Phyto-Berries™

A PILOT INTERVENTION STUDY

EVALUATING THE EFFECT OF PHYTO BERRIES® ON EARLY STAGE, ASYMPTOMATIC, NON STENOSING ATHEROSCLEROSIS PROGRESSION

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A B S T R A C T

Objective

The aim of this study is to evaluate the effect of daily consumption of a spray dried, mixed berry powdered beverage (PHYTO BERRIES®) on early stage asymptomatic, non stenosing atherosclerosis progression.

Subjects

A total of 120 volunteer subjects with pre-existing CVD risks factors were assigned into 4 groups over a period of 48 months.

Group 1	–	Control No placebo or randomisation was initiated. LifeStyle Management, Dietary Intervention & Exercise
Group 2	–	Aspirin 100mg / day
Group 3	–	PHYTO BERRIES® 5 grams / day
Group 4	–	PHYTO BERRIES® 5 grams / day with Aspirin 100mg / day

Results

The result of this pilot intervention study supports the recommendation that PHYTO BERRIES® is a significant suppressor of plaque progression in patients with early stage, asymptomatic non stenosing atherosclerosis with co-existing CVD risks factors such as elevated systemic inflammation markers, pre-hypertension & mild hyperlipidemia.

Introduction

Atherosclerosis is a coronary artery disease which is caused by buildup of a fatty materials called plaque on the inner walls of blood vessels resulting in the narrowing (stenosis), hardening & occlusion (blockage) of all blood vessels that supply blood & oxygen to the heart. Atherosclerosis is the underlying condition implicated in most myocardial infarctions & strokes.

In epidemiological & clinical studies, dietary anthocyanins have been associated with significantly improved cardiovascular risk profiles. Edible berries are the most abundant dietary source of anthocyanins. The genus of berries used for this evaluation are Strawberries, Blueberries, Black Raspberries, Red Raspberries, Mulberries, Red Cherries, Cranberries & Boysenberries. Juice extraction is obtained by crushing the entire fruit (flesh, leaves, seeds, colored skin) under 800 bar of pressure via a centrifuge. The sugar content within the juice is then completely removed via Ion Exchange Processing Method. The resultant sugar free juice is spray dried into crystalline fine powder using inert Nitrogen gas.

Participants & Methods

Selection of Subjects

120 volunteer subjects in the age group of 42 – 75 years having been diagnosed by their preferred cardiologists in their respective home states with the following CVD risk factor below for eligibility to this intervention pilot study:

UB Class IV – Early stage, non stenotic, asymptomatic atherosclerotic plaque formation with a localised thickening > 1.5mm producing lesser than < 50% diameter stenosis in at least one carotid bifurcation or one femoral bifurcation

Hyperlipidemia – 5.2 mmol/L to 7.8 mmol/L

Dosage

The recommended prophylactic dosage assigned to each subject is 5 grams of crystalline powder once a day after a meal.

Follow-Up

Subjects consulted with their cardiologists once every 6 months up to a total of 48 months for a repeat ultrasound scan, reporting of any adverse or favourable cardiovascular events & degree of compliance.

Ultrasound Class & Ultrasound Scoring

Both carotids & both femoral bifurcations were each assigned an ultrasound class (I-VI) and ultrasound score (2-10) to track their plaque progression or regression as shown in Table 1.

Assessment of atherosclerotic plaque progress

Plague progression is assessed by the changes in

– the sum of the ultrasonic score of all 4 bifurcations (both carotid bifurcations & both femoral bifurcations)

– the % of plaque that progressed from class IV to class V from baseline to the last follow up at 48 months.

Subject grouping is as illustrated in Table 2

Ultrasound Scanning Method

Non Invasive, High Resolution Doppler (B Mode) Ultrasound is a practical, safe and effective modality for scanning of carotid and femoral bifurcations for possible atherosclerotic plaque progression or regression. Carotid & femoral bifurcations are vulnerable locations for plaque lesion formation and are scanned using ultrasound imaging system in transverse and longitudinal planes. Maximum (IMT) intima media thickness was measured & noted. All ultrasonic scanning procedures were performed by each subject's cardiologist or physician in their respective home states throughout the United States & Canada.

Table 1: Ultrasonic Classes & Score

Ultrasound Class	Ultrasound Characteristics	Ultrasound Score
Class I	Normal artery, intimal surface is a straight line	2
Class II	Intimal irregularities with granulation, IMT (Intima Media Thickness) < 1mm	3
Class III	IMT (Intima Media Thickness) > 1mm	4
Class IV	Non stenotic atherosclerotic plaque. Thickening > 1.5mm producing < 50% diameter stenosis	6
Class V	Stenotic atherosclerotic plaque. Thickening > 50% diameter stenosis	8
Class VI	Symptomatic stenotic atherosclerotic plaque	10

Table 2: Grouping of Subjects

Group 1	Control Group No Placebo or Randomisation LifeStyle Management Dietary Intervention Exercise Regime
Group 2	Aspirin 100mg / day
Group 3	PHYTO BERRIES® 5 grams / day
Group 4	PHYTO BERRIES® 5 grams / day with Aspirin 100mg / day

Changes in systemic inflammation & CVD markers

Systemic inflammation is clinically proven to play a major role in the pathogenesis of atherosclerosis. Measurement of changes in HS-CRP, Homocysteine, Total Cholesterol, LDL, HDL & Hepatic Enzymes is necessary.

Changes in lipid peroxidation markers

Oxidative damage to both LDL and endothelial lining in blood vessels are also clinically proven in the development of atherosclerosis. The most representative serum marker for assessing degree of lipid peroxidation is serum malonaldehyde (MDA). Both inflammation markers & lipid peroxidation blood samples are drawn by subject's personal cardiologist and delivered directly to:

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Appendix 1

Group	Demographics of Subjects			
	Group 1 Control	**Group 2** Aspirin 100mg/day	**Group 3** Phyto Berries® 5grams/day	**Group 4** Phyto Berries® 5grams/day with Aspirin 100mg/ day
No of Subjects (N)	30	30	30	30
No of Subjects Withdrawn from study	2	1	0	0
No of Subjects Failed To Complete 48 months	6	7	1	2
No of Subjects Completed 48 months	22 (73%)	22 (73%)	29 (97%)	28 (93%)
Male	17	13	9	20
Female	5	9	20	8
Compliance	–	70%	90%	80%

Appendix 2

Group	Ultrasonic Score at Baseline and at 48 Months			
	Group 1 Control	**Group 2** Aspirin 100mg/day	**Group 3** Phyto Berries® 5grams/day	**Group 4** Phyto Berries® 5grams/day with Aspirin 100mg/day
Ultrasonic Score Sum of all 4 bifurcations				
At Baseline	20.0	22.3	20.80	21.55
At 48 Months	23.0	23.2	20.82	21.56
Difference	***3.0 (15.00%)***	***0.9 (4.04%)***	***0.02 (0.10%)***	***0.01 (0.05%)***

Appendix 3

Group	Plaque Progression from Class IV to Class V			
	Group 1 Control	**Group 2** Aspirin 100mg/day	**Group 3** Phyto Berries® 5grams/day	**Group 4** Phyto Berries® 5grams/day with Aspirin 100mg/day
No of Subjects Completed 48 Months	22	22	29	28
No of Subjects With at least 1 Plaque Progressed from Class IV to Class V	**7 (31.8%)**	**4 (18.2 %)**	**1 (3.5%)**	**1 (3.5%)**

Appendix 4

Parameters Tested	CVD Risk Factors & Systemic Inflammatory Markers		
	At Base Line	**At 3 Months**	**At 6 Months**
Total Cholesterol (mg/dL)	249.89	215.11 (– 14%)	200.08 (– 20%)
LDL (mg/dL)	172.93	145.19 (– 15.6%)	135.22 (– 21%)
Triglycerides (mg/dL)	210.54	174.66 (– 17%)	130.85 (– 38%)
HDL (mg/dL)	35.22	40.21 (+ 14%)	43.56 (+ 23.8%)
C-Reactive Protein (mg/L)	4.00	2.89 (– 27.5%)	1.61 (– 60%)
Homocysteine (mmol/L)	12.40	6.21(– 50%)	4.10 (– 66%)
Blood Glucose (mg/dL)	105.32	97.10 (– 7.6%)	83.90 (– 20%)
Hepatic Enzyme			
AST (IU/L)	40.54	25.12 (– 38%)	13.54 (– 66.6%)
ALT (IU/L)	39.98	28.87 (– 28%)	10.95 (– 75%)
GGT (IU/L)	61.21	45.11 (– 26%)	11.45 (– 81%)
MDA (malonaldehyde) (mmol/L)	1.89	0.36 (– 81%)	0.34 (– 82%)

Results

From 120 eligible subjects who volunteered for this study, 1 individual withdrew due to severe aspirin intolerance, 2 individuals also withdrew due to other non related medical conditions. 16 individuals had very poor compliance & failed to complete the 48 month study period. The remaining 101 eligible subjects were available for the entire 48 months of the pilot intervention study with reasonably good compliance of 70% to 90%.

In appendix 2 above, the ultrasonic score increased in group 1 (15%) & group 2 (4%). This is indicative of significant worsening of plaque progression in group 1 (control group) where no allopathic or nutritional intervention is prescribed to the subjects.

It can also be hypothesized that most patients in the control group experience difficulty in implementing lifestyle improvement strategies which ultimately led to significant worsening of their conditions. Group 2 who is prescribed aspirin only also experience an increase in plaque formation of 4%. This indicates that aspirin alone is insufficient in arresting plaque progression.

The ultrasonic score remained almost unchanged in group 3 (0.1%) & group 4 (0.05%). This is indicative that PHYTO BERRIES® when prescribed solely without aspirin, can significantly slow or even arrest the progression of atherosclerotic plaque.

In Appendix 3, it is clearly evident that PHYTO BERRIES® plays an extremely effective & important role in preventing new formations of arterial plaque.

The result of this pilot intervention study supports the recommendation that PHYTO BERRIES® is a significant & effective suppressor of plaque progression in patients with early stage, asymptomatic non stenosing atherosclerosis with co-existing CVD risks factors such as elevated systemic inflammation markers & mild hyperlipidemia.

Systemic Inflammation markers & Cardiovascular (DVD) markers

In appendix 4, PHYTO BERRIES® clearly exhibits significant anti inflammatory benefits while normalising hyperlipidemia & blood glucose in 3 months and achieving maximum blood lipid & blood glucose levels in 6 months concommitantly with a low carbohydrate diet, high protein, moderate fat diet.

In conjunction with an appropriate diet, PHYTO BERRIES® also aids in tremendously lowering ALT (Alanine Amino Transferase) which is a well known marker for NAFLD (Non Alcoholic Fatty Liver Disease).

In appendix 4, it shows a dramatic reduction in ALT by up to 28% in 3 months. This is also achieved with a low carbohydrate, high protein, moderate fat diet which focuses on achieving a stable insulin level.

Achieving steady insulin secretion is absolutely crucial for optimum lipid production & reversal of NAFLD.

Lipid Peroxidation markers

Oxidised LDL is the most common component of atherosclerotic plaque or lesions. Hence, managing lipid peroxidation is quickly becoming a major focus in preventing the formation of new arterial plaque.

The most accurate and representative marker of lipid peroxidation is Malondialdehyde (MDA). It can be seen in appendix 4 that PHYTO BERRIES® is a highly effective antioxidant which can significantly reduce lipid peroxidation as shown in major reductions in plasma MDA levels within 3 months.

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