

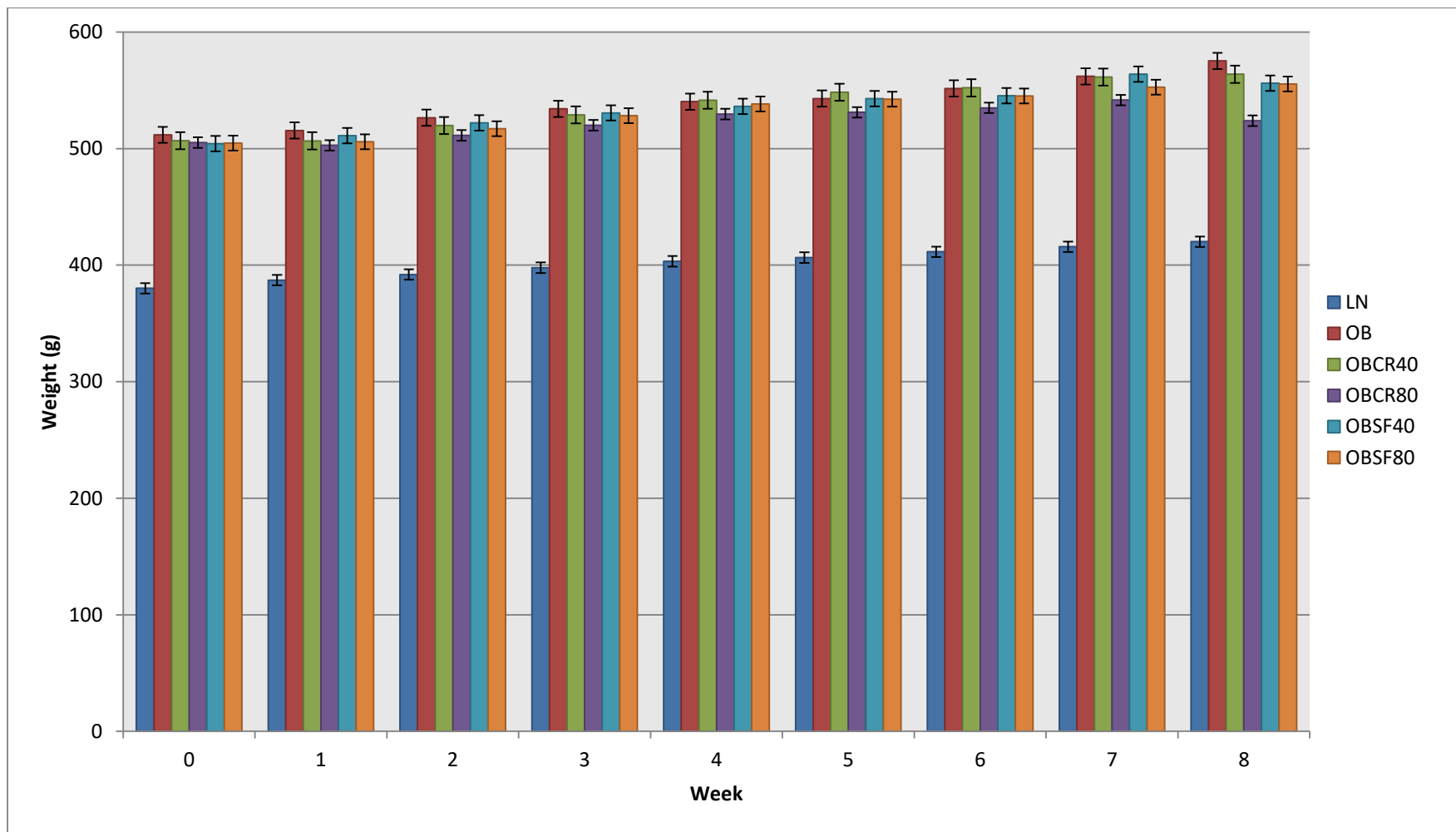
Supplementary Table S1: Composition of the diets fed to the animals [8]

Ingredients	Normal diet (g/kg diet)	High fat diet (g/kg diet)
Casein	200	200
DL-methionine	3	3
Corn starch	650	150
Sucrose	-	150
Cellulose	50	50
Corn oil	50	-
Beef tallow	-	400
Mineral mix	35	35
Vitamin mix	10	10
Choline bitartrate	2	2

Supplementary Table S2: Effect of saffron extract and crocin on the changes of food consumption at initial and the end of 8-week treatment [8]

Group	Week 0	Week 8	Change	p value
LN	132.40 ± 1.20	132.33 ± 1.20	-0.1	0.85
OB	115.60 ± 3.80	120.00 ± 1.60	4.4	0.85
OBCR40	106.80 ± 3.20	104.70 ± 0.20	-2.1	0.23
OBCR80	114.20 ± 2.30	103.60 ± 1.50	-10.6	0.01**
OBSF40	111.30 ± 6.60	103.50 ± 2.40	-7.8	0.12
OBSF80	114.50 ± 5.60	100.5 ± 0.50	-14	0.01**

Values are expressed as the mean ± SE (standard error of mean) of six rats; * p < 0.05, ** p < 0.01 (significance level)

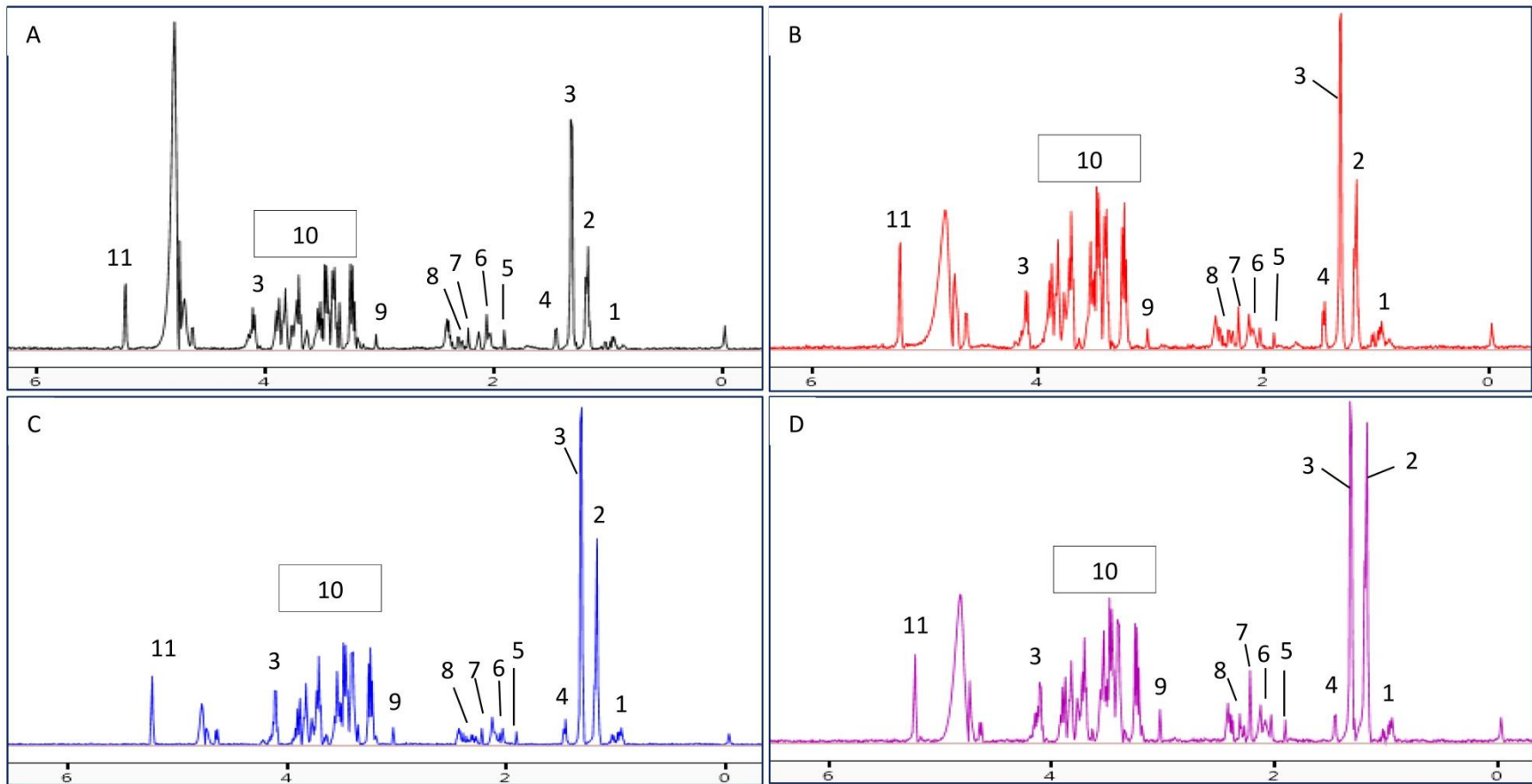


Supplementary Figure S1: Effect of saffron extract and crocin on body weight during 8 weeks of treatment [8]

Supplementary Table S3: Effect of saffron extract and crocin on biochemical parameters [8]

Biochemical Parameters					
	TG (mM/L)	TC (mM/L)	LDL (mM/L)	HDL (mM/L)	FBG (mM/L)
LN	2.23 ± 0.29	1.13 ±0.24	0.21 ±0.03	0.58 ±0.15	5.42 ± 0.67
OB	2.64 ±0.15	1.44 ±0.13	0.28 ±0.12	0.41 ±0.05	6.91 ± 0.61
OBCR40	2.08 ±0.41	1.35 ±0.18	0.24 ± 0.07	0.52 ± 0.06	5.80 ± 0.14
OBCR80	1.86 ±0.29*	1.07 ±0.08*	0.24 ± 0.06	0.39 ± 0.08	5.66 ± 0.62*
OBSF40	2.49 ±0.38	1.32 ±0.27	0.20 ± 0.03	0.49 ± 0.11	6.10 ± 0.82
OBSF80	2.28 ±0.26	1.03 ±0.24*	0.24 ± 0.08	0.33 ± 0.09	5.26 ± 0.38**

Triglycerides (TG), Total cholesterol (TC), Low density lipoprotein (LDL), High density lipoprotein (HDL), Fasting blood glucose (FBG), Lean group (LN), Obese group (OB), Obese + Crocin 40 mg/kg group (OBCR40), Obese + Crocin 80 mg/kg group (OBCR80), Obese + Saffron extract 40 mg/kg group (OBSF40) Obese + Saffron extract 80 mg/kg group (OBSF80) Value are expressed as mean ± SE of six rats * p < 0.05 vs negative control (OB), ** p < 0.01 vs negative control (OB)

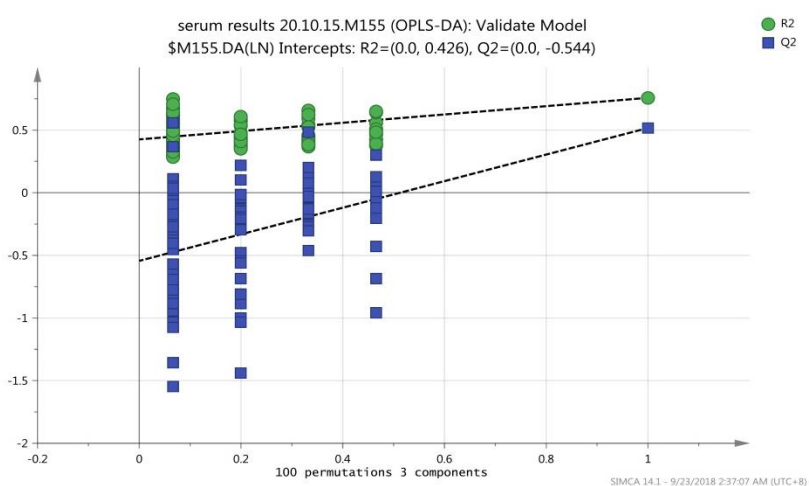


Supplementary Figure S2: Typical 500 MHz ^1H -NMR CPMG spectra of serum collected from a Lean group (A), Obese group (B), Obese + Crocin 80mg/kg group (C) and Obese + Saffron extract 80mg/kg group (D). 1. Valine 2. 3-hydroxybutyrate 3. Lactate 4. Alanine 5. Acetate 6. N-acetylglycoprotein 7. Methionine 8. Pyruvate 9. Creatinine 10. Glucose, 11. α -Glucose

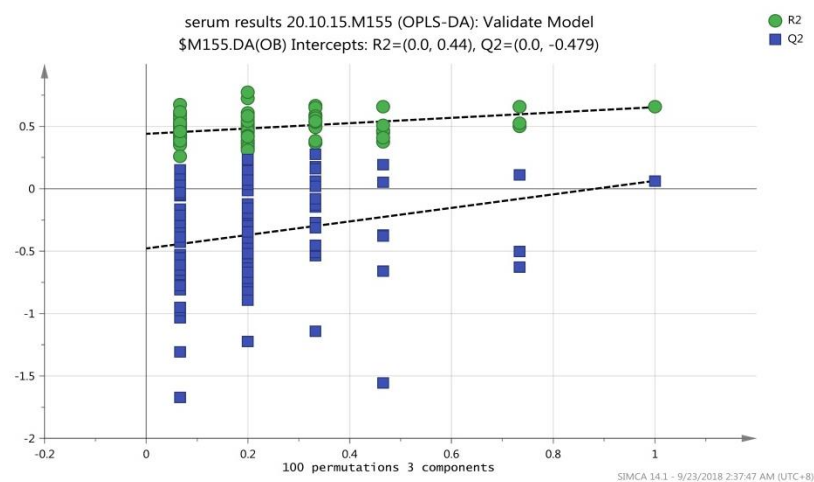
Supplementary Table S4: ¹H-NMR assignments of metabolites in rat serum

Metabolites	Chemical shifts (ppm)
Lactate	1.34 (d)
	4.11 (q)
3-Hydroxybutyrate	1.18 (d)
	2.31 (d)
	2.42 (dd)
	4.14 (m)
Creatinine	3.06 (s)
	4.06 (s)
Alanine	1.48 (d)
	3.78 (q)
Acetate	1.93 (s)
Methionine	2.16 (m)
	2.64 (t)
	2.13 (s)
<i>N</i> -acetylglycoprotein	2.03 (s)
Pyruvate	2.38 (s)
α D-Glucose	5.22 (d)
Valine	0.98 (d)
	1.04 (d)

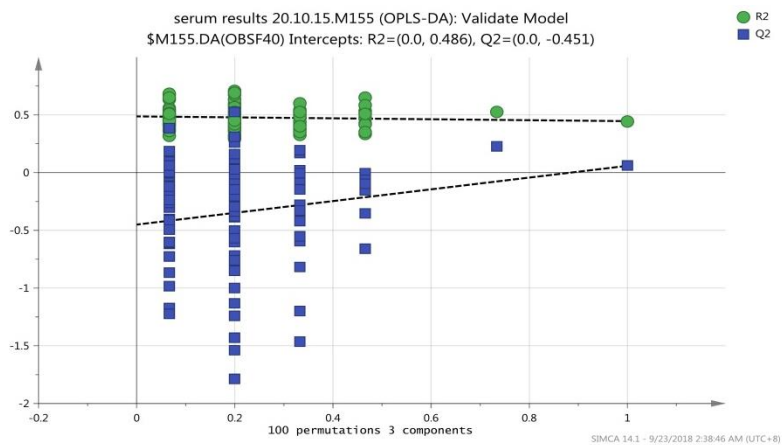
s: single; d: doublet; dd: doublet of doublets; t: triplet; m: multiplet



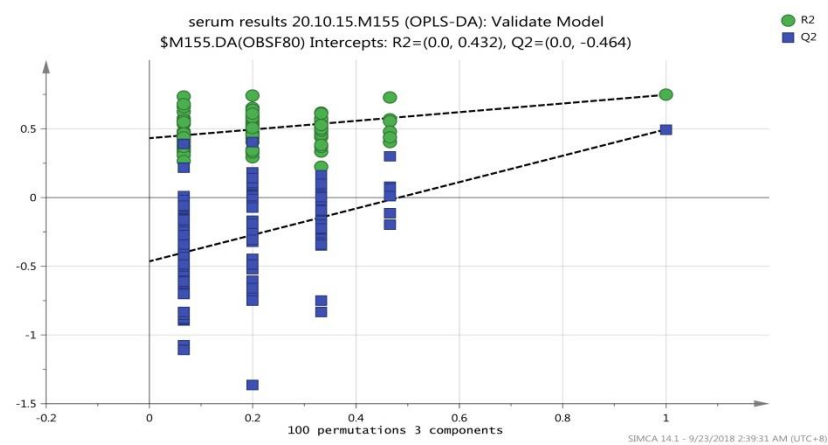
Supplementary Figure S3: Permutation Test (100 cycle) for PLS-DA model in lean rats (LN) after the 22nd week.



Supplementary Figure S4: Permutation Test (100 cycle) for PLS-DA model in obese rats (OB) after the 22nd week.



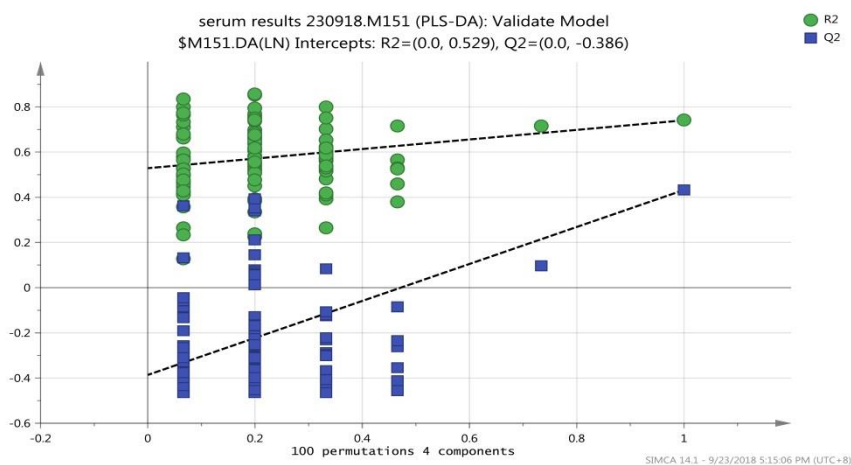
Supplementary Figure S5: Permutation Test (100 cycle) for PLS-DA model in obese rats treated with saffron extract (40 mg/kg) (OBSF40) after the 22nd week.



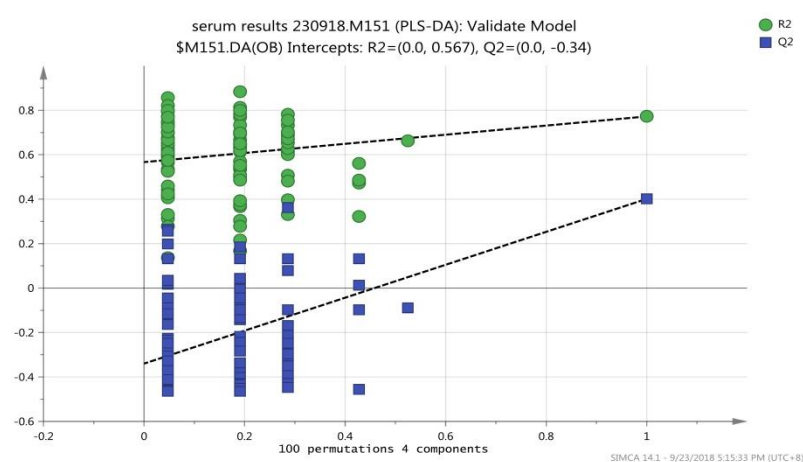
Supplementary Figure S6: Permutation Test (100 cycle) for PLS-DA model in obese rats treated with saffron extract (80 mg/kg) (OBSF80) after the 22nd week.

Supplementary Table S5: Misclassification table for PLS-DA model discriminating the lean group (LN), obese group (OB), obese rats treated with saffron extract (40 mg/kg) (OBSF40) and obese rats treated with saffron extract (80 mg/kg) (OBSF80) after the 22nd week.

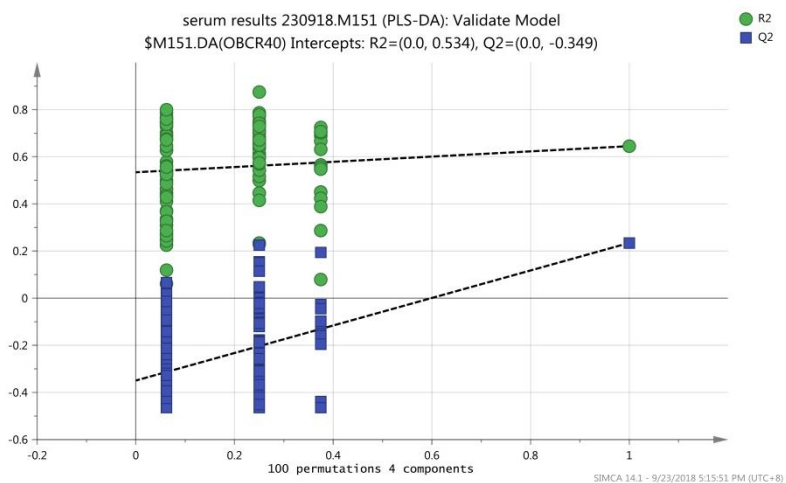
	Members	Correct	LN	OB	OBSF40	OBSF80	No class (YPred ≤ 0)
LN	5	100%	5	0	0	0	0
OB	5	100%	0	5	0	0	0
OBSF40	5	60%	0	1	3	1	0
OBSF80	5	100%	0	0	0	5	0
No class	22		12	5	4	1	0
Total	42	90%	17	11	7	7	0
Fisher's prob.	7.4e-008						



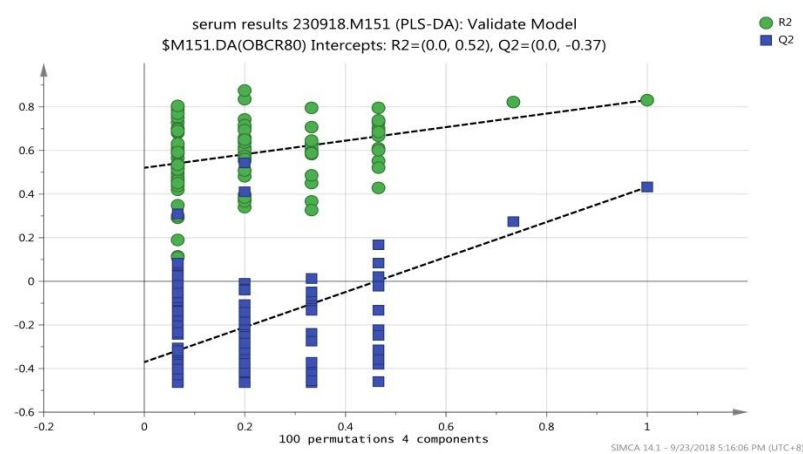
Supplementary Figure S7: Permutation Test (100 cycle) for PLS-DA model in lean rats (LN) after the 22nd week.



Supplementary Figure S8: Permutation Test (100 cycle) for PLS-DA model in obese rats (OB) after the 22nd week.



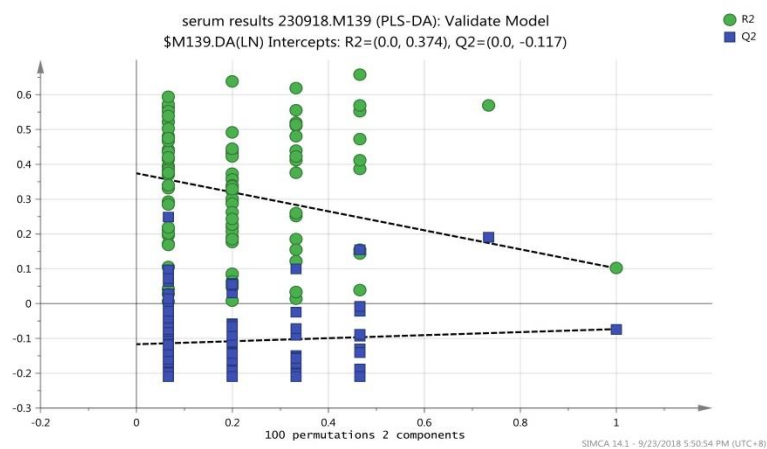
Supplementary Figure S9: Permutation Test (100 cycle) for PLS-DA model in obese rats treated with crocin (40 mg/kg) (OBCR40) after the 22nd week.



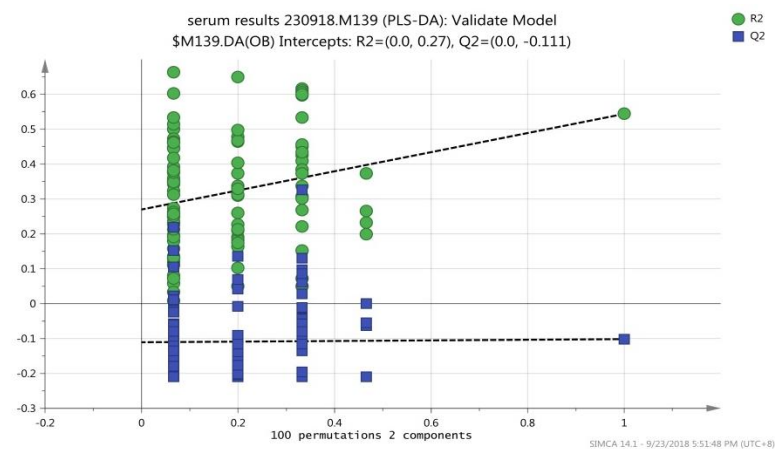
Supplementary Figure S10: Permutation Test (100 cycle) for PLS-DA model in obese rats treated with crocin (80 mg/kg) (OBCR80) after the 22nd week.

Supplementary Table S6: Misclassification table for PLS-DA model discriminating the lean group (LN), obese group (OB), obese rats treated with crocin (40 mg/kg) (OBCR40) and obese rats treated with crocin (80 mg/kg) (OBCR80) after the 22nd week.

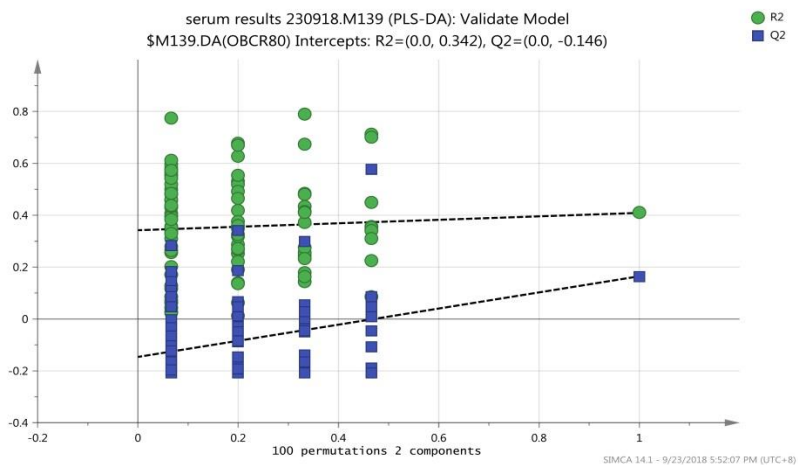
	Members	Correct	LN	OB	OBCR40	OBCR80	No class (YPred <= 0)
LN	5	80%	4	1	0	0	0
OB	6	100%	0	6	0	0	0
OBCR40	4	100%	0	0	4	0	0
OBCR80	5	100%	0	0	0	5	0
No class	22		5	12	2	3	0
Total	42	95%	9	19	6	8	0
Fisher's prob.	2.9e-009						



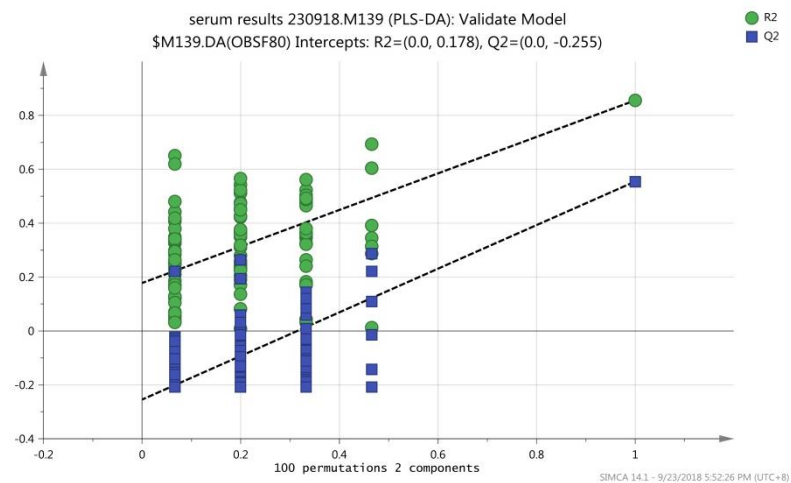
Supplementary Figure S11: Permutation Test (100 cycle) for PLS-DA model in lean rats (LN) after the 22nd week.



Supplementary Figure S12: Permutation Test (100 cycle) for PLS-DA model in obese rats (OB) after the 22nd week.



Supplementary Figure S13: Permutation Test (100 cycle) for PLS-DA model in obese rats treated with crocin (80 mg/kg) (OBCR80) after the 22nd week.



Supplementary Figure S14: Permutation Test (100 cycle) for PLS-DA model in obese rats treated with saffron extract (80 mg/kg) (OBSF80) after the 22nd week

Supplementary Table S7: Misclassification table for PLS-DA model discriminating the lean group (LN), obese group (OB), obese rats treated with saffron extract (80 mg/kg) (OBSF80) and obese rats treated with crocin (80 mg/kg) (OBCR80) after the 22nd week.

	Members	Correct	LN	OB	OBCR80	OBSF80	No class (YPred ≤ 0)
LN	5	0%	0	1	3	1	0
OB	5	100%	0	5	0	0	0
OBCR80	5	80%	0	1	4	0	0
OBSF80	5	100%	0	0	0	5	0
No class	22		0	10	8	4	0
Total	42	70%	0	17	15	10	0
Fisher's prob.	7.8e-005						