

Appendix – 1 INTERVENTION MODULE

Yoga module for T2D		Total: 60 min
Practice Name	Duration (min)	
1 Preparatory breathing, loosening & strengthening exercises) Urdhava-hastashvasan (Hand Stretch Breathing)) Kati-Shakti Vikasaka (Hip strengthening practices) (a) Forward and Backward bending (b) Twisting) Sarvangapushti (Limbs strengthening) (clockwise & anti-clockwise rotation)	10	
2 Surya Namaskara (Sun salutations)) 10 step fast Surya Namaskara 6 rounds) 12 step fast Surya Namaskara 1 round	10	
3 Asana practices	20	
) Trikonasana (Triangle pose)		
) Parivritta Trikonasana (Revolved Triangle pose)		
) Prasarita Padahasthasana (Wide-legged forward bend pose)		
) Mandukasana (Frog pose)		
) Vakrasana (Twisted pose)		
) Ardhamatsyendrasana (Half spinal twist pose)		
) Paschimothasana (Seated forward bend pose)		
) Ardha Ushtrasana (Half-Camel pose)		
) Bhujangasana (Cobra pose)		
) Dhanurasana (Bow pose)		
) Jatar Parivartanasana (Revolved abdomen twist pose)		
) Pavanamuktasana (Wind releasing pose)		
) Quick Relaxation Technique		
4 Kriya practices (cleansing practices)) Agnisara Kriya - 1 min) Kapalabhati - 60 breaths / minutes for 1 min followed by 1 min rest	3	
5 Pranayama practices) Nadishuddhi (Alternate nostril breathing) - 6 min) Bhramari (Humming bee breathing) - 4 min	10	
6 Deep Relaxation Technique - Shavasana (Corpse pose)	7	

Appendix-2INFORMEDCONSENT FORM



Informed Consent Form

based on WHO - ERC guidelines

SVYASA Prashanti Kutiram, Giddenahalli, Jigani Hobli, Anekal Taluk, Bengaluru - 560105, INDIA

Name of Principal Investigator: Dr. Ramesh M N

Informed Consent form for Yoga and Control groups

This Informed Consent Form is for men and women who we are inviting to participate in research on Yoga and its effect on Diabetes Mellitus related DNA damage & repair. The title of our research project is "*Role of yoga and its possible mechanism involved in Type 2 Diabetes mellitus related DNA damage and repair - A Randomized Control Trial* "

Name of Principal Investigator : Dr. Ramesh M N

Name of Organization : Swami Vivekananda Yoga Anusandhana Samsthana (SVYASA)

Name of Sponsor : University Grant Commission (UGC)

Name of Proposal and version : NA

This Informed Consent Form has two parts:

-) Information Sheet (to share information about the research with you)
-) Certificate of Consent (for signatures if you agree to take part)

You will be given a copy of the full Informed Consent Form

PART I: Information Sheet

Introduction

I am Dr. Ramesh M N working for the SVYASA University, a leading institution in the field of Yoga research. We are doing research on the effect of Yoga on the DNA damage & repair processes associated with Type 2 Diabetes Mellitus, which is affecting millions of our population adversely. Here, we would like to share information on the research that we do and invite you to be part of this research in case if you are interested to be part of that. You do not have to decide today whether or not you will participate in the research. Before you decide, you can talk to anyone you feel comfortable with about this research.

There may be some words that you do not understand. Please ask me to stop as we go through the information and I will take time to explain. If you have questions later, you can clarify them with me, or the resource persons associated with this study.

Purpose of the research

Number of people affected with diabetes is increasing at faster rate, particularly in India, and the present medical modalities are not able to contain the spread of the disease effectively. As Type 2 diabetes is closely associated with life style that we follow, we like to bring in alternative therapeutic system like Yoga, which is considered to be an effective approach in managing life style modification as part of the treatment. Hence, we like to understand how Yoga is working or helping in diabetes condition from modern scientific perspective, at molecular level as diabetes is considered to affect DNA damage & repair process.

Type of Research Intervention

Participants in this research is expected to practice a series of Surya Namaskar, Yoga asanas, Pranayamas (yogic breathing techniques) provided by a yoga instructor.

Participant selection

We are inviting all adults with Type 2 Diabetes Mellitus who are interested to participate in the research on the efficacy and mechanism of Yoga on T2DM related DNA damage & repair.

- *Do you know why we are asking you to take part in this study? Do you know what the study is about?*

Voluntary Participation

Your participation in this research is entirely voluntary. It is your choice whether to participate or not. You may change your mind later and stop participating even if you agreed earlier.

- *If you decide not to take part in this research study, do you know what your options are? Do you know that you do not have to take part in this research study, if you do not wish to? Do you have any questions?*

Include the following section only if the protocol is for a clinical trial:

Information on the Trial Drug: No Drug involve in trial but only a set of Yoga practices

You won't be asked to take any drugs as part of this study. But you can continue with your medicines, if any are there, as prescribed by your doctor. As part of this study, we request you to undergo certain yoga practices instructed by qualified yoga teachers.

Yoga practices are considered to be relatively safe to practise and not known to have any side effects. Also, if any practice is not appropriate for a particular condition (additional complication), it will be intimated to the participant and will be asked to either avoid or do it in a modified way.

Procedures and Protocol

A. Unfamiliar Procedures

If the protocol is for a clinical trial:

We need to compare the effect of Yoga on T2DM associated DNA damage & repair with non-Yoga practitioners and hence we need to compare the two groups. To do this, we will place people taking part in this research into two groups. The groups are selected by chance, as if by tossing a coin.

Participants in one group will be given the Yoga practices while participants in the other group don't practice Yoga but can continue with their regular exercises, if any. We will then compare which of the two has the best results.

The healthcare workers will be looking after you and the other participants very carefully during the study. If there is anything you are concerned about or that is bothering you about the research please talk to me or one of the other researchers)

If the protocol is for clinical research:

You will receive a Yoga therapeutic module specially designed and validated for Type 2 Diabetes Mellitus, instructed by trained and qualified Yoga instructor / teacher.

For any clinical study (if relevant):

We will take blood from your arm using a syringe and needle. Each time we will take about 15 ml.

In total, we will take about 30 ml. blood in twice, before and after 30 days of practice. At the end of the research, in 1 year, any leftover blood sample will be destroyed.

B. Description of the Process

-) In the first visit, a small amount of blood, equal to about 2 teaspoons (15 ml), will be taken from your arm with a syringe. We will also ask you a few questions about your general health and measure how tall you are and how much you weigh.*
-) At the next visit, which will be after 30 days of Yoga practice, a small amount of blood (15 ml) will be again collected and you will again be asked some questions about your health.*

Duration

The research takes place over 32 days in total. During that time, it will be necessary for you to come to the clinic/hospital/health facility 30 days, for 1 hours each day for yoga practice. Blood samples will be collected from you only twice in this study; once, before the start of intervention (30day yoga practice) and next, at the end of 30th day (after the intervention ends).

- Can you tell me if you remember the number of times that we are asking you to come to the hospital to complete the treatment? How much blood will be taken from your veins, using a syringe and needle? Over how many weeks? Etc. Do you have any other questions? Do you want me to go through the procedures again?*

Side Effects

As it is understood, Yoga practices don't have any side effects. We also inform you about the contra indications of the practices associated with any additional complications, in case if you have any. In case of any uneasiness or any complication you are free to stop the practice. If this is necessary, we will discuss it together with you and you will always be consulted before we move to the next step.

Risks

As such, we don't foresee any risks associated with yoga practices. But in case of any accidental fall or injury, we will provide you medical attention.

Benefits

If you participate in this research, you will have the following benefits:

-) Opportunity to use Yoga, one of the best life style modification programme for the treatment of T2DM at no cost to you.*
-) Learn Yoga practices which is also good for positive health and have an opportunity to share with family and friends*
-) Yoga practices, as such is very cost effective and impart a sense of confidence and well being*
-) Your participation helps us to further understand the benefits of Yoga from a scientific perspective and promote the same to affected people in the society as part of their treatment approaches.*

Reimbursements

We don't have any provision to provide any incentives for your participation in the study.

- Can you tell me if you have understood correctly the benefits that you will have if you take part in the study? Do you have any other questions?*

Confidentiality

We will maintain the information pertaining to all the participants confidentially.

The assessment sheets and blood sample obtained will be coded with a number. No identifying information will be associated with your sample. The code number will be kept confidentially by the principal investigator and will not be available to the staff of the study. All information obtained in this study is strictly confidential unless disclosure is required by law

- Did you understand the procedures that we will be using to make sure that any information that we as researchers collect about you will remain confidential? Do you have any questions about them?*

Sharing the Results

The knowledge that we get from doing this research can be shared with you through community meetings before it is made widely available to the public. Confidential information will not be shared. After these meetings, we will publish the results in order that other interested people may learn from our research.

Right to Refuse or Withdraw

You do not have to take part in this research if you do not wish to do so. You may also stop participating in the research at any time you choose. It is your choice and all of your rights will still be respected.

Whom to Contact

If you have any questions you may ask them now or later, even after the study has started. If you wish to ask questions later, you may contact any of the following:

Dr Ramesh M N, SVYASA University

Tel: 080-22639915

E-Mail: ramesh.mavathur@svyasa.org

This proposal has been reviewed and approved by Institutional Ethics Committee [IEC], which is a committee whose task it is to make sure that research participants are protected from harm. If you wish to find about more about the IRB, contact

Dr R Nagarathna,

Chairman,

Institutional Ethics Committee,

S-VYASA University

Ph: 080-22639983

- *Do you know that you do not have to take part in this study if you do not wish to? You can say No if you wish to? Do you know that you can ask me questions later, if you wish to? Do you know that I have given the contact details of the person who can give you more information about the study? Etc.*

You can ask me any more questions about any part of the research study, if you wish to. Do you have any questions?

PART II: Certificate of Consent

I have read the foregoing information, or it has been read to me. I have had the opportunity to ask questions about it and any questions that I have asked have been answered to my satisfaction. I consent voluntarily to participate as a participant in this research.

Print Name of Participant:

Signature of Participant:

Date:

If illiterate

A literate witness must sign (if possible, this person should be selected by the participant and should have no connection to the research team). Participants who are illiterate should include their thumb-print as well.

I have witnessed the accurate reading of the consent form to the potential participant, and the individual has had the opportunity to ask questions. I confirm that the individual has given consent freely.

Print name of witness:

AND

Thumb print of participant

Signature of witness:

Date:

Statement by the researcher/person taking consent

I have accurately read out the information sheet to the potential participant, and to the best of my ability made sure that the participant understands that the following will be done:

- 1. Intervention
- 2. Assessment
- 3.

I confirm that the participant was given an opportunity to ask questions about the study, and all the questions asked by the participant have been answered correctly and to the best of my ability. I confirm that the individual has not been coerced into giving consent, and the consent has been given freely and voluntarily.

A copy of this ICF has been provided to the participant.

Print Name of Researcher/person taking the consent:

Signature of Researcher /person taking the consent:

Date:

Appendix-3 INSTITUTIONAL ETHICS COMMITTEE [IEC]

Letter no.RES/IEC-SVYASA/119/2017



स्वामी विवेकानन्द योग अनुसंधान संस्थान
Swami Vivekananda Yoga Anusandhāna Samsthāna

(Declared as Deemed-to-be University under Section 3 of the UGC Act, 1956)

Eknath Bhavan, # 19, Gowdipuram Circle, Kompo Gowde Nagar, Bangalore - 560 019

Ph: 080 - 2981 2669, Telex: 080 - 2960 8645

E-mail: svyasa@svyasa.org Website: www.svyasa.org

RES/IEC-SVYASA/119/2017

05th June, 2018

To,
Dr. Ramesh M N,
Professor,
Division of Yoga and Life Sciences,
S-VYASA University,
Bengaluru.

Reference:

"Role of yoga and its possible mechanism involved in Type 2 Diabetes Mellitus related DNA damage and repair - A Randomized Control Trial"
- Committee Approval of the above-mentioned study.

Dear Dr. Ramesh M N,

We have received from you the following study related documents vide your letter dated 21 March 2018:

1	Project Proposal
2	Informed consent form

Ethics committee meeting was held on **27 March 2018** between 2:00 PM and 5:00 PM at Eknath Bhavan, Bengaluru. Above documents were examined and discussed in the meeting. After due consideration, the committee has decided to approve conducting the aforementioned study.



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Ph: 080 - 2661 2889, Telefax: 080 - 2660 8645

E-mail: svyasa@svyasa.org Website: www.svyasa.org

This is to confirm that neither Dr. Ramesh M N nor any staff participating in this study was involved in the voting procedures and decision making.


The Institutional Review Board / Institutional Ethics Committee (IEC) is expected to be informed about the progress of the study / any changes in the protocol and patient information / informed consent. The investigators are also expected to submit a copy of the final report to IEC for records.

This approval is valid up to the completion of the study at the site.

Please submit to the IEC, the status report of the study as per the SOPs.

The IEC is organized & operates according to the requirements of ICH-GCP, Indian Council of Medical Research Guidelines & Schedule Y.

Best Wishes,


Dr. Sanjib Kumar Patra,
Member Secretary,
Institutional Ethics Committee,
S-VYASA, Bengaluru.

APPROVED

INSTITUTIONAL ETHICS COMMITTEE
SVYASA, BANGALORE

Appendix – 4 Structural Equation Model (SEM) based Mediation Analysis Results

Structural Equation Model (SEM) based mediation analysis results obtained using ‘R’ statistical software (version 3.6.1) and ‘lavaan’ statistical package (version 0.6-5) is given below. Though, mediation involving only TM (DNA damage marker) is discussed in the article as it was sufficient to explain the question of mediation, mediation results involving OTM is also separately analysed and reported here.

SEM based mediation analysis results

lavaan 0.6-5 ended normally after 61 iterations

Estimator	ML
Optimization method	NLMINB
Number of free parameters	11
Number of observations	45
Model Test User Model:	
Test statistic	0.841
Degrees of freedom	1
P-value (Chi-square)	0.359
Model Test Baseline Model:	
Test statistic	40.603
Degrees of freedom	6
P-value	0.000
User Model versus Baseline Model:	
Comparative Fit Index (CFI)	1.000
Tucker-Lewis Index (TLI)	1.027
Loglikelihood and Information Criteria:	
Loglikelihood user model (H0)	-599.343
Loglikelihood unrestricted model (H1)	-598.922
Akaike (AIC)	1220.686
Bayesian (BIC)	1240.559
Sample-size adjusted Bayesian (BIC)	1206.079
Root Mean Square Error of Approximation:	
RMSEA	0.000
90 Percent confidence interval - lower	0.000
90 Percent confidence interval - upper	0.382
P-value RMSEA <= 0.05	0.385
Standardized Root Mean Square Residual:	
SRMR	0.036
Parameter Estimates:	
Standard errors	Bootstrap
Number of requested bootstrap draws	1000
Number of successful bootstrap draws	1000

Above results are for Tail Moment (TM) as the dependent variable

SEM mediation result using DNA damage marker - TM (Tail Moment)

		Estimate	Std.Err	z-value	P(> z)	ci.lower	ci.upper
Regressions:							
TM_post ~ Group	(c)	-0.150	2.112	-0.071	0.944	-4.230	4.318
OHdG_post ~ Group	(a1)	-60.395	15.118	-3.995	0.000	-90.069	-33.064
OGG1_post ~ Group	(a2)	17.550	8.006	2.192	0.028	1.294	33.316
TM_post ~ OHdG_post	(b1)	0.069	0.021	3.262	0.001	0.029	0.112
TM_post ~ OGG1_post	(b2)	-0.089	0.029	-3.114	0.002	-0.147	-0.038
Intercepts:							
.TM_post		4.660	5.103	0.913	0.361	-5.663	14.714
.OHdG_post		267.511	11.734	22.798	0.000	246.752	290.257
.OGG1_post		61.751	6.288	9.820	0.000	49.121	73.642
Variances:							
.TM_post		39.341	7.018	5.606	0.000	22.425	49.814
.OHdG_post		2732.351	501.464	5.449	0.000	1675.641	3630.262
.OGG1_post		691.350	151.244	4.571	0.000	380.215	986.621
Defined Parameters:							
a1b1		-4.174	1.789	-2.334	0.020	-8.412	-1.395
a2b2		-1.563	0.842	-1.856	0.063	-3.338	-0.104
totindefect		-5.737	2.019	-2.841	0.005	-10.173	-2.558
total		-5.886	2.197	-2.679	0.007	-10.417	-1.777

5.0 LIST OF PUBLICATIONS FROM THIS DOCTORAL THESIS

Article title	Authors	Journal	Publisher	Impact Factor
Role of Yoga and its Plausible Mechanism in the Mitigation of DNA Damage in Type-2 Diabetes: A Randomized Clinical Trial	Rajesh Nair, Dr. Mithila M V, Dr.Ramesh M N	Annals of Behavioral Medicine	Oxford University Press	4.480