Electronic Supplementary Material (ESI) for Food & Function.

Title:

A Minor Metabolite from *Curcuma longa* Effective for Metabolic Syndrome: Results from a Randomized, Double-blind, Placebo-Controlled Clinical Study

Author Names and Affiliations:

Muhammed Majeed[1,2], Kalyanam Nagabhushanam[2], T V Devarajan[3], Santhosh Saklecha[4],S. Venkata Krishna Reddy[5], Lakshmi Mundkur[1*]

[1]Sami-Sabinsa Group Limited, 19/1&19/2, I Main, II Phase, Peenya Industrial Area, Bengaluru, Karnataka 560058, India

[2]Sabinsa Corporation, 20 Lake Drive, East Windsor, NJ 08520, USA

[3]Apollo First Med Hospitals, 154, Poonamallee High Rd, Kilpauk, Chennai, Tamil Nadu 600010, India

[4]Santosh Hospital, 6, 1, Promenade Rd, Coles Park Pulikeshi Nagar, Bengaluru, Karnataka 560005, India

[5]Vijaya Super Specialty Hospital, 41-A, 16 II, Raghava Cine Complex Rd, Pogathota, Nellore, Andhra Pradesh 524001, India

Supplementary Methods

Inclusion and exclusion criteria

The inclusion criteria were as follows:

1.) IDF (International Diabetes Federation) 2006:

Waist ≥ 90 cm (men) or ≥ 80 cm (women) along with the presence of a minimum of two or more of the following:

a.) Fasting blood glucose greater than or equal to 5.6 mmol/L (100 mg/dl) or diagnosed diabetes

b.) HDL cholesterol < 1.0 mmol/L (40 mg/dl) in men, < 1.3 mmol/L (50 mg/dl) in women, or drug treatment for low HDL-C

c.) Blood triglycerides > 1.7 mmol/L (150 mg/dl) or drug treatment for elevated triglycerides

d.) Blood pressure > 130/85 mmHg or drug treatment for previously diagnosed hypertension.

2.) Male and/or female subjects aged between 30 to 65 years (both inclusive).

3.) BMI (≥) greater than or equal to 28 kg/m2 and less than or equal to (≤) 35 kg/m2.

4.) Willing to take up regular physical activity (for example: walking for 30 minutes daily for 5 days a week). 5. Subjects willing to agree to blood draws as per the protocol. 6. Able to give written informed consent.

7.) Willing to come for regular follow-up visits.

1.1.1. Exclusion criteria

The exclusion criteria were as follow:

1.) Intake of prescribed drugs in Ayurveda, Homeopathy, Naturopathy, Allopathy, etc., or prior surgery for obesity in the previous six months.

2.) Pathophysiologic/genetic syndromes associated with obesity (Cushing's syndrome, Turner's syndrome, Prader-Willi syndrome).

3.) Subjects who disagree to avoid drinking alcohol during the study period.

4.) Subjects with a diagnostic history of malignancy.

5.) Fasting Blood Glucose ≥ 150 mg/dl and HbA1c > 7%.

6.) Subjects with a history of clinically diagnosed Hypertension and with BP > 160 / 100 mm of Hg.

7.) Subjects diagnosed with thyroid disease, on medications for an underactive or overactive thyroid, and with TSH > 6 mIU/L.

8.) Subjects on lipid-lowering drugs.

9.) Subjects having a history of underlying Inflammatory arthropathy, Septic arthritis, Inflammatory joint disease, Gout, Pseudo gout, Paget's disease, Joint fracture, Acromegaly, Fibromyalgia, Wilsons disease, Ochronosis, Hemochromatosis, Heritable arthritic disorder or Collagen gene mutations or Rheumatoid arthritis.
10.) Subjects having a history of Coagulopathies, Cardiovascular diseases, Congestive heart failure, Pancreatitis, Lactic acidosis, Hepatomegaly with steatosis, Motor weakness, Peripheral sensory neuropathy, Psychiatric disorder, Severe Pulmonary Dysfunction (uncontrolled Bronchial Asthma and/or Chronic Obstructive Pulmonary Disorder [COPD].
11.) Have been diagnosed with an eating disorder, such as Anorexia nervosa, bulimia nervosa, Binge eating disorder, or Nocturnal eating disorder.
12.) History of any psychiatric disorders like Schizophrenia or bipolar disorder.
13.) Weight loss (-5%) in the last 3 months.
14.) Subjects on prolonged (> 4 weeks) medication with corticosteroids, antidepressants, anticholinergics, etc., or any other drugs that may influence the outcome of the study.
15.) Subjects with a concurrent serious hepatic disorder (defined as Aspartate Amino Transferase (AST) and/or Alanine Amino Transferase (ALT), Total Bilirubin, Alkaline Phosphatase (ALP)>2 times the upper normal limit) or Renal Disorders (defined as S. Creatinine>1.2mg/dL for females or >1.4 mg/dL for males and EGFR of 60 or less).
16.) History of hypersensitivity to any of the herbal extracts or dietary supplements.
17.) Pregnant / lactating woman.
18.) Subjects who have completed participation in any other clinical trial during the last six months.
19.) Any other condition that the Principal Investigator thinks may jeopardize the study.

Sample Size Determination:

We used an earlier research publication for the sample size calculations[1]. As per research publication, baseline values of Body Weight (kg) measured at baseline were:
Placebo Group baseline – Total Body weight mean=76.9, SD=11.08
Curcuma Caesia (Calebin A) Group baseline – Total Body weight mean=90.13, SD=14.75
We chose to mean=83.51 and SD=12.92 as being towards the centre of the two baseline results.

An SD=12.92 with mean=83.51 means the SD is about 0.2 times (base correlation) the size of the mean. That is, the coefficient of variation (CV) is 0. The mean Body weight value in the study is 83.51 and we assume the standard deviation is 12.92.
Using these inputs with 80% power and alpha=0.05 significance level assuming correlation of 0.2, the required total sample size is 60 for evaluation.
Allowing for 20% drop-out rate, the required sample size for recruitment is total of 72 in 1:1 ratio between two treatment groups (i.e., 36 per treatment group). We recruited 100 participants in a 1:1 ratio between two treatment groups (N=50 per treatment group)

Anthropometric measurements

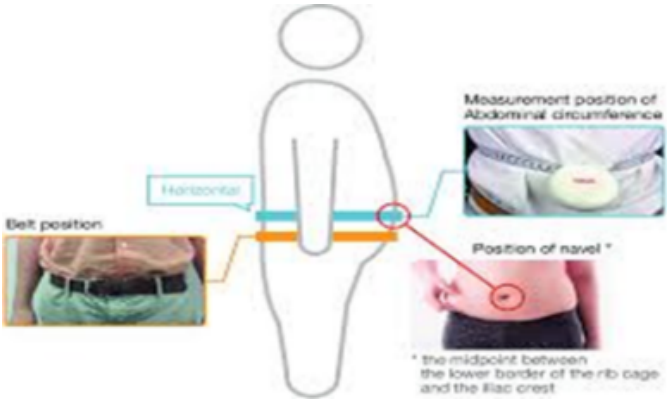
Body weight measurements

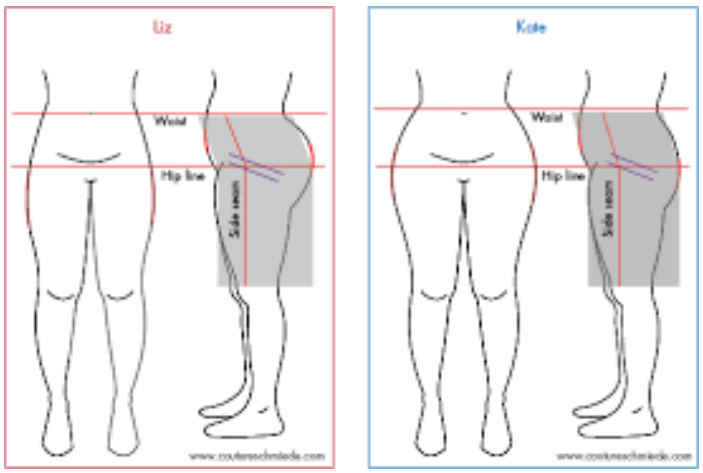
Weighing balance of same make and model was provided by the sponsor to each site. All the sites were bound to use the same for recording weight. Body weight measurement of the participants were taken in a surgical gown without footwear and other external apparel. Body Mass Index (BMI) is calculated by formula: BMI = kg/m2, where; kg = person's weight in kilograms and m2 = height in meters squared.

Waist and hip Circumference measurement

The measuring tape was placed horizontally around the waist just above the hip bone. The waist circumference was measured after breathing out.

To measure hip circumference, the outer garments, were removed, and the soft measuring tape was wrapped straight around the widest part of hips with feet put together. Hip circumference is the point at which the end of the tape meets the remaining length.





Laboratory measurements

SRL Diagnostics

SRL REFERENCE RANGE DOCUMENT - HEMATOLOGY

SRL Ltd.
Prime Square Building, Plot No 1,
Gaiwadi Industrial Estate,
S.V. Road, Goregaon (W)
Mumbai – 400 062,
Maharashtra, India

Test Name	Age	Gender	Reference Ranges	CH	CL	Unit	Instrument	METHODOLOGY
WHITE BLOOD CELL COUNT	18-99	M/F	4.0 - 10.0	> 30.0	< 2.0	thou/µL	UNICEL DXH 600	COULTER PRINCIPLE
RED BLOOD CELLS	18-99	F	3.8 - 4.8	NA	NA	mil/µL	UNICEL DXH 600	COULTER PRINCIPLE
		M	4.5 - 5.5	NA	NA			
HEMOGLOBIN	18-99	M	13.0 - 17.0	> 20.0	< 6.0	g/dL	UNICEL DXH 600	PHOTOMETRIC MEASUREMENT, CYANMETHEMOGLOBIN METH
		F	12.0 - 15.0	> 18.0	< 6.0			
MCV	18-99	M/F	83.0-101.0	101	23	fL	UNICEL DXH 600	DERIVED PARAMETER FROM RBC PARAMETER
MCH	18-99	M/F	27.0-32.0	32	27	pg	UNICEL DXH 600	CALCULATED PARAMETER
MCHC	18-99	M/F	31.5-34.5	34.5	31.5	g/dL	UNICEL DXH 600	CALCULATED PARAMETER
PLATELET COUNT	18-99	M/F	150 - 410	> 700	< 50	thou/µL	UNICEL DXH 600	ELECTRONIC IMPEDENCE & MICROSCOPY
HEMATOCRIT (PCV)	18-99	F	36 - 46	NA	NA	%	UNICEL DXH 600	Calculated Parameter
		M	40 - 50	NA	NA			
NEUTROPHILS (%)	18-99	M/F	40 - 80	NA	NA	%	UNICEL DXH 600	VCS TECHNOLOGY/ MICROSCCPY
LYMPHOCYTES (%)	18-99	M/F	20 - 40	NA	NA	%	UNICEL DXH 600	VCS TECHNOLOGY/ MICROSCCPY
MONOCYTES (%)	18-99	M/F	2-10	NA	NA	%	UNICEL DXH 600	VCS TECHNOLOGY/ MICROSCCPY
EOSINOPHILS (%)	18-99	M/F	1-6	NA	NA	%	UNICEL DXH 600	VCS TECHNOLOGY/ MICROSCCPY
BASOPHILS (%)	18-99	M/F	< 1 - 2	NA	NA	%	UNICEL DXH 600	VCS TECHNOLOGY/ MICROSCCPY
MEAN PLATELET VOLUME (MPV)	18-99	M/F	6.8-10.9	10.9	6.8	fL	UNICEL DXH 600	DERIVED PARAMETER FROM PLATELET HISTOGRAM
RED CELL DISTRIBUTION WIDTH (RDW)	18-99	M/F	11.6-14.0	14	11.6	%	UNICEL DXH 600	DERIVED PARAMETER FROM RBC HISTOGRAM

Verified by

Dr. Reena Mittal
Senior Consultant - Haematopathologist, Haematology & Flow Cytometry

Approved by

Dr. Simi Bhatia
Director - Goregaon Reference Lab., Senior histopathologist,
Head Auto-Immune section

Test Name	Age	Gender	Reference Ranges	CH	CL	Unit	Instrument	Methodology
TRIGLYCERIDES	0 - 99	M/F	<150 (NORMAL) 150-199 (BORDERLINE HIGH) 200-499 (HIGH) >/=500 (VERY HIGH)	NA	NA	mg/dL	COBAS 8000	Spectrophotometry, enzymatic Endpoint with glycerol blank
CHOLESTEROL TOTAL	0 - 99	M/F	< 200 (DESIRABLE) 200 - 239 (BORDERLINE HIGH) >/= 240 (HIGH)	NA	NA	mg/dL	COBAS 8000	Spectrophotometry, Enzymatic Colorimeric Cholesterol Oxidase Esterase Peroxidase
Cholesterol,HDL	0 - 99	M/F	< 40 (LOW HDL CHOLESTEROL) >/= 60 (HIGH HDL CHOLESTEROL)	NA	NA	mg/dL	COBAS 8000	Spectrophotometry, Homogenous Direct Enzymatic Colorimetric
Cholesterol,LDL Direct	0 - 99	M/F	<100 OPTIMAL 100-129 NEAR OR ABOVE OPTIMAL 130-159 BORDERLINE HIGH 160-189 HIGH >/=190 VERY HIGH	NA	NA	mg/dL	COBAS 8000	Spectrophotometry, Homogeneous Enzymatic Colorimetric
VLD. (Calculated)	0 - 99	M/F	</= 30	NA	NA	mg/dL	COBAS 8000	Calculated Parameter
SODIUM	1 year - 18 year	M/F	138 - 145	160	120	mmol/L	COBAS 8000	ISE Indirect
	18 year - 99 year	M/F	136 - 145	160	120			
POTASSIUM	1 year - 18 year	M/F	3.4 - 4.7	6.2	2.8	mmol/L	COBAS 8000	ISE Indirect
	18 year - 99 year	M/F	3.5 - 5.1	6.2	2.8			
Chloride	0 days - 28 days	M/F	97 - 110	120	80	mmol/L	COBAS 8000	ISE Indirect
	28 days - 99 year		98 - 106					
EGFR	18-99	M/F	> 60	NA	NA	mL/min/1.73m2	COBAS 8000	Calculated Parameter
Hs-CRP	18 year - 99 year	M/F	Low risk for CAD: < 1.00 Average risk for CAD: 1.00 - 3.00 High risk for CAD: > 3.00	NA	NA	mg/L	BEHRING NEPHELOMETER II	Nephelometry, Particle- Enhanced Immunonephelometry

Verified by

Dr. Kshama Pimpalgaonkar
Head Dept. of Biochemistry

Approved by

Dr. Sini Bhatia
Director - Goregaon Reference Lab., Senior histopathologist,
Head Auto-immune section

Test Name	Age	Gender	Reference Ranges	CH	CL	Unit	Instrument	Methodology
TRIGYLCERIDES	0 - 99	M/F	<150 (NORMAL) 150-199 (BORDERLINE HIGH) 200-499 (HIGH) >/=500 (VERY HIGH)	NA	NA	mg/dL	COBAS 8000	Spectrophotometry, enzymatic Endpoint with glycerol blank
CHOLESTEROL TOTAL	0 - 99	M/F	< 200 (DESIRABLE) 200 - 239 (BORDERLINE HIGH) >/= 240 (HIGH)	NA	NA	mg/dL	COBAS 8000	Spectrophotometry, Enzymatic Colorimeric Cholesterol Oxidase Esterase Peroxidase
Cholesterol,HDL	0 - 99	M/F	< 40 (LOW HDL CHOLESTEROL) >/= 60 (HIGH HDL CHOLESTEROL)	NA	NA	mg/dL	COBAS 8000	Spectrophotometry, Homogenous Direct Enzymatic Colorimetric
Cholesterol,LDL Direct	0 - 99	M/F	<100 OPTIMAL 100-129 NEAR OR ABOVE OPTIMAL 130-159 BORDERLINE HIGH 160-189 HIGH >/=190 VERY HIGH	NA	NA	mg/dL	COBAS 8000	Spectrophotometry, Homogeneous Enzymatic Colorimetric
VLD_ (Calculated)	0 - 99	M/F	</= 30	NA	NA	mg/dL	COBAS 8000	Calculated Parameter
SODIUM	1 year - 18 year	M/F	138 - 145	160	120	mmol/L	COBAS 8000	ISE Indirect
	18 year - 99 year	M/F	136 - 145	160	120			
POTASSIUM	1 year - 18 year	M/F	3.4 - 4.7	6.2	2.8	mmol/L	COBAS 8000	ISE Indirect
	18 year - 99 year	M/F	3.5 - 5.1	6.2	2.8			
Chloride	0 days - 28 days	M/F	97 - 110	120	80	mmol/L	COBAS 8000	ISE Indirect
	28 days - 99 year		98 - 106					
EGFR	18-99	M/F	> 60	NA	NA	mL/min/1.73m2	COBAS 8000	Calculated Parameter
Hs-CRP	18 year - 99 year	M/F	Low risk for CAD: < 1.00 Average risk for CAD: 1.00 - 3.00 High risk for CAD: > 3.00	NA	NA	mg/L	BEHRING NEPHELOMETER II	Nephelometry, Particle- Enhanced Immunonephelometry

Verified by

Dr. Ashama Pimpalgaonkar
Head Dept. of Biochemistry

Approved by

Dr. Simi Bhatia
Director - Goregaon Reference Lab., Senior histopathologist,
Head Auto-immune section

SRL Diagnostics

SRL REFERENCE RANGE DOCUMENT - BIOCHEMISTRY

SRL Ltd
Prime Square Building, Plot No 1,
Gaiwadi Industrial Estate, S.V. Road, Goregaon
(W)
Mumbai – 400 062, Maharashtra, India

Test Name	Age	Gender	Reference Ranges	CH	CL	Unit	Instrument	Methodology
T3	18 years-20 years	M	91.0 - 218.0	218	91	ng/dL	COBAS 8000	COMPETITIVE ELECTROCHEM LUMINESCENCE IMMUNOASSAY
	> 20 years-99 years		80.0 - 200.0	200	80			
	18 years-20 years	F	Non-Pregnant Women 91.0 - 218.0 Pregnant Women 1st Trimester105.0 - 230.0 2nd Trimester129.0 - 262.0 3rd Trimester135.0 - 262.0	218	91			
	> 20 years-99 years		Non-Pregnant Women 80.0 - 200.0 Pregnant Women 1st Trimester105.0 - 230.0 2nd Trimester129.0 - 262.0 3rd Trimester135.0 - 262.0	200	80			
T4	18 years-20 years	M	5.91 - 13.20	13.20	5.91	µg/dL	COBAS 8000	COMPETITIVE ELECTROCHEM LUMINESCENCE IMMUNOASSAY
	> 20 years-99 years		5.10 - 14.10	14.10	5.10			
	18 years-20 years	F	Non Pregnant Women 5.91 - 13.20 Pregnant Women 1st Trimester: 7.33 - 14.80 2nd Trimester: 7.93 - 16.10 3rd Trimester: 6.95 - 15.70	13.20	5.91			
	> 20 years-99 years		Non-Pregnant Women 5.10 - 14.10 Pregnant Women 1st Trimester: 7.33 - 14.80 2nd Trimester: 7.93 - 16.10 3rd Trimester: 6.95 - 15.70	14.10	5.10			
TSH	18 years-20 years	M	0.510 - 4.300	4.300	0.510	µIU/mL	COBAS 8000	SANDWICH ELECTROCHEM LUMINESCENCE IMMUNOASSAY
	> 20 years-99 years		0.270 - 4.200	4.200	0.270			
	18 years-20 years	F	Non Pregnant Women 0.510 - 4.300 Pregnant Women 1st Trimester: 0.330 - 4.590 2nd Trimester: 0.350 - 4.100 3rd Trimester: 0.210 - 3.150	4.300	0.510			
	> 20 years-99 years		Non Pregnant Women 0.27 - 4.20 Pregnant Women 1st Trimester: 0.33 - 4.59 2nd Trimester: 0.35 - 4.10 3rd Trimester: 0.21 - 3.15	4.200	0.270			

Verified by
22/10/22
Dr. Kshama Pimpalgaonkar
Head Dept. of Biochemistry

Approved by
Dr. Simi Bhatia
Director - Goregaon Reference Lab., Senior histopathologist,
Head Auto-Immune section

SRL Diagnostics

SRL REFERENCE RANGE DOCUMENT - URINALYSIS

SRL Ltd.
Prime Square Building, Plot No 1,
Gaiwadi Industrial Estate, S.V. Road Goregaon (W)
Mumbai – 400 062.

Test Name	Age	Gender	Reference Ranges	CH	CL	Unit	Instrument	Methodology
Colour	18-99	M/F	-	NA	NA	-	AVE 772 INTEGRATED AUTOMATED SYSTEM	Urine Routine & Microscopy Examination ny Integrated Automated System.
Appearance	18-99	M/F	-	NA	NA	-	AVE 772 INTEGRATED AUTOMATED SYSTEM	Urine Routine & Microscopy Examination ny Integrated Automated System.
pH	18-99	M/F	5.0 –7.5	NA	NA	-	AVE 772 INTEGRATED AUTOMATED SYSTEM	Urine Routine & Microscopy Examination ny Integrated Automated System.
Specific Gravity	18-99	M/F	1.010 - 1.030	NA	NA	-	AVE 772 INTEGRATED AUTOMATED SYSTEM	Urine Routine & Microscopy Examination ny Integrated Automated System.
Glucose	18-99	M/F	Not Detected	> +++	NA	-	AVE 772 INTEGRATED AUTOMATED SYSTEM	Urine Routine & Microscopy Examination ny Integrated Automated System.
Protein	18-99	M/F	Not Detected	> +++	NA	-	AVE 772 INTEGRATED AUTOMATED SYSTEM	Urine Routine & Microscopy Examination ny Integrated Automated System.
Ketone	18-99	M/F	Not Detected	> +++	NA	-	AVE 772 INTEGRATED AUTOMATED SYSTEM	Urine Routine & Microscopy Examination ny Integrated Automated System.
Blood	18-99	M/F	Not Detected	> ++	NA	-	AVE 772 INTEGRATED AUTOMATED SYSTEM	Urine Routine & Microscopy Examination ny Integrated Automated System.
Bilirubin	18-99	M/F	Not Detected	>+++	NA	-	AVE 772 INTEGRATED AUTOMATED SYSTEM	Urine Routine & Microscopy Examination ny Integrated Automated System.
Urobilinogen	18-99	M/F	Normal	NA	NA	-	AVE 772 INTEGRATED AUTOMATED SYSTEM	Urine Routine & Microscopy Examination ny Integrated Automated System.

Nitrite	18-99	M/F	Not Detected	NA	NA	-	AVE 772 INTEGRATED AUTOMATED SYSTEM	Urine Routine & Microscopy Examination ny Integrated Automated System.
Leukocytes	18-99	M/F	Not Detected	NA	NA	-	AVE 772 INTEGRATED AUTOMATED SYSTEM	Urine Routine & Microscopy Examination ny Integrated Automated System.
WBC (Pus cells)	18-99	M/F	<5	NA	NA	cells/hpf	AVE 772 INTEGRATED AUTOMATED SYSTEM	Urine Routine & Microscopy Examination ny Integrated Automated System.
Epithelial Cells	18-99	M/F	<5	NA	NA	cells/hpf	AVE 772 INTEGRATED AUTOMATED SYSTEM	Urine Routine & Microscopy Examination ny Integrated Automated System.
RBC	18-99	M/F	Not Detected	>++	NA	cells/hpf	AVE 772 INTEGRATED AUTOMATED SYSTEM	Urine Routine & Microscopy Examination ny Integrated Automated System.
Casts	18-99	M/F	Not Detected	>++	NA	/lpf	AVE 772 INTEGRATED AUTOMATED SYSTEM	Urine Routine & Microscopy Examination ny Integrated Automated System.
Crystal	18-99	M/F	Not Detected	NA	NA	/hpf	AVE 772 INTEGRATED AUTOMATED SYSTEM	Urine Routine & Microscopy Examination ny Integrated Automated System.
Yeast	18-99	M/F	Not Detected	NA	NA	-	AVE 772 INTEGRATED AUTOMATED SYSTEM	Urine Routine & Microscopy Examination ny Integrated Automated System.
Bacteria	18-99	M/F	Not Detected	NA	NA	-	AVE 772 INTEGRATED AUTOMATED SYSTEM	Urine Routine & Microscopy Examination ny Integrated Automated System.

Verified by

Dr. Kshama Pimpalgaonkar
Head Dept. of Biochemistry

Approved by

Dr. Simi Bhatia
Director - Goregaon Reference Lab., Senior histopathologist,
Head Auto-immune section

PARAMETER	**ACTIVE** (N=47)		**PLACEBO** (N=47)	
	Day 0	**Day90**	**Day 0**	**Day90**
Liver Function Test				
Total Bilirubin (mg/dL)	0.60±0.23	0.61±0.29	0.96±2.55	0.58±0.23
Alkaline Phosphatase (IU/L)	113.63±45.44	114.21±43.89	117.06±41.12	113.67±41.78
AST-SGOT (U\L)	24.14±12.59	22.65±9.03	22.02±8.63	23.12±8.23
ALT – SGPT (U\L)	28.17±22.61	22.82±14.84	23.21±10.01	24.10±12.06
Renal Function Test				
Serum Creatinine (mg/dL)	0.90±0.18	0.92±0.8	0.89±0.21	0.89±0.19
Urea (mg/dL)	19.59±4.86	18.93±3.29	19.09±4.32	21.96±18.11
Uric Acid (mg/dL))	5.43±1.21	5.55±1.33	5.24±1.37	5.25±1.19
eGFR (mL/min/1.73m^2)	89.05±24.28	86.17±20.69	95.04±33.41	92.72±23.70
Sodium (mmol/L)	139.02±2.83	138.14±2.94	136.51±14.65	138.34±4.16
Potassium (mmol/L)	4.80±0.80	4.62±0.32	4.68±0.35	4.57±0.38
Chloride (mmol/L)	100.97±2.98	101.31±2.85	101.25±2.62	101.08±3.50

Supplementary Results

Supplementary Table 1 : Liver and kidney function tests performed at screening and final visits for active and placebo groups.

Values are expressed as Mean ± SD or median and inter-quartile range based on normal distribution. Independent T-test or Mann-Whitney U test was used to compute the difference between the groups. No significant difference was observed between Screening and final visit in both Calebin A and placebo groups.

PARAMETER	ACTIVE (N=47)		PLACEBO (N=47)	
	Day 0	**Day90**	**Day 0**	**Day90**
Hemoglobin (g/dL)	14.23±1.54	14.18±1.55	13.88±1.85	13.80±1.71
RBC (Million/µL)	4.85±0.31	4.91±0.56	4.88±0.44	4.94±0.36
Platelet Count (lakhs/mm^3)	2.50±0.59	2.53±0.55	2.72 ±0.54	3.10 ±0.66
Packed Cell Volume (%)	44.50±4.87	45.19±5.33	44.10±5.64	44.22±5.17
Mean Cell Volume (fL)	90.34±7.56	90.54±7.95	88.33±8.77	87.56±9.34
Mean Platelet Volume (fL)	9.88±1.70	10.19±1.52	9.98±1.56	9.95±1.61
Mean Corpuscular Hemoglobin (pg)	28.34±2.51	28.54±2.26	27.49±2.84	27.31±2.99
Mean Corpuscular Hemoglobin Concentration (g/dL)	33.57±1.76	33.52±1.85	33.21±1.98	33.17±2.16
Total Leukocyte Count (cell/mm^3)	8.82±2.85	8.51±2.48	9.28±2.56	8.92±2.34
Lymphocytes (%)	28.19±7.24	29.65±8.72	28.29±8.18	28.57±6.24
Eosinophils (%)	3.72±1.83	3.80±3.14	3.70±1.91	3.91±2.26
Monocytes (%)	4.06±2.66	3.88±2.89	4.29±2.85	4.36±3.03
Neutrophils (%)	63.74±8.67	61.58±14.13*	63.42±10.37	63.04±8.48
Basophils (%)	0.25±0.48	0.33±0.52	0.31±0.69	0.38±0.57

Supplementary Table 2: Hematological parameters for active and placebo groups.

Values are expressed as Mean ± SD. No significant difference was observed between Screening and final visit in both Calebin A and placebo groups, except neutrophil% which decreased in Calebin A group. *P<0.05;

Supplementary Table 3: **Urine analysis for active and placebo groups**.

PARAMETER	ACTIVE (N=47)		PLACEBO (N=47)	
	Screening Visit	**Visit 5**	**Screening Visit**	**Visit 5**
Colour				
Pale Yellow	32 (68.08 %)	32 (68.08 %)	37 (80.43 %)	30 (66.67 %)
Reddish	11 (23.40 %)	10 (21.27 %)	6 (13.04 %)	8 (17.78 %)
Yellow	4 (8.51 %)	5 (10.63 %)	3 (6.52 %)	7 (15.56 %)
Appearance				
Clear	37 (78.72 %)	33 (70.21 %)	35 (74.46 %)	34 (75.56 %)
Slightly Turbid	10 (21.27 %)	14 (29.78 %)	12 (25.53 %)	10 (22.22 %)
Turbid		0 (0.00 %)		1 (2.22 %)
Protein				
Present (+)	3 (6.38 %)	0 (0.00 %)	1 (2.17 %)	3 (6.81 %)
Negative (-)	32 (68.08 %)	36 (76.59 %)	32 (69.56 %)	31 (70.45 %)
Trace	1 (2.12 %)		3 (6.52 %)	
Nil	11 (23.40 %)	11 (23.40 %)	10 (21.73 %)	10 (22.72 %)
Glucose				
Positive	3 (6.38 %)	1 (2.12 %)	0 (0.00 %)	0 (0.00 %)
Negative	33 (70.21 %)	35 (74.46 %)	37 (78.72 %)	35 (77.78 %)
Nil	11 (23.40 %)	11 (23.40 %)	10 (21.27 %)	10 (22.22 %)
Ketone Bodies				
Positive	0 (0.00 %)	2 (4.25 %)	1 (2.12 %)	1 (2.22 %)
Negative	47 (100.00 %)	45 (95.74 %)	46 (97.87 %)	44 (97.78 %)
Urobilinogen				
Normal	36 (76.59 %)	23 (48.93 %)	37 (78.72 %)	24 (53.33 %)
Negative	11 (23.40 %)	24 (51.06 %)	10 (21.27 %)	21 (46.67 %)
Bilirubin				
Normal		1 (2.12 %)		1 (2.27 %)
Negative		46 (97.87 %)		43 (97.72 %)

Nitrites				
Positive	5 (10.63 %)	7 (14.89 %)	4 (8.51 %)	5 (11.11 %)
Negative	42 (89.36 %)	40 (85.10 %)	43 (91.48 %)	40 (88.89 %)
Cast				
Present	0 (0.00 %)		1 (2.12 %)	
Absent	36 (76.59 %)	36 (76.59 %)	36 (76.59 %)	35 (77.78 %)
Nil	11 (23.40 %)	11 (23.40 %)	10 (21.27 %)	10 (22.22 %)
Crystals				
Present	4 (8.51 %)	3 (6.38 %)	4 (8.51 %)	4 (88.89 %)
Absent	32 (68.08 %)	33 (70.21 %)	33 (70.21 %)	31 (68.89 %)
Nil	11 (23.40 %)	11 (23.40 %)	10 (21.27 %)	10 (22.22 %)
Specific Gravity	1.02±0.006	1.01±0.007	1.01±0.006	1.02±0.007
pH	6.23±0.45	6.24±0.40	6.32±0.57	6.30±0.38
Epithelial Cells				
0 – 1	13 (27.65 %)	13 (27.65 %)	12 (25.53 %)	9 (19.14 %)
1 – 2	9 (19.14 %)	8 (17.02 %)	8 (17.02 %)	11 (23.40 %)
2 – 3	4 (8.51 %)	10 (21.27 %)	10 (21.27 %)	8 (17.02 %)
3 – 4	7 (14.89 %)	6 (12.76 %)	5 (10.63 %)	7 (14.89 %)
3 – 5	7 (14.89 %)	4 (8.0510 %)	5 (10.63 %)	6 (12.76 %)
4 – 5	1 (212.00 %)	3 (6.38 %)	2 (4.25 %)	1 (2.12 %)
4 – 6	2 (4.25 %)	1 (2.12 %)	3 (6.38 %)	2 (4.25 %)
5 – 7	0 (0.00 %)	1 (2.12 %)	2 (4.25 %)	0 (0.00 %)
6 – 8	2 (4.25 %)		0 (0.00 %)	
8 – 10	2 (4.25 %)	0 (0.00 %)	0 (0.00 %)	1 (2.12 %)
Nil		1 (2.12 %)		17 (36.17 %)
RBC				
1 – 0	1 (2.12 %)	2 (4.25 %)	1 (2.12 %)	1 (2.22 %)
1 – 2	0 (0.00 %)	2 (4.25 %)	1 (2.12 %)	2 (4.44 %)
20 – 30	1 (2.12 %)	0 (0.00 %)	0 (0.00 %)	1 (2.22 %)
5 – 7	0 (0.00 %)	1 (2.12 %)	2 (4.25 %)	1 (2.22 %)
8 – 10		1 (2.12 %)		0 (0.00 %)
Not Detected	34 (72.34 %)	30 (63.82 %)	33 (70.21 %)	30 (66.67 %)

Nil	11 (23.40 %)	11 (23.40 %)	10 (21.27 %)	10 (22.22 %)

Values are expressed as N (percentage). No significant difference was observed between Screening and final visit in both Calebin A and placebo groups

1. M. Muhammed, M. Anju, P. Anjali, L. Prachi Subhash and V. *Kiran Kumar, EFFICACY AND TOLERABILITY OF A NOVEL FORMULATION FOR WEIGHT MANAGEMENT IN OBESE SUBJECTS: A RANDOMIZED, DOUBLE BLIND, PLACEBO CONTROLLED, CLINICAL STUDY, *International Journal of Ayurveda and Pharma Research*, 2016, **4**.