(mg/total feces)
Corn starch	6.0± 0.5[d]	17.7± 3.1[d]	8.3± 0.3[b]	25.1± 2.0[d]
Dehulled adlay	7.2± 0.4[c]	30.4± 3.6[c]	9.3± 0.5[a]	38.0± 2.9[b]
Corn starch+Cholesterol	14.8± 1.7[b]	61.7± 9.4[b]	8.5± 0.6[b]	33.7± 4.1[c]
Dehulled adlay+Cholesterol	16.9± 1.0[a]	80.1± 17.1[a]	9.8± 0.5[a]	46.8± 4.2[a]

[1]Results are expressed as mean ± SD. for n=7~8 rats per each dietary group. Values in the same column with the superscript letter are significantly different ($p<0.05$).
[2]See Table 1-1.

表八、糖尿病大白鼠餵食不同實驗飼料六週後，盲腸內容物中短鏈脂肪酸的含量

Table 8. The amount of short-chain fatty acid (SCFA) in cecal content of diabetic rats fed different experiment diets for 6 weeks.[1]

Diet[2]	Acetate	Propionate	Butyrate	Total SCFA	Acetate	Propionate	Butyrate	Total SCFA
	(u mole/g cecal content)				(u mole/total cecal content)			
Corn starch	30.3± 3.6[d]	9.5± 1.6[c]	5.3± 1.2[b]	45.2± 4.7[c]	164.2± 66.9[b]	50.6± 18.6[c]	28.1± 10.0[c]	243.1± 93.8[c]
Dehulled adlay	39.3± 6.2[c]	13.3± 3.9[c]	7.2± 1.8[a]	59.8± 7.3[b]	93.8± 22.0[d]	32.5± 13.0[b]	17.7± 7.7[b]	144.2± 39.1[b]
Corn starch +cholesterol	49.5± 4.7[b]	7.3± 1.2[d]	2.5± 0.8[c]	59.3± 5.5[b]	220.2± 87.5[a]	32.8± 15.4[b]	11.4± 5.8[c]	264.6± 106.6[a]
Dehulled adlay +cholesterol	56.2± 9.1[a]	10.5± 2.1[b]	2.4± 0.9[c]	69.1± 10.2[a]	137.7± 53.1[c]	25.7± 10.4[c]	5.9± 3.3[d]	169.4± 66.9[b]

[1]Result are expressed as mean± SD. for n=7~9 rats in each dietary group. Value in the same column with the different superscript letter are significantly different ($p<0.05$).