Cardiometabolic Health Benefits of Rice Bran Oil

Dr. Sankar Devarajan, MD (Bio), Ph.D, FAHA, FADA

Associate Professor

Nutrition and Dietetics Program

Department of Human Sciences

University of Arkansas at Pine Bluff, USA

Former Regional Head, WHO

Bioactive Components of Rice bran Oil

- Rice bran oil (RBO) presents several advantages over other cooking oils due to the presence of many bioactive antioxidant components which are responsible for its oxidative stability and health benefits.
- The crude RBO encompasses a rich unsaponifiable fraction (~5%), which consists of sterols (43%), triterpene alcohols (28%), 4-methyl-sterols (10%) and other less polar components.
- The phytosterols include β-sitosterol, campesterol, stigmasterol, squalene and γ-oryzanol. γ-Oryzanol is often recognized as the most active component of RBO.
- RBO is also a rich source of vitamin E (both tocopherols and tocotrienols) as well as contains variable quantities of tocotrienols, especially β- and γ-tocotrienols.
- γ-Oryzanol has similar functions as vitamin E.

Significance of RBO in Human Health

- RBO is gaining popularity because of its better cooking characteristics, prolonged shelf life and well-balanced fatty acid composition as well as the presence of bioactive substances.
- RBO is commonly used in many Asian cultures, where it is regarded as “premium edible oil”. In Japan, RBO is commonly known as a “heart oil”, whereas in Western countries, it has attained the status of a “healthy food” (CAC 2003). It is also now becoming popular in the USA and other parts of the world because of its relatively low price and many health benefits.
- RBO has been shown to have the potential to lower cholesterol, blood pressure and blood glucose and can help to reduce inflammation and symptoms of metabolic syndrome as well.

- RBO has been shown to be effective in the prevention and management of cardiovascular disease (CVD) risk factors if consumed as part of a healthy diet. It may also help to boost the immune system and prevent diabetes, cardiovascular diseases, cancer and premature ageing.
- Studies have reported that RBO diet relieves the menopausal symptoms, increases the cognitive function and may lower the incidence of allergic reactions.

RBO-Perspectives in Cardiometabolic Diseases Management

Anti-hyperlipidaemic and Hypocholesterolaemic Effect of RBO

- Studies have shown that the intake of RBO reduced the plasma TC, TG and LDL-C and increased the HDL-C levels in rodents, rabbits, non-human primates and humans.
- RBO have been shown to have beneficial effects on lipid metabolism in terms of their antioxidant, hypolipidaemic and anti-atherogenic properties.
- The bioactive phytosterols, γ- oryzanol and tocotrienols in RBO are responsible for its anti-hyperlipidaemic properties. The phytosterols, in particular the ss-sitosterol and 4-desmethylsterols and not the 4,4′-dimethylsterols in RBO, have been shown to reduce the plasma TC and LDL-C levels.

- It has been studied that the supplementation of high-cholesterol diet with γ-oryzanol showed an increased bile flow and total bile acid excretion with simultaneous 20% decrease in cholesterol absorption which suggest that the bioactive γ-oryzanol and some other components in the unsaponifiable fraction of RBO such as tocotrienols and tocopherols can increase the faecal excretion of bile acids and neutral sterols.
- Supplementation of RBO with γ-oryzanol appeared to be strongly associated with alleviating the cardiovascular disease risk factors in animal models, especially when fed a high-fat diet.
- Use of physically refined RBO may be attributed to decreased cholesterol absorption and not to the hepatic cholesterol synthesis. It has been suggested that a reduction in fatty streak formation, the early signs of atherosclerosis with physically refined RBO, may be due to its non-triglyceride fraction.

- γ-Oryzanol rich RBO significantly reduced plasma lipid hydroperoxides and triglycerides in high-fat diet fed hamsters. These results indicated that γ-oryzanol might have potentiated the lowering of plasma LDL and VLDL levels and may also help to raise the HDL cholesterol.
- The cholesterol-lowering efficacy of RBO is much superior that is apparently judged based on its fatty acid composition.
- γ-Oryzanol is considered as the possible fundamental component of RBO due to its anti-atherosclerotic action. It inhibits the intestinal absorption of cholesterol, increases the bile flow and accelerates the excretion of cholesterol in the faeces.
- Data from the animal studies confirmed the anti-hyperlipidaemic properties of γ-oryzanol and its overall impact to lower the CVD risk.

RBO in Clinical Trials on Humans

- Earlier studies have reported the anti-hyperlipidaemic properties of RBO in healthy young Japanese women. This study showed that the daily use of 60 g of a blend of RBO and safflower oil (70:30) was more effective in lowering the plasma TC levels; even only after 7 days of treatment!
- Data from various studies in which RBO was given for 4-14 weeks period indicated that the RBO at a dose level up to 50 g/day was effective in reducing the TC, LDL-C, TG and apolipoprotein levels with a simultaneous increase in HDL-C.
- Ishihara and his colleagues evaluated the impact of γ-oryzanol supplementation on 40 women with postmenopausal syndrome. Treatment with 300 mg of γ-oryzanol/day for 4-8 weeks showed a significant decrease in plasma TC, LDL-C and TG levels with a simultaneous increase in HDL-C.

- It was observed that the patients who used RBO showed 16% and 25% decrease in plasma TC and 32% and 35% reduction in plasma TG after 15 and 30 days of treatment, respectively,
- Double-blind 12-wk long clinical trial on hypercholesterolaemic human subjects, who were given a supplement of tocotrienol-rich fraction that was obtained from specially processed RBO, together with a standard National Cholesterol Education Program (NCEP) Step-1 diet, indicated a significant decrease in plasma TC and LDL-C.
- It appears that the RBO and its bioactive components may be able to safely improve the plasma lipid profile in hypercholesterolaemic patients.
- Various clinical trials have clearly indicated that the consumption of RBO-rich diets can significantly improve the levels of HDL-C in hypercholesterolaemic human subjects.

- A recent study has reported the effects of RBO versus statins on blood glucose, HbA1C and serum lipid profiles in patients with type 2 diabetes. The RBO group was given a low-calorie diet, and the patients consumed 30 g/day RBO. They also used RBO as the main cooking oil for 6 months. The patients in atorvastatin group received a low-calorie diet together with 40 mg/day of atorvastatin drug for 6 months. The diabetic and moderately hyperlipidaemic patients showed significant increase in the fasting and postprandial blood glucose, HbA1C and liver transaminase levels on atorvastatin, whereas there was a reduction in all these parameters in RBO group. This study concluded that the use of RBO together with dietary modifications may be effective in reduce the incidence of cardiovascular diseases.

Anti-diabetic Effect of RBO

- Tocotrienol-rich fraction of RBO has been shown to act as an antioxidant to effectively decrease the HbA1C.
- Tocotrienols in RBO are considered to lower blood TC concentrations by inhibiting the HMG-CoA reductase activity.
- Tocotrienols have cardioprotective properties by improving the postischaemic ventricular functions and reducing the myocardial infarction. The bioactive components and antioxidants present in RBO as well as its oleic acid and conjugated linoleic acid contents may help to boost the metabolic rate, regulate the blood glucose and lipid profile, reduce inflammation, lose weight and may control obesity.
- γ-Oryzanol can regulate the secretion of insulin and blood glucose levels by normalizing the liver enzyme activities and therefore may lower the risk of hyperglycaemia.

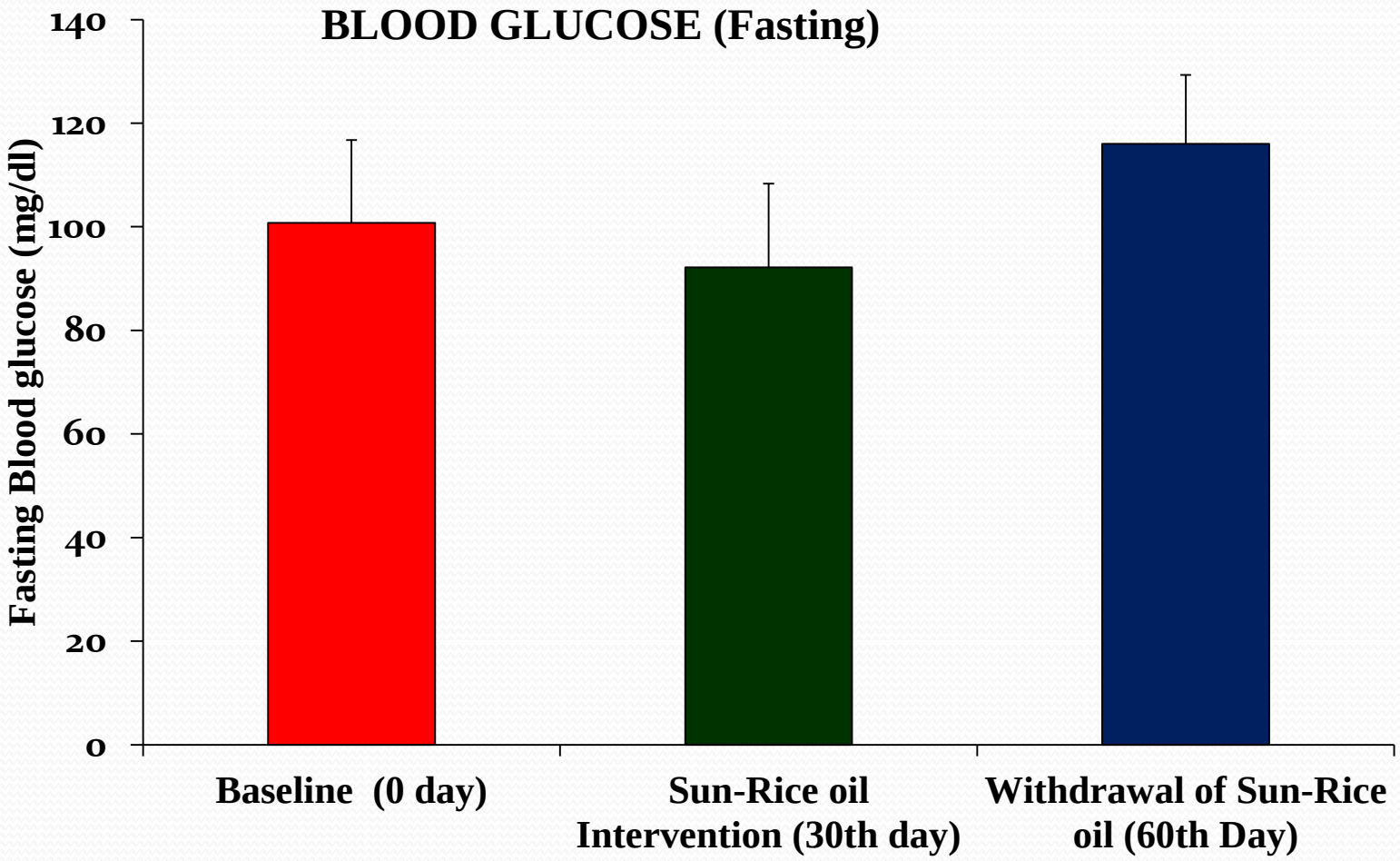
- Pigmented rice berry bran oil may have beneficial effects on diabetes by reducing the oxidative stress.
- RBO is effective in ameliorating the neuropathic pain in diabetic patients.
- RBO has been shown to inhibit hyperinsulinemia
- ADA recommends that in order to improve the hyperlipidaemia and to prevent heart-related diseases, the diabetic patients should consume those vegetable oils, which contain high amounts of oleic acid.
- RBO, because of its optimal fatty acid composition and bioactive components, which have high absorption capacity in the GI tract, can not only inhibit the intestinal absorption of cholesterol and block the synthesis of cholesterol analogues, and increase the excretion of its metabolites from the body and thus may reduce the incidence of cardiovascular diseases.

Effects of RBO on Oxidative Stress

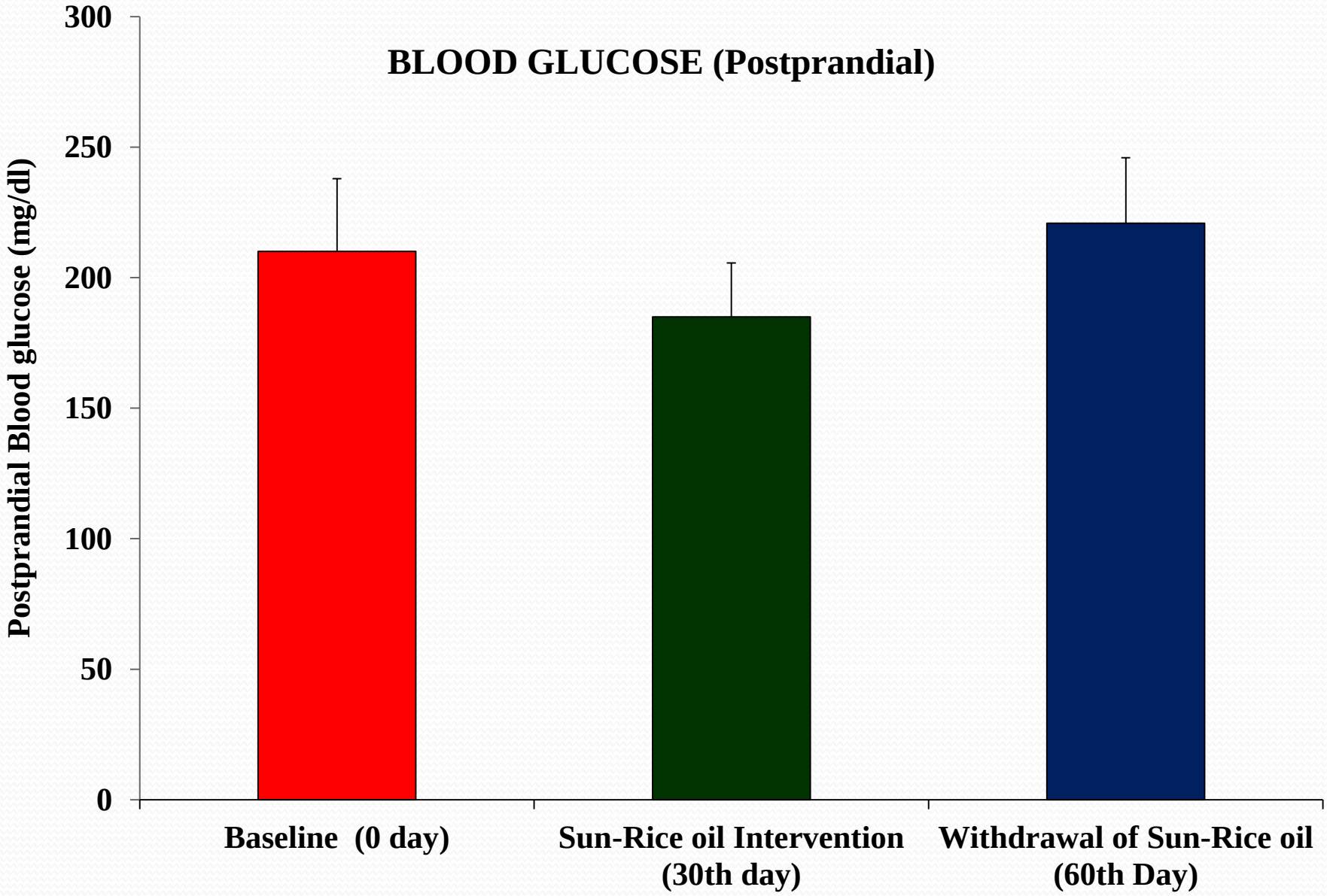
- RBO and its high antioxidant potential can better help to prevent cellular lipid and protein oxidation.
- It has been concluded that rice bran extracts including RBO have great nutraceutical potential in the prevention of mitochondrial dysfunctions and may attenuate the oxidative stress in neurodegenerative diseases.
- Tocotrienols exhibit stronger antioxidant activity which is attributed to their high capacity to donate phenolic hydrogen to various free radicals.
- RBO diets can improve the antioxygenic potential and may protect against oxidative stress.
- Bioactive components of RBO may exert synergistic effect in combating the reactive oxygen species (ROS) and may therefore help in the prevention of cellular oxidative damage.

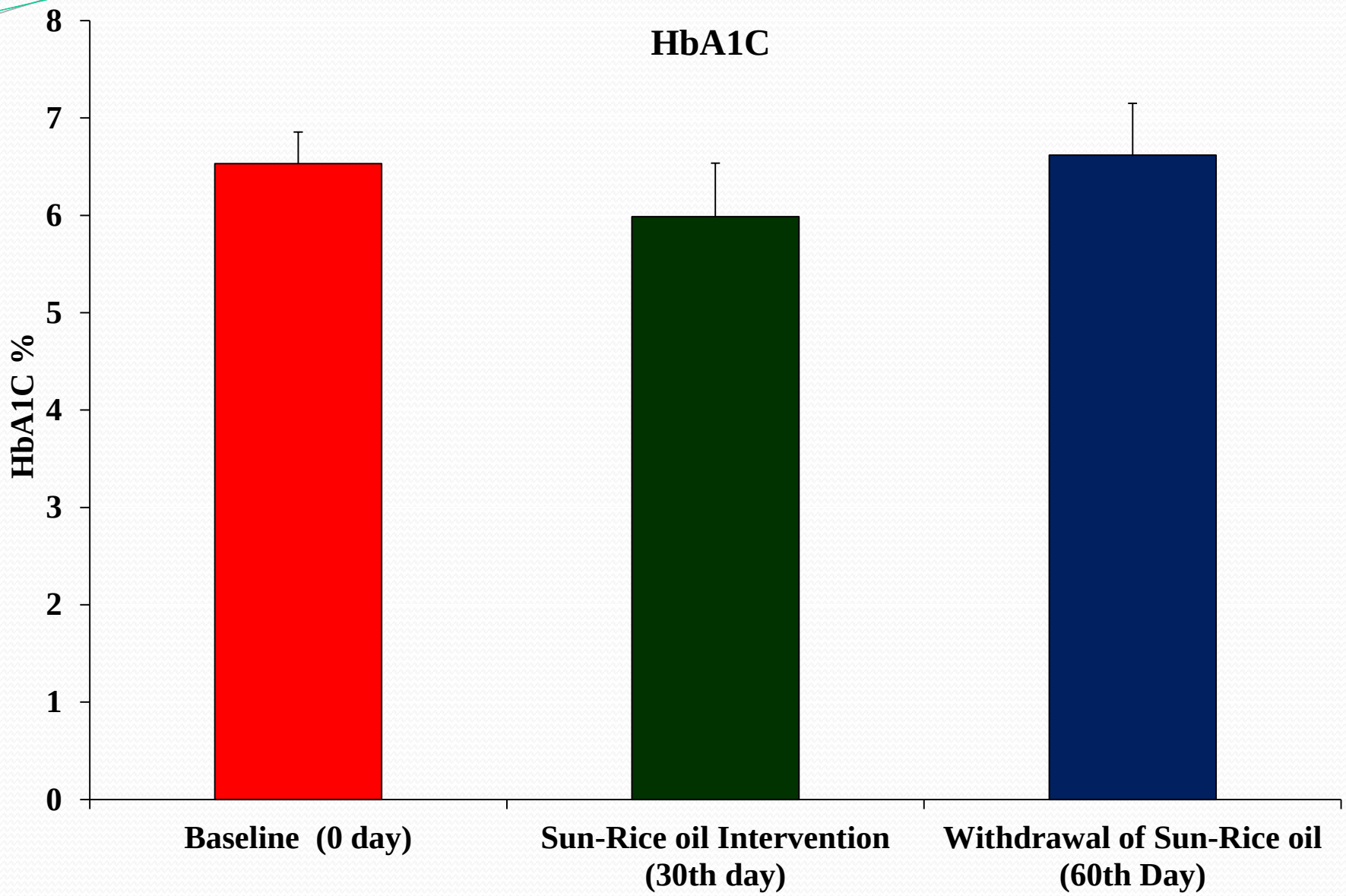
Health Benefits of RBO Blends

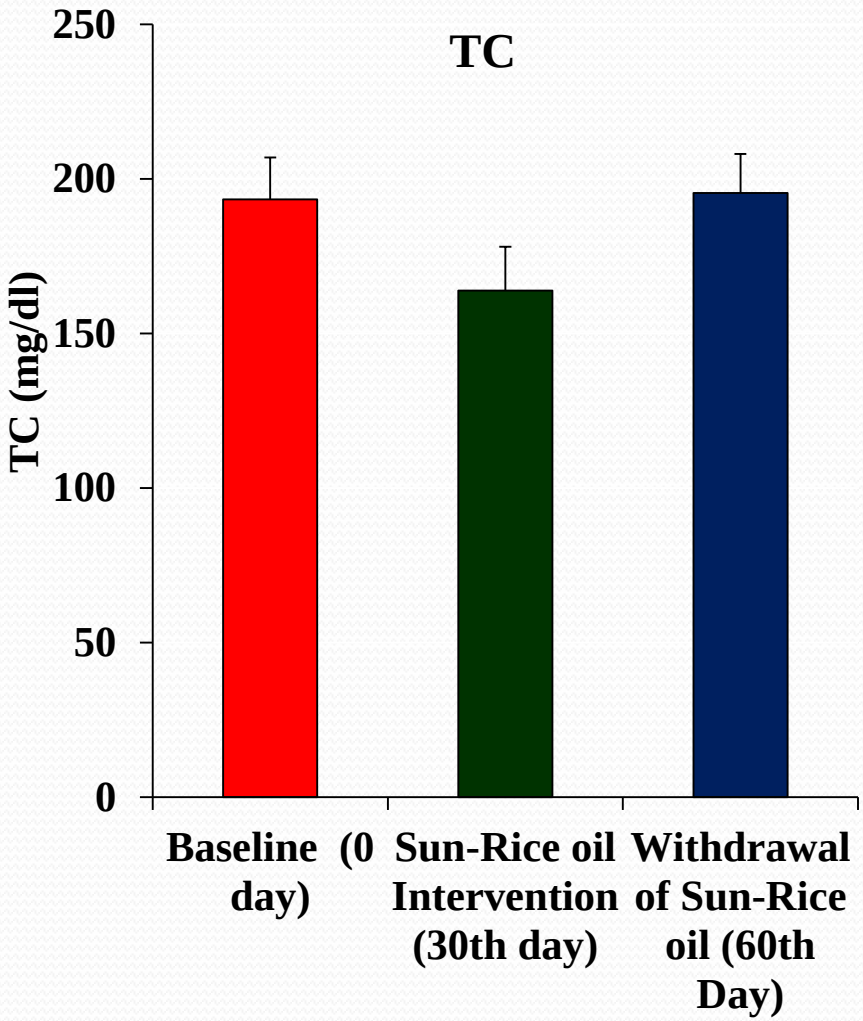
Effect RBO and Sunflower oil blend in Type 2 Diabetes

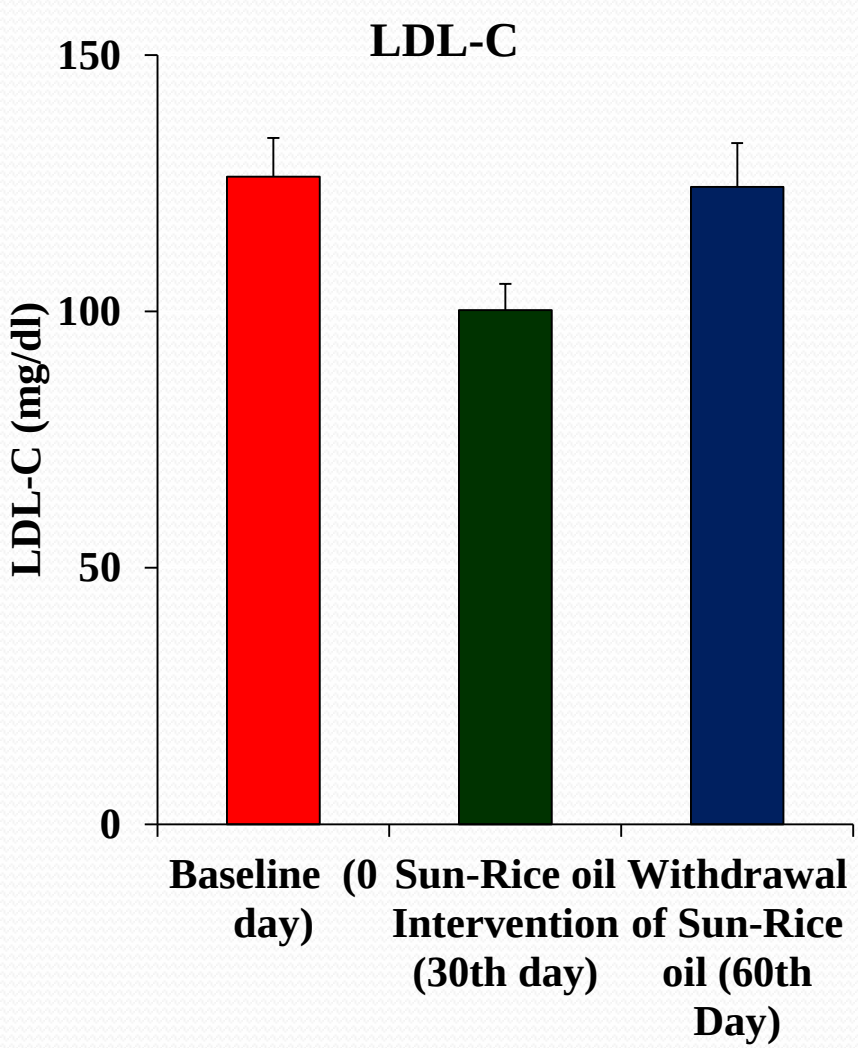


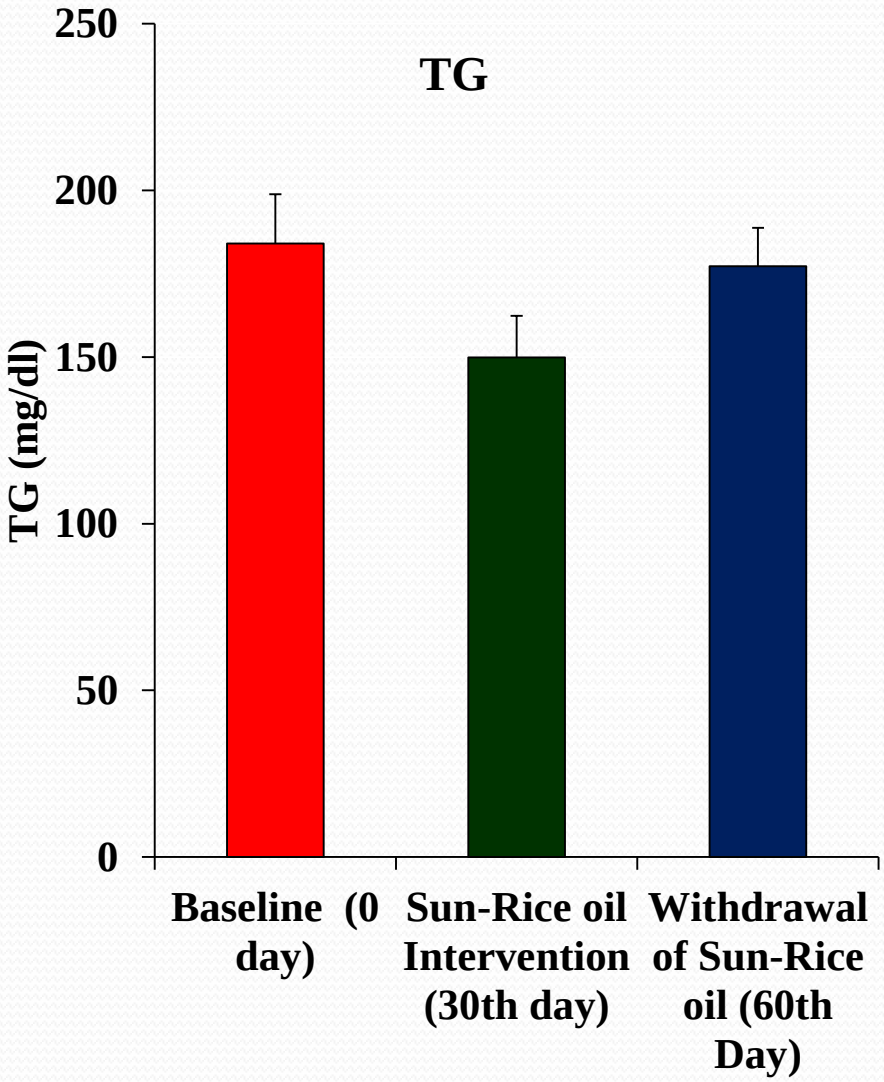
Sankar Devarajan et al (Under Publication in Biomedicine and Pharmacotherapy)

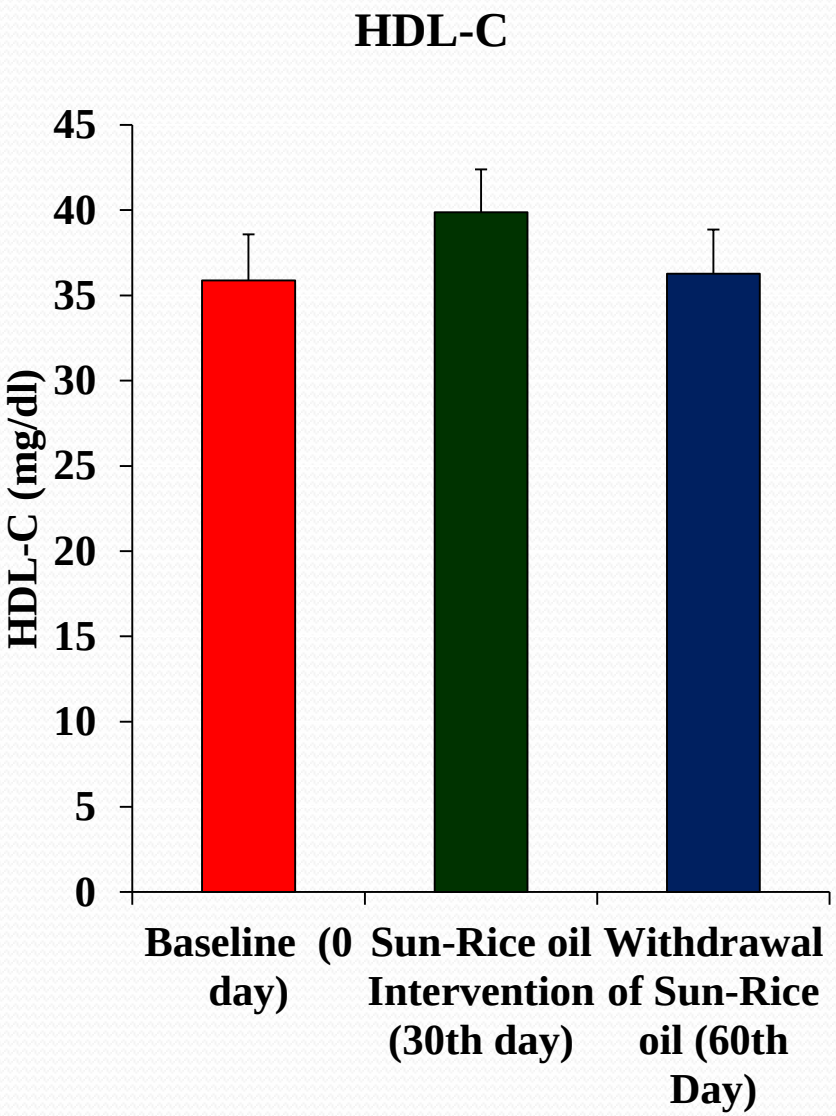

BLOOD GLUCOSE (Postprandial)
Postprandial Blood glucose (mg/dl)
300
250
200
150
100
50
0
Baseline (0 day)
Sun-Rice oil Intervention (30th day)
Withdrawal of Sun-Rice oil (60th Day)


HbA1C
HbA1C %
8
7
6
5
4
3
2
1
0
Baseline (0 day)
Sun-Rice oil Intervention (30th day)
Withdrawal of Sun-Rice oil (60th Day)


TC
250
200
150
100
50
0
TC (mg/dl)
Baseline (0 day)
Sun-Rice oil Intervention (30th day)
Withdrawal of Sun-Rice oil (60th Day)

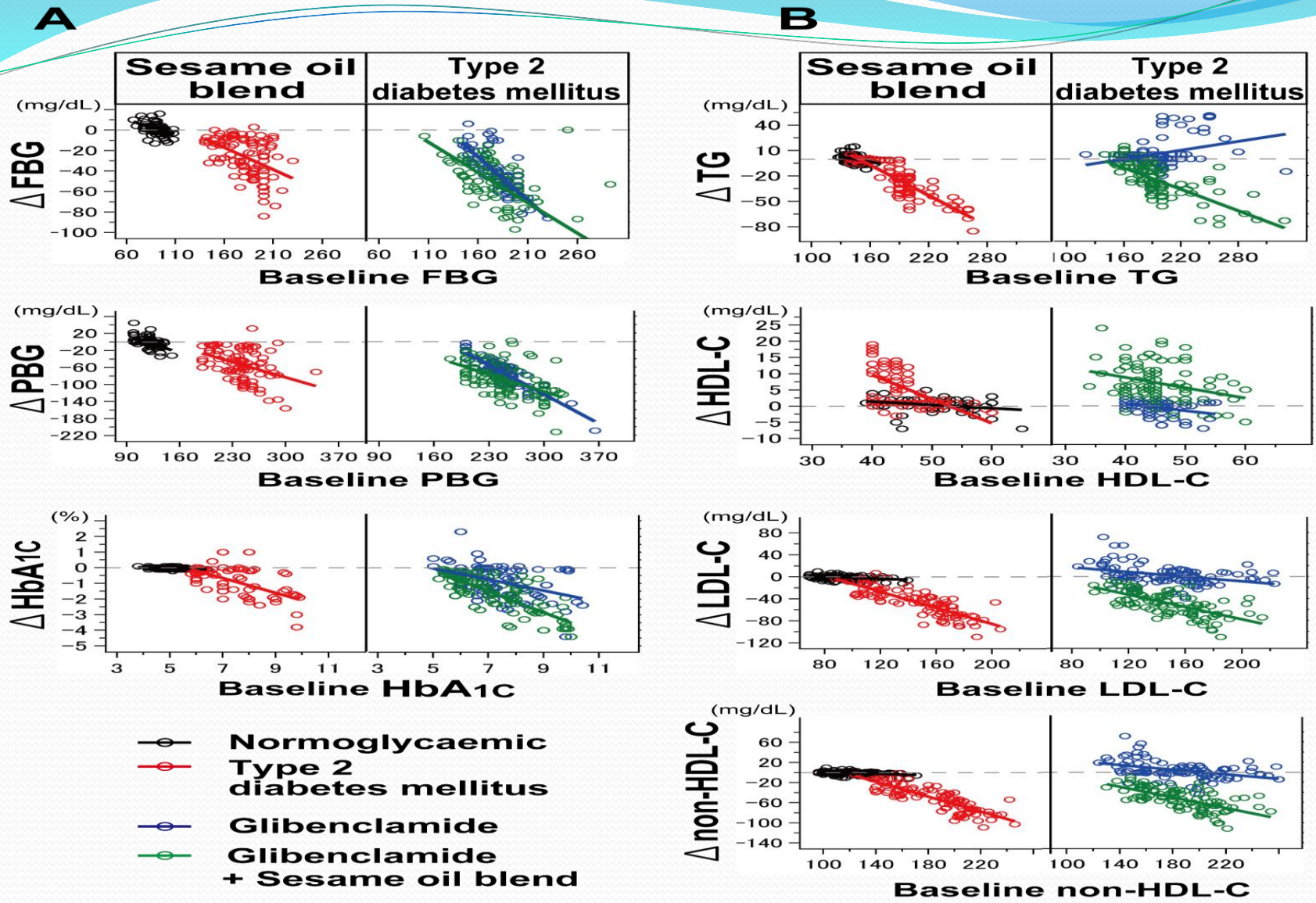

LDL-C
150
100
50
0
LDL-C (mg/dl)
Baseline (0 day)
Sun-Rice oil Intervention (30th day)
Withdrawal of Sun-Rice oil (60th Day)


TG
250
200
150
100
50
0
TG (mg/dl)
Baseline (0 day)
Sun-Rice oil Intervention (30th day)
Withdrawal of Sun-Rice oil (60th Day)


HDL-C
45
40
35
30
25
20
15
10
5
0
HDL-C (mg/dl)
Baseline (0 day)
Sun-Rice oil Intervention (30th day)
Withdrawal of Sun-Rice oil (60th Day)

Effect RBO and Sesame oil blend on Type 2 Diabetes

Parameters	Sesame Oil Blend			Type 2 diabetes mellitus patients		
	Normal subjects (n=100)	Type 2 diabetes mellitus patients (n=100)		Glibenclamide (n=100)	Glibenclamide + Sesame oil blend (n=100)	
	Study 1		Group* period interaction (P value)	Study 2		Group* period interaction (P value)
Fasting plasma glucose (mg/dL)						
0days	95 ± 8	181 ± 20 †		180 ± 18	184 ± 37	
wk-4		162 ± 24 *		153 ± 14 *	150 ± 30 *	
wk-8	93 ± 7	155 ± 21 * †	<0.001	137 ± 12 *	128 ± 26 * †	0.04
Post prandial plasma glucose (mg/dL)						
0days	121 ± 10	242 ± 26 †		246 ± 27	248 ± 37	
wk-4		219 ± 28 *		220 ± 24 *	210 ± 41 * †	
wk-8	119 ± 10	189 ± 36 * †	<0.001	175 ± 14 *	161 ± 37 * †	0.02
HbA1c (%)						
0days	5.1 ± 0.5	7.3 ± 1.2 †		7.3 ± 1.2	7.2 ± 1.4	
wk-8	5.0 ± 0.4	6.5 ± 1.0 * †	<0.001	6.4 ± 1.2 *	5.6 ± 0.9 * †	<0.001
Total cholesterol (mg/dL)						
0days	172 ± 14	230 ± 27 †		230 ± 31	231 ± 26	
wk-8	170 ± 14	184 ± 16 * †	<0.001	233 ± 29	185 ± 20 * †	<0.001
Triglyceride (mg/dL)						
0days	148 ± 8	193 ± 29 †		195 ± 30	196 ± 34	
wk-8	145 ± 8	166 ± 15 * †	<0.001	198 ± 39	170 ± 24 * †	<0.001
HDL-C (mg/dL)						
0days	49 ± 5.5	45.1 ± 4.5 †		44.8 ± 3.9	45.1 ± 5.6	
wk-8	49.4 ± 5.3	50.9 ± 5.1 *	<0.001	44.4 ± 3.9	52.2 ± 6.5 * †	<0.001
LDL-C (mg/dL)						
0days	94 ± 15	147 ± 28 †		146 ± 31	147 ± 27	
wk-8	92 ± 15	100 ± 16 * †	<0.001	149 ± 30	99 ± 20 * †	<0.001
Non-HDL-C (mg/dL)						
0days	123 ± 16	185 ± 28 †		186 ± 31	186 ± 26	
wk-8	121 ± 15	133 ± 16 * †	<0.001	189 ± 29	133 ± 21 * †	<0.001



Sankar Devarajan et al. 2016, Am J Med, 129; 731-739

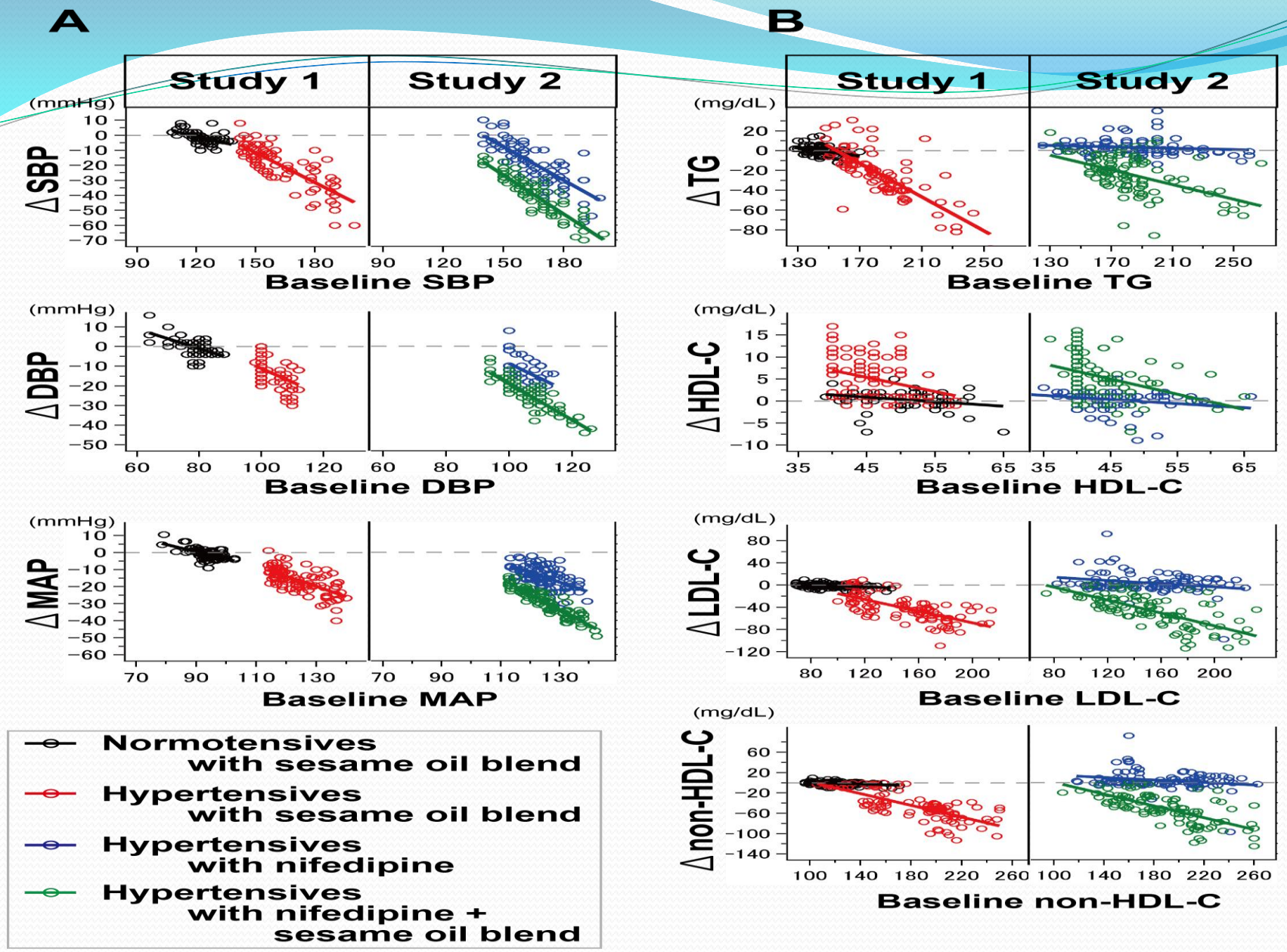
Using a blend of unrefined sesame oil and physically refined rice bran oil (20:80) as cooking oil in patients with type 2 diabetes mellitus

- Lowers blood glucose (FBG 14.36%; PPG 21.9% and HbA1C 10%)
- Lowers TC (20%), LDL-C (31%) and TG (13%)
- Increases HDL-C by (12%)
- Shows an additive effect with Glibenclamide for highly significant reduction of blood glucose (FBG 30%; PPG 35% and HbA1C 22%).

Sankar Devarajan et al. 2016, Am J Med, 129; 731-739

Effect RBO and Sesame oil blend on Hypertension

	Normotensives			Hypertensives			
	Sesame oil blend (n=100)	Sesame oil blend (n=100)		Nifedipine (n=100)	Nifedipine + Sesame oil blend (n=100)		
	Study 1		Group* period interaction (P value)	Study 2			Group* period interaction (P value)
SBP (mmHg)							
0 days	122 ± 6	164 ± 17 †		164 ± 14	164 ± 14		
15 days		155 ± 14 *		153 ± 12 *	149 ± 12 * †		
30 days		149 ± 13 *		149 ± 11 *	134 ± 9 * †		
45 days		145 ± 8 *		146 ± 6 *	127 ± 7 * †		
60 days	120 ± 5	143 ± 10 * †	<0.001	146 ± 8 *	125 ± 6 * †		<0.001
DBP (mmHg)							
0 days	79 ± 4	104 ± 5 †		104 ± 5	106 ± 7 †		
15 days		98 ± 4 *		97 ± 5 *	95 ± 5 * †		
30 days		94 ± 4 *		96 ± 5 *	91 ± 6 * †		
45 days		92 ± 5 *		93 ± 5 *	85 ± 5 * †		
60 days	79 ± 4	90 ± 6 * †	<0.001	92 ± 6 *	81 ± 4 * †		<0.001
MAP (mmHg)							
0 days	94 ± 4	124 ± 8 †		124 ± 6	125 ± 8		
15 days		117 ± 6 *		116 ± 6 *	113 ± 6 * †		
30 days		112 ± 6 *		114 ± 6 *	105 ± 6 * †		
45 days		110 ± 5 *		111 ± 5 *	99 ± 5 * †		
60 days	93 ± 3	108 ± 6 * †	<0.001	110 ± 6 *	96 ± 3 * †		<0.001
TC (mg/dL)							
0 days	172 ± 14	230 ± 33 †		231 ± 32	232 ± 34		
60 days	171 ± 14	188 ± 23 * †	<0.001	235 ± 32 *	186 ± 25 * †		<0.001
TG (mg/dL)							
0 days	145 ± 8	182 ± 23 †		186 ± 30	184 ± 27		
60 days	145 ± 8	159 ± 15 * †	<0.001	189 ± 31 *	159 ± 24 * †		<0.001
HDL-C (mg/dL)							
0 days	49.4 ± 5.5	45.9 ± 5.0 †		43.8 ± 5.9	43.8 ± 5.3		
60 days	49.8 ± 5.3	51.0 ± 5.6 *	<0.001	44.2 ± 5.9	49.2 ± 5.5 * †		<0.001
LDL-C (mg/dL)							
0 days	94 ± 15	149 ± 29 †		150 ± 33	151 ± 34		
60 days	92 ± 15	108 ± 22 * †	<0.001	153 ± 33	106 ± 25 * †		<0.001
non-HDL-C (mg/dL)							
0 days	123 ± 16	184 ± 34 †		187 ± 33	188 ± 34		
60 days	121 ± 15	137 ± 24 * †	<0.001	191 ± 34 *	137 ± 26 * †		<0.001



Sankar Devarajan et al. 2016, J Clin Lipidol, 10; 339-349

Using a blend of unrefined sesame oil and physically refined rice bran oil (20:80) as cooking oil in mild-to-moderate hypertensive patients

- Lowers blood pressure (SBP 12.8%; DBP 13.5% and MAP 12.9%)
- Lowers total cholesterol (18.3%), low-density lipoprotein cholesterol (27.5%), triglycerides (12.6%) and non-high-density lipoprotein cholesterol (25.4%)
- Increases high-density lipoprotein cholesterol (11%)
- Shows an additive effect with nifedipine for highly significant reduction of blood pressure (SBP 23.8%; DBP 23.6% and MAP 23.2%).

Sankar Devarajan et al. 2016, J Clin Lipidol, 10; 339-349

Conclusion

- Dietary strategies are considered as the first line of defense in the prevention and management of diabetes, cardiovascular diseases. RBO with its excellent fatty acid composition and bioactive antioxidants has demonstrated beneficial effects to improve the plasma lipid profile.
- Consumption of RBO has been shown to have a direct relationship with its antihypertensive, antidiabetic and lipid-lowering efficacies.
- As evidenced from several observational and clinical studies, it is well documented that the RBO has an imperative role in the prevention, management and control of cardiometabolic diseases, and therefore RBO would certainly be a valuable dietary addition as functional food.

On going Research with Rice Bran components

Screening of Rice Bran components for Chymase Inhibitory Indications: Selectivity of the Functional Potentiality Food compounds for Depressor Effect

USDA-Capacity Building Grant 2017
Project Director-Dr. Sankar Devarajan ($ 500,000)

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