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BENEFICIAL EFFECTS OF *MORINDA CITRIFOLIA* LINN. (NONI) LEAF EXTRACT ON OBESITY, DYSLIPIDEMIA AND ADIPONECTINEMIA IN RATS WITH METABOLIC SYNDROME

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ABSTRACT: Pharmacological activities have been reported for the fruit, leaf and root extracts of *Morinda citrifolia* L. (Noni); however, the plant has not been widely studied for its antidyslipidemic effects on obesity and metabolic syndrome (MS). **Objective:** to evaluate the effects of aqueous *M. citrifolia* leaf extract on obesity and adipose tissue cell dynamics associated with triacylglycerol and adiponectin levels in Wistar rats with MS. **Methodology:** four groups of rats were used; control, metabolic syndrome (MS), *M. citrifolia* (Mc) and *M. citrifolia* plus sucrose (Mc-Suc). The dose of extract was 200 mg/kg of body weight for 2 weeks. **Results:** we observed differences in the weights of abdominal fat between the Mc and MS groups. The Mc-Suc and Mc groups showed significantly lower triacylglycerol concentrations than the MS group. Moreover, the adiponectin serum concentrations were higher in control, Mc-Suc and Mc groups than in the MS group. Finally, the MS group showed an increase in the percentage of fat cells with areas between 1001 and 1501 μm^2 compared with the Mc and Mc-Suc groups. **Conclusion:** ingestion of the aqueous extract from dried *M. citrifolia* leaves decreases abdominal fat and triacylglycerols associated with increased adiponectin levels and changes to adipose tissue cell dynamics.

INTRODUCTION: *Morinda citrifolia* Linn. (Rubiaceae), commonly known as “noni,” likely originated in the Indonesian archipelago and has been used for over 2000 years for its medicinal effects; this plant is distributed throughout the tropical and subtropical regions of the world¹.

A wide variety of pharmacological activities have been reported for extracts from *M. citrifolia* Linn. fruit, leaves and roots, however; the plant has not been widely studied for its antidyslipidemic effects with regards to obesity and adiponectin levels in Wistar rats with sucrose-induced metabolic syndrome. The sucrose-induced metabolic syndrome model represents the dietary intake of sucrose of humans, e.g., refined sugar in beverages and soft drinks, which is associated with the development of overweight status and obesity.

Obesity is a multifactorial disorder reflecting the complex interactions between genes and

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environment, e.g., lifestyle², and is associated with a high risk of chronic diseases such as diabetes, cardiovascular disease, dyslipidemia, neurological alterations, chronic kidney disease and certain cancers³. In 2010, IASO/IOTF analysis⁴ estimated that approximately one billion adults were overweight and that 475 million were obese. Patients who are overweight or obese are characterized by the abnormal development of adipose tissue⁵⁻⁸.

Adipose tissue produces a number of bioactive substances (adipokines), including tumor necrosis factor (TNF)- α , leptin, resistin, and adiponectin⁹. The size of individual adipocytes and distribution of sizes within a population have attracted attention with regards to their physiological impacts, and studies have shown that adipocyte size may affect behaviors such as adipokine secretion¹⁰.

Adiponectin is a 30 kDa protein that is abundantly secreted from adipocytes and circulates as three oligomeric complexes at high concentrations in the blood (3–30 $\mu\text{g/mL}$)¹¹. Unlike other adipokines, adiponectin is protective against the development of metabolic disorders, including obesity, insulin resistance, type 2 diabetes and related atherosclerotic vascular disease¹²⁻¹⁴. In rodent models, deletion of adiponectin is associated with increased inflammatory actions under conditions of stress such as over-nutrition and ischemic insult¹⁵⁻¹⁷. The circulating levels of adiponectin are markedly reduced in obese^{18, 19}, diabetic, and hypertensive patients²⁰ and in patients with coronary artery disease^{21, 22}, as well as in experimental animal models of insulin resistance and diabetes^{23, 24}. Additionally, a number of clinical observations have noted that hypo-adiponectinemia is associated with impaired endothelial-dependent vasodilation²⁵, hypertension²⁶, myocardial infarction²⁷, and coronary artery disease²⁸. Consequently, the present study aimed to investigate the effects of *Morinda citrifolia* leaf extract on obesity and changes to adipose tissue cell dynamics that are associated with dyslipidemia and adiponectinemia in rats with sucrose-induced metabolic syndrome.

MATERIALS AND METHODS:

Collection and preparation of plant material: Dried *M. citrifolia* leaves were collected in San

Bartolo Tuxtepec (18°05'35.69" N, 96°06'30.07" W) from the Papaloapan region of Oaxaca, Mexico. Taxonomic identification was performed by the curator of the Herbarium of CIIDIR-OAX, and a sample copy was deposited in their research laboratory for future reference. The plants were washed with tap water, dried on sheets of newspaper for 16 - 20 days, and then pulverized using a mechanical mill to obtain a powder that was subsequently hydrated.

Preparation of crude extract: To prepare the crude extracts, 50 g of dried and ground plants was added to 150 mL of distilled water in a flask and allowed to stand for 24 h. The solids were then separated from the liquid using filter paper and then discarded. The solvent was removed using reduced pressure on a rotary evaporator to obtain 15 g of crude extract. The crude extract was then stored in amber colored bottles at 8 °C until use.

Sucrose-induced metabolic syndrome model: A total of 20 weaning male Wistar rats (Harlan Teklad), 21 days of age, were individually housed and maintained on a 12-h light/dark cycle at 25 °C. Animal maintenance and handling methods were in accordance with the 1985 National Institutes of Health Guide for the Care and Use of Laboratory Animals. Animals were divided into two groups: the control group (C; $n=5$), which received a standard diet (Lab Diet CA.170481 Harlan Teklan Inc.), and the metabolic syndrome group (MS; $n=15$), which received the standard diet plus 40% sucrose, which was added to the drinking water; the animals were fed *ad libitum* for 10 weeks.

Experimental design: The animals with induced metabolic syndrome (MS), described above, were divided into two groups. Both groups received a standard diet and *Morinda citrifolia* L. extract (200 mg/kg) for 2 weeks; the first group (Mc-Suc; $n=5$) received *M. citrifolia* extract and sucrose in the drinking water *ad libitum*, and the second group (Mc; $n=5$) received *M. citrifolia* extract without sucrose in the drinking water. The metabolic syndrome group (MS; $n=5$) received 40% sucrose in the drinking water, while the control group (C; $n=5$) received purified water without sucrose. At the end of the experimental period, fasted animals were killed by decapitation, and metabolic syndrome parameters were assayed. All animal

experiments were conducted under institutional ethical guidelines.

Blood Samples: At the end of treatment period, blood samples from 18-hour-fasted animals were carefully collected to avoid hemolysis. The blood was centrifuged at 1086 X g for 10 min, and serum samples were kept at -20 °C until analysis.

Analytical Methods: Serum glucose concentrations were measured using the glucose oxidase method²⁹. Total cholesterol and HDL were measured using enzymatic reagents³⁰. Triacylglycerols, uric acid, total proteins (PTOT), albumin, and globulin were determined by colorimetric or enzymatic methods using an RA 10,000 Autoanalyzer (Bayer Diagnostics, Tarrytown, NY, USA). Finally, serum adiponectin levels were measured using an ELISA assay for rat adiponectin (Quantikine, R&D Systems).

Adipocyte Size Measurements: Random samples of abdominal adipose tissue were fixed in neutral formalin (10% formaldehyde and 0.1 M phosphate buffer, pH 7) for 24 h at room temperature. The samples were embedded in paraffin, and serial 7 mm sections were then cut using a microtome and stained with hematoxylin and eosin. Photomicrographs were obtained at a 40X magnification using an optical microscope (Axioimagen A2, Zeiss) with an Olympus digital camera at a 5.1-megapixel resolution. Adipocyte

areas were measured using the AxioVision Real 4.6 software (Zeiss Software, Inc.), and expressed as μm^2 . Areas were measured for adipocytes that were completely enclosed within the field, using five fields per rat. The average adipocyte area was calculated for each rat, and group means were determined from the individual averages for comparisons between the groups.

Data analysis: Data are presented as the mean \pm SD. Statistical significance was determined by analysis of variance, and Tukey's multiple range test was used for comparison of means ($P < 0.05$). The Fisher test was utilized for the relative distribution of adipocyte areas ($P < 0.001$).

RESULTS:

Experimental Model: The metabolic syndrome model was generated by administration of drinking water containing 40% sucrose to male Wistar rats for 10 weeks. **Table 1** shows a significant difference in the body weight change for rats with (MS group) and without (C group) sucrose ingestion. At 1 week, a moderate increase in body weight was observed for the MS group, but at 5 and 10 weeks, the MS group body weights were significantly higher ($P < 0.05$) than those of the C group. **Table 2** shows the differences in liquid consumption, as well as food and caloric intake, between the two groups ($P < 0.05$) at 1, 5 and 10 weeks of sugar ingestion.

TABLE 1: BODY WEIGHTS (g) OF SUCROSE-FED AND CONTROL RATS AT 1, 5 AND 10 WEEKS

Weeks	Control Group(n=5)	MS Group(n=15)	Increase
1	81 \pm 11 ^a	120 \pm 10 ^b	39 \pm 1
5	170 \pm 11 ^a	218 \pm 13 ^b	48 \pm 2
10	175 \pm 13 ^a	224 \pm 33 ^b	49 \pm 3

^{ab} $P < 0.05$ indicates difference compared with the control group

TABLE 2: LIQUID CONSUMPTION AND FOOD AND CALORIC INTAKE IN SUCROSE-FED (MS GROUP) AND CONTROL (C GROUP) RATS

Parameter	Control Group (n=5)			MS Group (n=5)		
	1	5	10	1	5	10
Liquid consumption	38.48 \pm 6.21 ^a	25.36 \pm 6.18 ^a	29.22 \pm 7.01 ^a	28.13 \pm 4.07 ^a	28.10 \pm 1.92 ^a	28.99 \pm 3.20 ^a
Liquid consumption equivalent (kcal)	----	----	----	45.00 \pm 6.51	44.96 \pm 3.07	46.38 \pm 5.12
Food consumption	30.79 \pm 2.76 ^a	21.83 \pm 1.96 ^a	19.05 \pm 3.23 ^a	2.24 \pm 1.0 ^b	7.19 \pm 1.91 ^b	6.88 \pm 2.58 ^b
Food consumption equivalent (kcal)	117.00 \pm 10.48 ^a	82.95 \pm 7.44 ^a	72.38 \pm 12.27 ^a	46.51 \pm 3.80 ^b	27.20 \pm 7.25 ^b	26.14 \pm 9.80 ^b
Total calories	117.00 \pm 10.48 ^a	82.95 \pm 7.44 ^a	72.38 \pm 12.27 ^a	91.51 \pm 10.31 ^a	72.16 \pm 10.32 ^a	72.52 \pm 14.92 ^a

The parameters are expressed in ml/day/100 g bw¹; kcal/day/ 100 bw^{2,4,5} and g/day/ 100 bw³.

Bw = body weight. ^{ab} $P < 0.05$ indicates difference from week 1, 5 and 10, compared with the control group

Effects of *Morinda citrifolia* L. extracts: After the rat sucrose-induced metabolic syndrome model was established, the effects of dietary supplementation with *Morinda citrifolia* L. leaf extract were analyzed. **Table 3** shows statistically significant differences between the abdominal fat weights of

the Mc and MS groups (8.05 ± 1.43 vs. 15.03 ± 4.80 g; $P < 0.05$). The Mc-Suc and Mc groups showed significantly lower triacylglycerol concentrations (45% and 68%, respectively, $P < 0.05$) than the MS group. No differences were observed for the other parameters (**Table 4**).

TABLE 3: BODY AND ABDOMINAL FAT WEIGHTS OF RATS FED EXPERIMENTAL DIETS FOR 2 WEEKS

Parameter	Control Group (n=5)	MS Group (n=5)	Mc-Suc Group (n=5)	Mc Group (n=5)
Body weight (g)	246 ± 16 ^a	226 ± 14 ^a	205 ± 48 ^a	206 ± 17 ^a
Abdominal fat weight (g)	3.83 ± 1.92 ^{ab}	15.03 ± 4.80 ^a	16.20 ± 5.95 ^a	8.05 ± 1.43 ^b
Pericardial fat weight (g)	----	----	0.20 ± 0.01	0.60 ± 0.01
Index of adiposity	1.55	6.65	7.90	3.90

Index of adiposity: (Abdominal fat weight / body weight) x 100

^{ab} $P < 0.05$ indicates difference compared with the control group

TABLE 4: SERUM PARAMETERS IN RATS FED EXPERIMENTAL DIETS PLUS MORINDA CITRIFOLIA EXTRACTS FOR 2 WEEKS

Parameter	Control Group (n=5)	MS Group (n=5)	Mc-Suc Group (n=5)	Mc-Group (n=5)
Glucose (mg/dl)	122.33±24.00 ^b	170.00±37.78 ^{ab}	190.67±15.18 ^a	107.33±24.00 ^b
Cholesterol (mg/dl)	189.33±38.07 ^a	145.33±15.89 ^a	137.33±46.61 ^a	146.33±47.12 ^a
Triacylglycerols (mg/dl)	105.06±15.75 ^b	255.55±38.33 ^a	140.88±21.13 ^b	83.55±12.53 ^b
HDL (mg/dl)	76.33±7.51 ^a	63.67±9.29 ^a	55.67±19.73 ^a	62.00±25.51 ^a
Uric acid (mg/dl)	2.63±1.35 ^a	3.03±0.49 ^a	2.63±0.04 ^a	2.06±0.028 ^a
Albumin (g/dl)	5.36±0.05 ^a	5.80±0.26 ^a	5.20±0.17 ^a	5.00±1.01 ^a
Globulin (mg/dl)	2.76±0.25 ^a	2.76±0.20 ^a	2.43±0.40 ^a	2.40±0.81 ^a
Creatinine (mg/dl)	0.68±0.04 ^a	0.58±0.03 ^a	0.61±0.01 ^a	0.69±0.12 ^a
Urea (mg/dl)	37.66±2.30 ^{ab}	27.33±8.62 ^b	20.66±1.52 ^b	48.66±12.58 ^a
PTOT (g/dl)	8.13±0.31 ^a	8.56±0.45 ^a	7.63±0.35 ^a	7.40±1.83 ^a

^{ab} $P < 0.05$ indicates difference compared with the control group (C group)

As shown in **Fig. 1**, the adiponectin serum concentration was higher for the C, Mc-Suc and Mc groups than for the MS group. Additionally, abdominal fat weights were negatively correlated with serum adiponectin for the Mc-Suc ($r = -0.85$), Mc ($r = -0.62$), MS ($r = -0.88$) and control groups ($r = -0.99$) ($P < 0.05$). Finally, **Fig. 2** shows the

relative distribution of adipocyte areas in samples from abdominal adipose tissues. The SM group displayed a significant increase in the percentage of fat cells, with areas between 1001 and 1501 μm^2 compared with the group control, and significant differences compared with the Mc and Mc-Suc groups ($p < 0.001$).

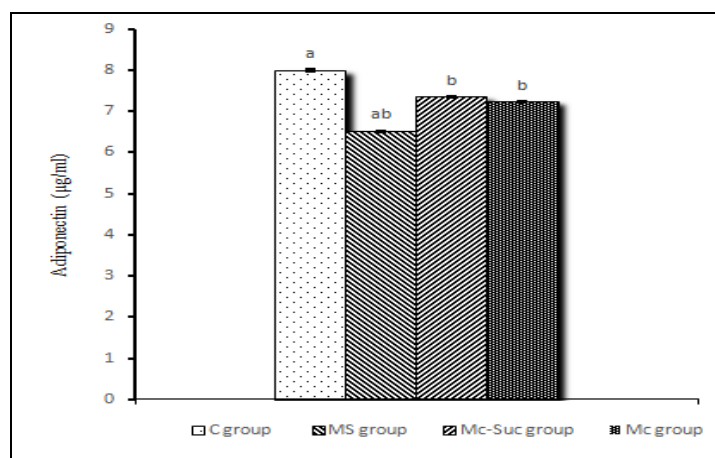


FIG. 1: SERUM ADIPONECTIN IN RATS FED EXPERIMENTAL DIETS FOR 2 WEEKS

^{ab} $P < 0.05$ indicates difference compared with the control group (C group)

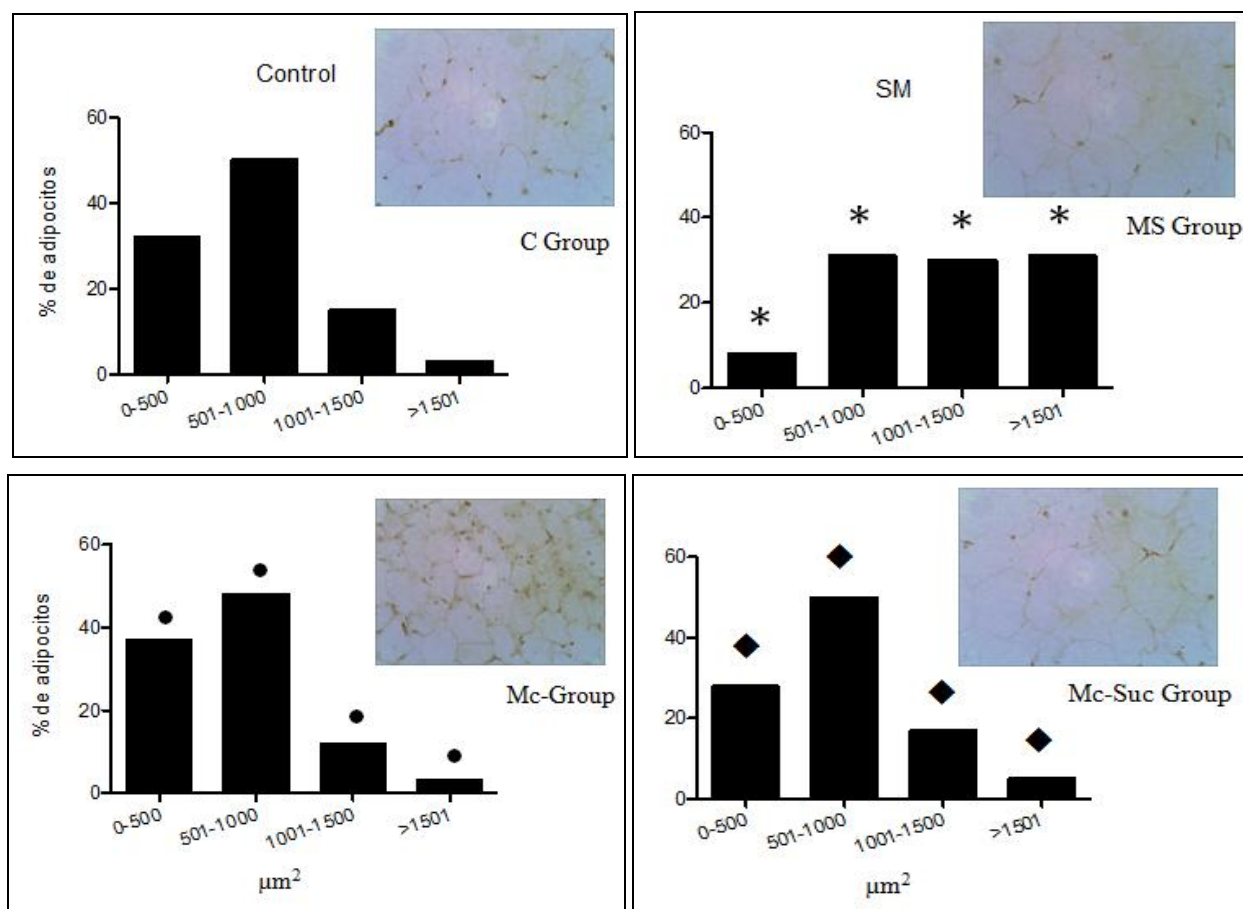


FIG. 2: HISTOGRAM OF THE FREQUENCY OF THE RELATIVE DISTRIBUTION OF ADIPOCYTE SIZES. DIFFERENCES BETWEEN C GROUP vs. MS, *MS vs. *Mc and *Mc-Suc. Fisher P < 0.001.

DISCUSSION: Our research evaluated the effects of an aqueous extract of dried *Morinda citrifolia* leaves on obesity, dyslipidemia, and adiponectinemia in a Wistar rat animal model of metabolic syndrome. This model was induced by high sucrose intake *via* drinking water, leading to the development of abdominal obesity, hypertriglyceridemia and hypoadiponectinemia.

These results are consistent with those reported by Aguilera *et al.*, who used similar concentrations of sucrose in drinking water and observed increased abdominal fat, dyslipidemia and high levels of tumor necrosis factor alpha (TNF) ³¹.

With regards to the body weights of rats receiving *M. citrifolia*, **Table 3** shows that body weight did not differ among the groups (p < 0.05). Reports in the literature using other animal models, *e.g.*, hamsters, reported that for a high cholesterol diet, there were no changes in body weight upon administration of noni juice ^{32, 33}. In contrast, this work shows that rats consuming different dietary energy sources such as sucrose or proteins can have

the same body weight but different abdominal fat contents.

The rats that received the aqueous extract of dried of *M. citrifolia* leaves and consumed sucrose (Mc-Suc group) showed equal abdominal fat contents compared to the metabolic syndrome group (MS group); moreover, the group that received the extract without the co-administration of sucrose displayed a significant reduction in abdominal fat compared with the metabolic syndrome group (MS group, p < 0.05). These data indicate that *M. citrifolia* extract inhibits the accumulation of fat; however, the suspension of sucrose intake could also contribute to this result.

It is important to relate these results to the cellular dynamics of adipose tissue prior to the changes in the total weight of body fat, and these results will be discussed later. With regards to serum triglyceride levels, we found that the rats given the *M. citrifolia* extract without sucrose intake displayed a significant decrease compared with the metabolic syndrome group (MS group, P < 0.05).

Similarly, the group of rats given extract and sucrose (Mc-Suc group) showed lower triglyceride levels compared with the metabolic syndrome group (MS group), which showed a significant elevation of these lipids. Similarly, the rats given extract and sucrose (Mc-Suc group) showed lower triglycerides levels compared with the MS group ($P < 0.05$).

Studies have evaluated the effects of *M. citrifolia* on lowering triglycerides in humans as well as in mouse and hamster animal models and observed a significant lowering of triglycerides. Wang *et al.*, 2012³⁴ reported that noni juice improved lipid profiles and other risk markers in smokers, particularly cholesterol, triglycerides and high sensitivity C-reactive protein. Mandukhail *et al.*, 2010 studied the antidyslipidemic effect of *Morinda citrifolia* (Noni) fruit leaf and root extracts, finding a reduction in triglyceride levels that could be attributed to the plant antioxidant capacity. The active constituents responsible for the antioxidant and antidyslipidemic activities include iridoids³⁵; several polyphenols belonging to the coumarin³⁶ and scopoletin³⁷.

Other proposed antidyslipidemic mechanisms for *Morinda citrifolia* or its active constituents are the inhibition of HGM Co-A, as this enzyme plays a key role in controlling lipid levels in plasma and other tissues¹⁵ and activation of AMPK³⁸, as its phosphorylation leads to increased glucose uptake and lipid oxidation in muscle cells^{39,40}.

Finally, concerning the relative distribution of fat cell areas, there was clearly an increase in the percentage of fat cells with areas greater than 1000 μm^2 caused by the sucrose intake, while the groups receiving the *M. citrifolia* extract with and without sucrose intake were similar to the control group.

The above result leads us to hypothesize that the *M. citrifolia* extract participates in the cellular dynamics of adipose tissue and therefore the amount of abdominal fat in rodents, tending to reverse metabolic syndrome components.

These results are similar to those of other studies that associated adipocyte size and distribution with several diseases. Size distribution differences were linked with a diabetic phenotype⁴¹, hepatic

steatosis⁴² and inflammation. Several other studies showed that individual adipocyte sizes may impact behaviors such as adipokine secretion²⁴. Previous reports have dealt with the issue of size dynamics, examining how adipocyte population size shifts under various dietary conditions and among different rat strains^{43,44}.

The above result is similar to the results for adiponectinemia, which was increased in the group receiving *M. citrifolia*; these adiponectin levels may contribute to decreased adipocyte inflammation under conditions of stress caused by overnutrition⁴⁵, in this case, sucrose intake. Additionally, this study found a negative correlation between abdominal fat weight and adiponectin concentration that could contribute to metabolic syndrome reversal.

CONCLUSION: The ingestion of the *Morinda citrifolia* L. (Noni) dried leaf aqueous extract decreases abdominal fat and serum triglycerides in rats with metabolic syndrome, and this effect is associated with increased adiponectin levels and changes to adipose tissue cell dynamics.

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REFERENCES:

1. Ross IA: Medicinal plants of the world. Chemical constituents, traditional and modern medicinal uses. Humana Press, Totowa 2001.
2. Guiducci L, Denoth F, Liistro T, Iozzo P: Obesity: the epidemic of the new millennium between genetics and environment. *Recent Prog Med*, 2013; 104(9):467-75.
3. Couto E, Boffetta P, Lagiou P *et al.*: Mediterranean dietary pattern and cancer risk in the EPIC cohort. *British Journal of Cancer*, 2011; 9:1493-1499.
4. International Obesity Taskforce (2010). The Global Epidemic. IASO/ IOTB. Available at: <http://www.iaso.org/iotf/obesity/obesitytheglobalepidemic/> [accessed July, 2014].
5. Garaulet M, Hernandez-Morante JJ, Tebar FJ, Zamora S: Relation between degree of obesity and site-specific adipose tissue fatty acid composition in a Mediterranean population. *Nutrition*, 2011; 27(2):170-6.
6. Melanson KJ, Summers A, Nguyen V, Brosnahan J, Lowndes J, Angelopoulos TJ, Rippe JM: Body

- composition, dietary composition, and components of metabolic syndrome in overweight and obese adults after a 12-week trial on dietary treatments focused on portion control, energy density, or glycemic index. *Nutr J*, 2012; 27; 11:57.
7. Xia MF, Chen Y, Lin HD, Ma H, Li XM, Aleteng Q, Li Q, Wang D, Hu Y, Pan BS, Li XJ, Li XY, Gao X: A indicator of visceral adipose dysfunction to evaluate metabolic health in adult Chinese. *Sci Rep*, 2016; 1; 6:38214.
 8. Yang L, Samarasinghe YP, Kane P, Amiel SA, Aylwin SJ: Visceral adiposity is closely correlated with neck circumference and represents a significant indicator of insulin resistance in WHO grade III obesity. *Clin Endocrinol (Oxf)*, 2010; 73(2):197-200.
 9. Nakamura K, Fuster JJ, Walsh K: Adipokines: a link between obesity and cardiovascular disease. *J Cardiol*, 2014; 63(4):250-9.
 10. Zhang Y, Zitsman JL, Hou J, Fennoy I, Guo K, Feinberg J, Leibel RL: Fat cell size and adipokine expression in relation to gender, depot, and metabolic risk factors in morbidly obese adolescents. *Obesity (Silver Spring)*, 2014; 22(3):691-7.
 11. Tsao TS, Tomas E, Murrey HE, Hug C, Lee DH, Ruderman NB *et al.*: Role of disulfide bonds in Acrp30/adiponectin structure and signaling specificity. Different oligomers activate different signal transduction pathways. *J Biol Chem*, 2003; 278:50810–50817.
 12. Mai S, Walker GE, Brunani A, Guzzaloni G, Grossi G, Oldani A, Aimaretti G, Scacchi M, Marzullo P: Inherent insulin sensitivity is a major determinant of multimeric adiponectin responsiveness to short-term weight loss in extreme obesity. *Sci Rep*, 2014; 24; 4:5803.
 13. Goto M, Goto A, Morita A, Deura K, Sasaki S, Aiba N, Shimbo T, Terauchi Y, Miyachi M, Noda M, Watanabe S: Low-molecular-weight adiponectin and high-molecular-weight adiponectin levels in relation to diabetes. *Obesity (Silver Spring)*, 2014; 22(2):401-7.
 14. Eglit T, Lember M, Ringmets I, Rajasalu T: Gender differences in serum high-molecular-weight adiponectin levels in metabolic syndrome. *Eur J Endocrinol*, 2013; 15; 168(3):385-91.
 15. Maeda N, Shimomura I, Kishida K, Nishizawa H, Matsuda M, Nagaretani H, *et al.*: Diet-induced insulin resistance in mice lacking adiponectin/ACRP30. *Nat Med*, 2002; 8:731–737.
 16. Shibata R, Sato K, Pimentel DR, Takemura Y, Kihara S, Ohashi K *et al.*: Adiponectin protects against myocardial ischemia-reperfusion injury through AMPK- and COX-2-dependent mechanisms. *Nat Med*, 2005; 11:1096–1103.
 17. Nawrocki AR, Rajala MW, Tomas E, Pajvani UB, Saha AK, Trumbauer ME, *et al.*: Mice lacking adiponectin show decreased hepatic insulin sensitivity and reduced responsiveness to peroxisome proliferator-activated receptor gamma agonists. *J Biol Chem*, 2006; 281: 2654–2660.
 18. Arita Y, Kihara S, Ouchi N, Takahashi M, Maeda K, Miyagawa J, Hotta K, Shimomura I, Nakamura T, Miyaoka K, Kuriyama H, Nishida M, Yamashita S, Okubo K, Matsubara K, Muraguchi M, Ohmoto Y, Funahashi T, Matsuzawa Y: Paradoxical decrease of an adipose-specific protein, adiponectin, in obesity. 1999. *Biochem Biophys Res Commun*, 2012; 31; 425(3):560-4.
 19. De Rosa A, Monaco ML, Capasso M, Forestieri P, Pilone V, Nardelli C, Buono P, Daniele A: Adiponectin oligomers as potential indicators of adipose tissue improvement in obese subjects. *Eur J Endocrinol*, 2013; 1; 169(1):37-43.
 20. Baden MY, Yamada Y, Takahi Y, Obata Y, Saisho K, Tamba S, Yamamoto K, Umeda M, Furubayashi A, Tsukamoto Y, Sakaguchi K, Matsuzawa Y: Association of adiponectin with blood pressure in healthy people. *Clin Endocrinol (Oxf)*, 2013; 78(2):226-31.
 21. Xia K, Guo L, Zhao Z, Md Sayed AS, Li F, Yang T: Plasma level of adiponectin in coronary heart disease patients combined with abnormal glucose metabolism, 2012; 37(2):179-84.
 22. Durrani S, Shah J, Khan MA, Jan MR: Relationship of adiponectin level with lipid profile in type-2 diabetic men with coronary heart disease. *J Ayub Med Coll Abbottabad*, 2015; 27(1):32-5.
 23. Lee S, Zhang H, Chen J, Dellsperger KC, Hill MA, Zhang C: Adiponectin abates diabetes-induced endothelial dysfunction by suppressing oxidative stress, adhesion molecules, and inflammation in type 2 diabetic mice. *Am J Physiol Heart Circ Physiol*, 2012; 303(1):H106-15
 24. Lee S, Zhang H, Chen J, Dellsperger KC, Hill MA, Zhang C: Adiponectin abates diabetes-induced endothelial dysfunction by suppressing oxidative stress, adhesion molecules, and inflammation in type 2 diabetic mice. *Am J Physiol Heart Circ Physiol*, 2012; 303:H106– 115.
 25. Du Y, Li R, Lau WB, Zhao J, Lopez B, Christopher TA, Ma XL, Wang Y: Adiponectin at Physiologically Relevant Concentrations Enhances the Vasorelaxative Effect of Acetylcholine via Cav-1/AdipoR-1 Signaling. *PLoS One*, 2016; 29; 11(3):e0152247.
 26. Brambilla P, Antolini L, Street ME, Giussani M, Galbiati S, Valsecchi MG, Stella A, Zuccotti GV, Bernasconi S, Genovesi S: Adiponectin and hypertension in normal-weight and obese children. *Am J Hypertens*, 2013; 26(2):257-64.
 27. Lindberg S, Mogelvang R, Pedersen SH, Bjerre M, Frystyk J, Flyvbjerg A, Galatius S, Jensen JS: Relation of serum adiponectin levels to number of traditional atherosclerotic risk factors and all-cause mortality and major adverse cardiovascular events (from the Copenhagen City Heart Study). *Am J Cardiol*, 2013; 15; 111(8):1139-45.
 28. Hui E, Xu A, Chow WS, Lee PC, Fong CH, Cheung SC, Tse HF, Chau MT, Cheung BM, Lam KS: Hypoadiponectinemia as an independent predictor for the progression of carotid atherosclerosis: a 5-year prospective study. *Metab Syndr Relat Disord*. 2014; 12(10):517-22.
 29. Barham D, Trinder P: An improved color reagent for the determination of blood glucose by the oxidase system. *Analyst*, 1972; 97:142-5.
 30. Assman G: Current diagnosis of hyperlipidemias. *Internist (Berl)*, 1979; 20:559-64.
 31. Alexander-Aguilera A, Berruezo S, Hernández-Díaz G, Angulo O, Oliart-Ros R: Dietary n-3 polyunsaturated fatty acids modify fatty acid composition in hepatic and abdominal adipose tissue of sucrose-induced obese rats. *J Physiol Biochem*, 2011; 67(4):595-604.
 32. Lin YL, Chang YY, Yang DJ, Tzang BS, Chen YC: Beneficial effects of noni (*Morinda citrifolia* L.) juice on livers of high-fat dietary hamsters. *Food Chem*, 2013; 31-8.
 33. Lin YL, Chou CH, Yang DJ, Chen JW, Tzang BS, Chen YC: Hypolipidemic and antioxidative effects of noni (*Morinda citrifolia* L.) juice on high-fat/cholesterol-dietary hamsters. *Plant Foods Hum Nutr*, 2012; 3:294-302.
 34. Wang MY, Peng L, Weidenbacher-Hoper V, Deng S, Anderson G, West BJ: Noni juice improves serum lipid profiles and other risk markers in cigarette smokers. *Scientific World Journal*, 2012.

35. Viljoen A, Mncwani N, Vermaak I: Anti-inflammatory iridoids of botanical origin. *Curr Med Chem.* 2012; 19(14): 2104-27.
36. Gupta RK1, Patel AK: Do the health claims made for *Morinda citrifolia* (Noni) harmonize with current scientific knowledge and evaluation of its biological effects. *Asian Pac J Cancer Prev.* 2013; 14(8): 4495-9.
37. Shaw CY, Chen CH, Hsu CC, Chen CC, Tsai YC: Antioxidant properties of scopoletin isolated from *Sinomonium acutum*. *Phytother Res.* 2003; 7:823-5.
38. Lee SY, Park SL, Hwang JT, Yi SH, Nam YD, Lim SI: Antidiabetic Effect of *Morinda citrifolia* (Noni) Fermented by Cheonggukjang in KK-A(y) Diabetic Mice. *Evid Based Complement Alternat Med.* 2012.
39. Zang M, Zuccollo A, Hou X, et al.: AMP-activated protein kinase is required for the lipid-lowering effect of metformin in insulin-resistant human HepG2 cells. *Journal of Biological Chemistry.* 2004; 279(18): 4647898-47905.
40. Cuthbertson DJ, Babraj JA, Mustard KJW, et al.: 5-Aminoimidazole – 4 - carboxamide 1-β-D-ribofuranoside acutely stimulates skeletal muscle 2-deoxyglucose uptake in healthy men. *Diabetes.* 2007; 56(12): 2078-2084.
41. Fang L, Guo F, Zhou L, Stahl R, Grams J: The cell size and distribution of adipocytes from subcutaneous and visceral fat is associated with type 2 diabetes mellitus in humans. *Adipocyte.* 2015; 4(4):273-9.
42. Kursawe R., Eszinger M., Narayan D., Liu T., Bazuine M., Cali AMG et al.: Cellularity and adipogenic profile of the abdominal subcutaneous adipose tissue from obese adolescents: association with insulin resistance and hepatic steatosis. *Diabetes.* 2010; 59(10): 2288-2296.
43. Jo J, Gavrilova O, Pack S, Jou W, Mullen S, Summer AE, et al.: Hypertrophy and/or hyperplasia: dynamics of adipose tissue growth. *Plos Comput Biol.* 2009; 5(10): e1000324.
44. Jo J, Guo J, Liu T, Mullen S, Hall KD, Cushman SW; et al.: Hypertrophy-Driven adipocyte death overwhelms recruitment under prolonged weight gain. *Biophys. J.* 2010; 98(11):3535-3544.
45. Lee S, Park Y, Dellsperger KC, Zhang C: Exercise training improves endothelial function via adiponectin-dependent and independent pathways in type 2 diabetic mice. *Am J Physiol Heart Circ Physiol.* 2011; 301:H306-314.

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