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Effect of Photo-Bio modulation on lipid profile in Patients with type 2 diabetes mellitus: A Randomized Clinical Trial

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ABSTRACT

Objective: to investigate the low level laser therapy (LLLT) efficiency by using laser watch as an adjunctive therapy of dyslipidemia in type 2 diabetes mellitus (T2DM) patients.

Methods: The study included sixty adult patients with diabetic dyslipidemia of both gender. They were split into two groups. Study group received anti diabetic drugs along with laser watch therapy (3 sessions /week for 12 weeks), while control group received only anti diabetic drugs. Blood sugar (FBS, 2HPP and HbA1C) and lipid panel (TG, TC, LDL and HDL) were measured before and at completion of the study.

Results: A significant improvement in blood sugar and serum lipid profile was seen in both groups ($P < 0.001$), the study group, however, displayed more significant outcomes ($P < 0.001$).

Conclusion: LLLT using laser watch can be used as a complementary treatment for dyslipidemia in T2DM patients to improve blood lipid profile and blood sugar.

Keywords: *laser watch, low level Laser therapy, Type 2 diabetes mellitus (T2DM), Lipid profile.*

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INTRODUCTION

Diabetes mellitus (DM) necessitates ongoing medical attention as it has reached epidemic levels (1). According to the Diabetes Atlas, 2020, there are 463 million patients with DM globally. They also stated that patients will count up to 578 and 640 million patients by 2030 and 2040 respectively (2). T2DM represents more than 90% of diabetes cases worldwide and is characterized by persistently hyperglycemia due to lack of or resistance to insulin (3). Diabetic patients are at risk of both micro and macro-vascular hazards that leads to early death (4).

Dyslipidemia is very common among diabetic patients affecting around 72-85 % of patients (5). Increased plasma triglyceride (TG), low high density lipoprotein (HDL) cholesterol levels, and an increase in low density lipoprotein (LDL) cholesterol particles are the defining characteristics of diabetic dyslipidemia. Insulin resistance or insufficiency affects important enzymes and metabolic pathways involved in lipid metabolism that leads to increased free fatty acid flow (6). Dyslipidemia increases the mortality risk in diabetes patients as it increases atherosclerosis risk and consequently increases incidence of stroke and cardiovascular risk (7). Consequently for preventing that, it requires early detection and effective care of dyslipidemia (8).Treatment of dyslipidemia includes dietary modifications, physical activity, good glycemic control and lipid-lowering medications (9).

Photo-bio modulation (PBM) or LLLT is secured noninvasive technique that does not produce heat, sound or vibration. It produces a single wavelength of light that has the characteristics of brightness, mono-chromaticity, directionality and spatial and temporal coherence (10). LLL has 300-10,600 nm wavelength, 0-5000 Hz pulse rate, its 0.00-0.1 W power output, 0.01-100 J/cm2 dosage and 0.01-10 W/cm2 intensity (11).

Transcutaneous laser blood irradiation impacts the entire body because the laser light is focused continuously on a region with undamaged skin and many blood vessels (like the forearm) (12). The laser watch is the newest innovation in laser medicine and is applied before the wrist (13). It increases the arterio-venous oxygen difference and enhances oxidation of pyruvate and glucose. It stimulates synthesis of nitric oxide (NO) and adenosine triphosphate (ATP) (14). It enhances microcirculation, reduces tissue hypoxia, promotes tissue oxygenation, restores normal tissue metabolism that makes laser watch has numerous therapeutic applications in multiple and complex diseases as DM (15-16). According to Litscher's study, using laser watch lowers levels of glucose, cholesterol, LDL, and very low density lipoprotein (VLDL) and improves the immune and hormonal functions (13).

Thus, the purpose of study to investigate the effectiveness of laser watches along with standard medical treatment in treatment of diabetic dyslipidemia.

PATIENTS AND METHODS

Participants and study design

A randomized clinical trial was carried out between July 2021 and February 2022. Regardless of gender or body mass index (BMI), sixty clinically stable patients with T2DM and dyslipidemia (LDL more than130 mg/dl - HDL less than 50 mg/ dl-TG more than 150 mg/dl - Total cholesterol (TC) more than or equal 200 mg/dl) were enrolled in the trial. Their HA1C levels were ≥ 7 % and ≤ 9 % and they had begun their medical treatment more than a year ago. Also, their ages ranged from 40 to 60. The patients were selected from the internal medicine outpatient clinics of Kasr Al-Aini Hospital

Participants had none of the following exclusion conditions: taking specific drugs that could alter the validity of the test results or influencing blood cholesterol and weight as corticosteroids or diuretics; uncontrolled diseases as liver or renal failure, cardiovascular instability (unstable angina, myocardial infarction, severe hypo- or hypertension, arrhythmias and congestive heart failure) and severe autonomic neuropathy, as they would impact response to treatment; photosensitivity reaction; active infection, wound, burn, allergy or another external injury to laser treatment area; smokers and alcoholics; hypothyroidism; anemia, hemorrhagic disorders or history of cancer; pregnant women, breast-feeding, or planning pregnancy before the study ended; mental illness as schizophrenia or dementia.

The patients were assigned into two equal groups randomly: the study group (n=30) had LLLT on the wrist for 12 weeks (3 sessions /week) along with hypoglycemic drugs (Metformin and vildagliptin), while the control group (n=30), received only hypoglycemic drugs.

A coworker who was both independent of the study and blinded to it carried out the randomization by taking sealed, opaque envelopes from a box and randomly placing the group description into each of them.

All study participants were given information on the procedure, hazards, and anticipated benefits. Before enrollment a written consent was signed by all participants. All participants underwent a thorough examination prior to beginning the study. The Ethical Committee of the Faculty of Physical Therapy at Cairo University reviewed and authorized the study (P.T.REC/012/003313).

Evaluation procedures

Anthropometric measurement

Body weight, height and waist circumference (WC) was measured at baseline and BMI was calculated using the following formula:

BMI= weight (kg) / [height (m)] 2 (17)

Laboratory analysis

Assessment of blood sugar and lipid profile was done for both groups before and after study completion (after 12 weeks).

Intervention with low level laser treatment

A semiconductor LLL medical device, laser watch (model: BS-W11, China), that is utilized for irradiation of extravascular blood through ulnar and radial vessels. The application parameters and characteristics of laser watch radiation are represented in table 1.

Medical device experts at the National Institute of Laser Enhanced Sciences, Cairo University, Egypt, analyzed and examined the device to certify that it has collimation, coherence, and monochromatic qualities.

TABLE 1: The application parameters and characteristics of laser watch radiation

Parameters	**Value**
Site of applications:	At wrist of the non-dominant hand to prevent interference with daily activities of the patients
Monochromatic wave length (nm)	650
Maximum power produced by a single laser output (W)	0.005
A spot's diameter (cm)	0.2
A spot's size (cm^2)	0.03
Power density (w/cm^2)	0.16
Radiation time (s)	1800
Energy density (J/cm^2)	288
Energy (J)	8.64
Mode for terminal laser output	Continuous
Session Duration	Thirty minutes
Laser beams numbers	Ten
Time	Patients need to fast four hours in the morning prior the session to prevent rise in blood sugar levels
Total duration of treatment	Three times a week for 12 consecutive weeks
Type of beam	(Red) infrared laser light
Instability of the terminal laser output	± Ten percentage
Mode of display	Liquid crystal display
Safety class	3R-class laser product, internally powered supply apparatus

Calculation of sample size

G*Power statistical program (version 3.1.9.2; Germany) was used to calculate the sample size. Type I error frequency was established at 5% (= 0.05), while the type II error frequency was established at 80% power (β = 0.2).The ideal sample number was found to be n = 60.

STATISTICAL ANALYSIS

Data were processed through using statistical package for the Social Sciences (SPSS) version 28. Unpaired t test and Mann-Whitney test were used for comparisons between groups for normally distributed quantitative variables and non-normally distributed quantitative variables respectively. Paired t test and Wilcoxon signed rank test were used for comparisons between pre and post values in each group .Chi square ($\chi 2$) test was performed for comparing categorical data. P-values less than 0.05 were considered as statistically significant

RESULTS

Data was extracted from 60 patients with diabetic dyslipidemia that completed the study. Recruitment, exclusion, evaluation, and intervention are all illustrated in (Figure 1)

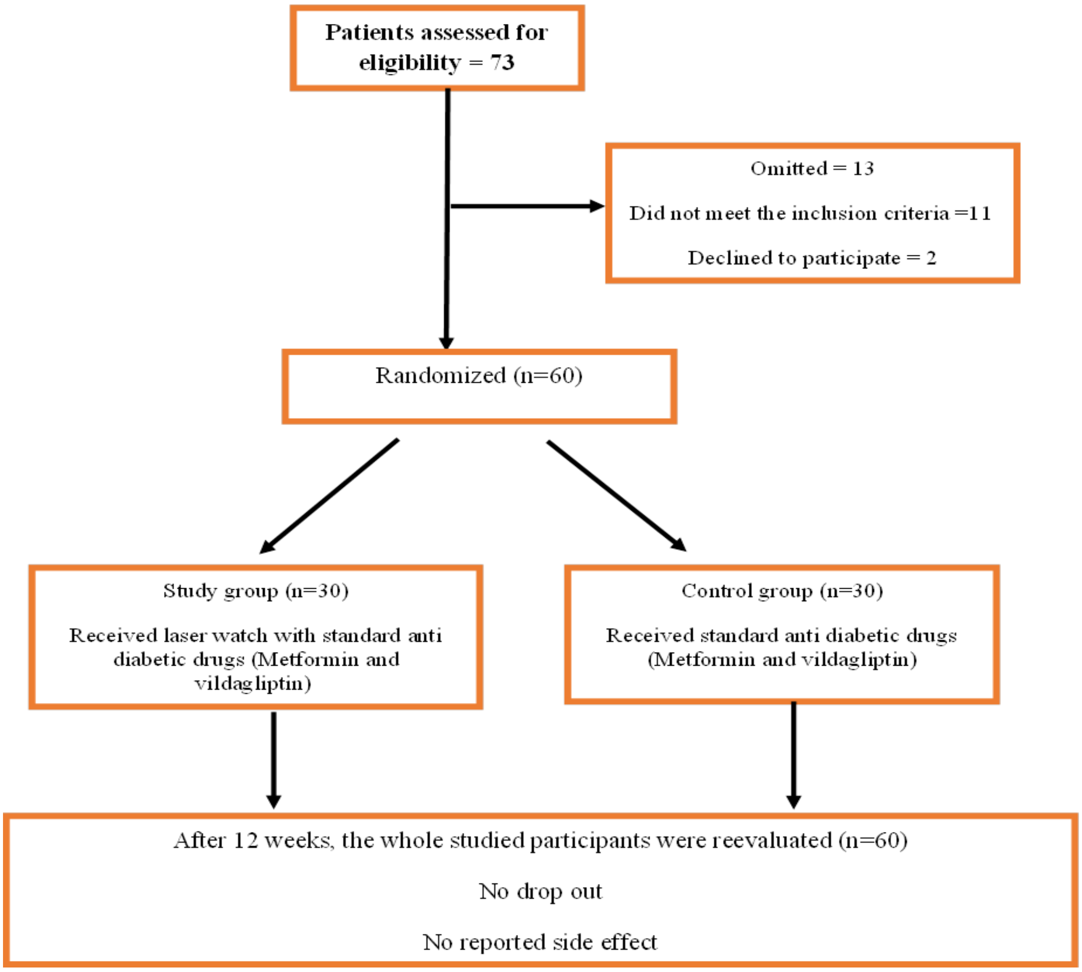

FIGURE 1: Flow chart of studied participants

Baseline factors such as age, height, weight, BMI, WC, blood sugar (HBA1c, FBS, 2HPP), and lipid profile levels (TG, T. CHOL, LDL, HDL,T. CHOL/HDL, and LDL-C/HDL) did not significantly differ between the groups (P value > 0.05), as demonstrated in table 2.

TABLE 2: The study participants' baseline characteristics

Characteristics (Mean ± SD)	Study group (N=30)	Control group (N=30)	P value
Females/males [N (%)]	22 (73%) / 8 (27%)	23 (76.6%) / 7 (23.3%)	0.874
Age (y)	53.7 ± 3.78	54.15 ± 4.15	0.66
Height (m)	1.61± 0.05	1.62± 0.06	0.183
Weight (Kg)	73.28 ± 6.8	73.55 ± 8.53	0.746
BMI (kg/m2)	28.6±33.57	28.03±3.8	0.52
Male **WC** (cm) Female	104.18± 2.79 94.63 8± 3.07	104.25± 3.22 93.888± 3.83	0.957 0.546
HBA1C (%)	7.54 ± 0.30	7.52 ± 0.26	0.760
FBG (mg/dl)	155.19 ± 6.29	153.8 2± 5.07	0.379
2h PPBG (mg/dl)	217.59 ± 10.42	219.32 ± 9.38	0.520
TG (mg/dl)	178.44 ± 15.84	177.29 ± 15.35	0.327
T. CHOL (mg/dl)	219.81± 10.87	218.36 ± 11.47	0.076
LDL	140.00 ± 7.35	140.32 ± 7.02	0.498
HDL Male Female	38.00 ± 2.14 41.88 ± 5.06	37.75 ± 2.22 40.62 ± 3.90	0.787 0.440
T. CHOL / HDL Male Female	5.78 ± 0.53 5.24 ± 0.87	5.79 ± 0.63 5.37 ± 0.62	0.566 0.926
LDL-C/HDL Male Female	3.68 ± 0.42 3.34 ± 0.59	3.71 ± 0.48 3.45 ± 0.37	0.820 0.458

WC: Waist circumference, BMI: body mass index, HBA1C, Hemoglobin A1C, FBG: Fasting blood sugar, 2hPPBS: 2hour post prandial blood sugar, T. CHOL: total cholesterol, TG: triglyceride, HDL: high-density lipoprotein, LDL: low-density lipoprotein.

As demonstrated in table 3, there was a significant reduction in HbA1C, FBG, and 2HPP following the treatment in both groups, with more significant outcomes in the study group in comparison to the control group (p < 0. 001).

TABLE 3: Blood sugar levels comparison before and after the intervention (12 Weeks).

Variable	Study group (n=30)				control group (n=30)				P value between groups
	Pre Mean ± SD	Post Mean ± SD	% change	P value	Pre Mean ± SD	Post Mean ± SD	% change	P value	
HBA1c	7.54 ± 0.30	6.36 ± 0.22	-15.7	<0.001	7.52 ± 0.26	6.91 ± 0.21	-8.11	<0.001	<0.001
FBG	155.19 ± 6.29	128.52 ± 4.91	-17.18	<0.001	153.8 2± 5.07	141.32 ± 3.50	-8.12	<0.001	<0.001
2h PPBG	217.59 ± 10.42	182.37 ± 7.79	-16.18	<0.001	219.32 ± 9.38	201.96 ± 6.87	-7.91	<0.001	<0.001

HBA1C: Hemoglobin A1C, FBG: Fasting blood sugar, 2hPPBS: 2hour post prandial blood sugar.

In comparison to the control group, there was a more substantial rise in HDL concentration and a significant decrease in TG, T.CHOL, LDL, T. CHOL/HDL, and LDL-C/HDL in the study group (P< 0.001), as shown in table (4)

TABLE 4: Comparison of Pre and post intervention for Lipid Components

	Study group (n=30)				**control group (n=30)**				**P value between groups**
	Pre	**Post**	**% change**	**P value**	**Pre**	**Post**	**% change**	**P value**	
	Mean± SD	**Mean ± SD**			**Mean± SD**	**Mean ± SD**			
TG	178.44 ± 15.84	155.96 ± 14.78	-12.59	<0.001	177.29 ± 15.35	166.39 ± 14.43	-6.14	<0.001	0.011
T. CHOL	219.81± 10.87	199.19 ± 10.49	-9.38	<0.001	218.36 ± 11.47	208.75 ± 10.43	-4.40	<0.001	<0.001
LDL	140.00 ± 7.35	120.59 ± 7.13	-13.86	<0.001	140.32 ± 7.02	131.14 ± 5.97	-6.54	<0.001	<0.001
HDL									
Male	38.00 ± 2.14	43.91 ± 2.07	15.55	<0.001	37.75 ± 2.22	40.67 ± 2.42	7.73	<0.001	<0.001
Female	41.88 ± 5.06	47.50 ± 4.24	13.4	<0.001	40.62 ± 3.90	43.44 ± 3.85	6.94	<0.001	<0.001
T. CHOL / HDL									
Male	5.78 ± 0.53	4.53± 0.31	-21.62	<0.001	5.79 ± 0.63	5.13 ± 0.42	-11.39	<0.001	<0.001
Female	5.24 ± 0.87	4.19 ± 0.39	-20.03	<0.001	5.37 ± 0.62	4.80 ± 0.47	-10.61	<0.001	<0.001
LDL-C/HDL									
Male	3.68 ± 0.42	2.39±0.19	-35.05	<0.001	3.71 ± 0.48	3.22 ± 0.33	-13.20	<0.001	<0.001
Female	3.34 ± 0.59	2.53 ± 0.26	-24.25	<0.001	3.45 ± 0.37	3.01 ± 0.28	-12.75	<0.001	<0.001

T. CHOL: total cholesterol, TG: triglyceride, HDL: high-density lipoprotein, LDL: low-density lipoprotein.

DISCUSSION

Among the main reasons for cardiovascular diseases and fatality in DM is dyslipidemia (18). LLLT has been suggested to decrease cholesterol-genesis and hence lower cholesterol and triglyceride levels (19). The aim of the study was to investigate effect of laser watch on T2DM lipid profile.

The study's findings suggested that using laser watch and hypoglycemic drugs dramatically lowers blood sugar in T2DM patients (FBS, 2HPP, and HbA1C). These reductions were 17.18%, 16.18%, and 15.7%, respectively, as opposed to 8.12%, 7.91%, and 8.11% among control group (P < 0.001). Additionally, study group had even more substantial results than the control group, with both having statistically significant increases in HDL and decreases in

TG, TC and LDL. Within study group, TC, TG and LDL decreased by 9.38%, 12.59%, and 13.86%, respectively, while HDL increased by 15.55% in males and 13.4% in females compared to baseline readings. In contrast to control group, TC, TG, and LDL declined by 4.4%, 6.14, and 6.54%, respectively, while HDL increased by 7.73% in men and 6.94% in women ($P < 0.001$).

Our findings support Serry et al conclusions that extravascular laser blood irradiation by laser watch lowers blood sugar, with decreases in FBG and HbA1C of 14.95 and 15.42%, respectively in comparison to 8.77 and 8.28% in the control group (20).

Our results also support a meta-analysis conducted by Kazemikhoo et al and other studies that suggested that intravenous laser therapy dramatically lowers blood glucose levels in T2DM and can be utilized as added therapy (21-23).

Up to our Knowledge, This is the initial investigation on the effect of a laser watch on lipid profile in T2DM as a result; we relied on previously published research on the impact of transcutaneous or intravenous laser blood irradiation (ILIB) on lipid profiles.

According to Hakami et al, LLLT has an impact on the in vitro lipid and glycemic profiles of chosen healthy participants. Consequently, the application of LLLT may have therapeutic benefits for DM and dyslipidemia (24).

Melekhovets et al reported that ILIB decreases level of TG, TC and LDL in patients with dyslipidemia solely or with hypothyroidism, and this is consistent with our findings. However, ILIB was used for just one month as opposed to our trial where laser watch was used for 12 weeks (25).

Additionally, Liu observed that patients with cerebral infarction or coronary heart disease who get intranasal laser therapy have improved blood lipid profiles (26).

In a pilot investigation, the impact of systemic trans-mucosal and/or transcutaneous laser therapy on lipid profiles (TC, HDL, LDL, and TG) and blood sugar at 30 and 60 days was examined. The findings demonstrated the safety of using ILIB for controlling lipid profile and blood glucose, regardless of the irradiation route (either trans mucosal or transcutaneous) (27), Results therefore agree with us and with previous reports (12, 19).

Said and Elnhas came to the conclusion that LLLT applied to the abdomen has reported a substantial drop in TG, TC, and LDL with percentages of improvement (decrease) 13.26%, 7.28%, and 6.79%, respectively, and non-significant effect on HDL (28) and are therefore in keeping with prior results (19, 29-33). This somewhat matches our findings, however we observed a higher percentage of improvement, and HDL levels greatly improved, correlating with previous studies that also showed a considerable rise in HDL (34-36).

This improvement can also be explained by the fact that lasers promote lipid peroxidation and boost superoxide generation. The lipids in the cell membrane are degraded by increased generation of reactive oxygen species. Lipids and fatty material enter the interstitial space through temporary pores created in the cell membrane, where the lymphatic system eliminates the fatty waste [37]. It might be accounted for by the possibility that the LLLT could modify the intracellular redox state and the potential of the mitochondria membrane, leading to an increase in the rate of ADP-ATP exchange. By modifying the transcription factors necessary for the expression of crucial genes involved in the biosynthetic pathway, these mitochondrial alterations may decrease cholesterol genesis (19, 29).

Maahs et al stated that better control of blood glucose can partially improve diabetes dyslipidemia (38). With good glycemic control in DM, LDL catabolism increased and VLDL levels decreased due to decreased glycation and increased LDL receptors, which in turn resulted in lower levels of TC and TG (39-40). This can explain improvement of lipid profile in the control group.

Despite that the outcomes are encouraging; the trial had certain limitations due to the small number of patients enrolled. As a result, more research with more participants and longer periods of follow- are required.

CONCLUSION

The study's overall findings show that using a laser watch as an additional therapy beside standard treatment to treat people with T2DM and dyslipidemia is safe and effective.

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CONFLICTS OF INTEREST

No authors have disclosed any conflicts of interest.

REFERENCES

1. American Diabetes Association. Introduction: Standards of medical care in diabetes – 2018. Diabetes Care. 2018; 41(Suppl. 1):S1–S2; doi: 10.2337/dc18-Sint01
2. IDF Diabetes Atlas 2019: Worldwide toll of diabetes. [Jun; 2020]; http://www.diabetesatlas.org/en/sections/worldwide-toll-of-diabetes.html 2020. Federation I. D. (2019). IDF diabetes atlas ninth. Dunia: IDF.
3. Baynest HW. Classification, pathophysiology, diagnosis and management of diabetes mellitus. J Diabetes Metab. 2015; 6(5):1000541; doi: 10.4172/2155-6156.1000541.
4. Whiting DR, Guariguata L, Weil C, Shaw J. IDF diabetes atlas: global estimates of the prevalence of diabetes for 2011 and 2030. Diabetes Res Clin Pract. 2011 Dec; 94(3): 311-21. doi: 10.1016/j.diabres.2011.10.029. Epub 2011 Nov 12. PMID: 22079683.
5. Jialal I, Singh G. Management of diabetic dyslipidemia: An update. World J Diabetes. 2019 May 15; 10(5):280-290. doi: 10.4239/wjd.v10.i5.280. PMID: 31139315; PMCID: PMC6522756.
6. Mithal A, Majhi D, Shunmugavelu M, Talwarkar PG, Vasnawala H, Raza AS. Prevalence of dyslipidemia in adult Indian diabetic patients: A cross sectional study (SOLID). Indian J Endocrinol Metab. 2014 Sep; 18(5): 642-7. doi: 10.4103/2230-8210.139220. PMID: 25285280; PMCID: PMC4171886.
7. Qi L, Ding X, Tang W, Li Q, Mao D, Wang Y. Prevalence and Risk Factors Associated with Dyslipidemia in Chongqing, China. Int J Environ Res Public Health. 2015 Oct 26; 12(10):13455-65. doi: 10.3390/ijerph121013455. PMID: 26516874; PMCID: PMC4627042.
8. Lazarte J, Hegele RA. Dyslipidemia management in adults with diabetes. Canadian journal of diabetes. 2020 Feb 1; 44(1):53–60. doi: 10.1016/j.jcjd.2019.07.003.
9. Banach M, Surma S, Reiner Z, Katsiki N, Penson PE, Fras Z, et al. Personalized management of dyslipidemias in patients with diabetes—it is time for a new approach (2022). Cardiovasc Diabetol.2022: 21, 263 https://doi.org/10.1186/s12933-022-01684-5.
10. Verma SK, Maheshwari S, Singh RK, Chaudhari PK. Laser in dentistry: an innovative tool in modern dental practice. Natl J Maxillofac Surg. 2012; 3(2):124–132; doi: 10.4103/0975-5950.111342.
11. Lin F, Josephs SF, Alexandrescu DT, Ramos F, Bogin V, Gammill V, et al. Lasers, stem cells, and COPD. J Transl Med. 2010 Feb; 8:16; doi: 10.1186/1479-5876-8-16. PMID: 20158898; PMCID: PMC2830167.
12. Makela AM. Theoretical backgrounds for light application in diabetes. Laser Florence; 2004.
13. Litscher G, Litscher D. A laser watch for simultaneous laser blood irradiation and laser acupuncture at the wrist. Integr Med Int. 2016; 3(1–2):75–81; doi: 10.1159/00044 8099.
14. Farivar S, Malekshahabi T, Shiari R. Biological effects of low level laser therapy. J Lasers Med Sci. 2014; 5(2):58– 62; doi: 10.22037/JLMS.V5I2.5540.
15. Litscher G, Bahr F, Litscher D. Yellow laser stimulation on the skull – first evidence of microcirculatory changes in the laboratory [in German]. Akupunktur & Aurikulomedizin. 2015; 41(1):33–36; doi: 10.1007/s15009-015- 5319-y.
16. Hamblin MR. Ultraviolet irradiation of blood: “The cure that time forgot”? Adv Exp Med Biol. 2017; 996:295– 309; doi: 10.1007/978-3-319-56017-5_25.
17. Haslam DW, Wittert G, Seiler S, Tønnessen E. Fast Facts: Obesity. Intervals, thresholds, and long slow distance: the role of intensity and duration in endurance training. Sportscience.2009: 13: 32-53.
18. Mehta RK, Koirala P, Mallick RL, Parajuli S, Jha R. Dyslipidemia in Patients with Type 2 Diabetes Mellitus in a Tertiary Care Centre: A Descriptive Cross-sectional Study. JNMA J Nepal Med Assoc. 2021 Apr 30; 59(236):305-309. doi: 10.31729/jnma.6278. PMID: 34508529; PMCID: PMC8369597.
19. Jackson FR, Roche GC and Wisler K. Reduction in cholesterol and triglyceride serum levels following low-level laser irradiation: a non-controlled, nonrandomized pilot study. Am J Cosmet Surg. 2010; 27:177-84.

20. Serry ZM, El-Khashab SO, El-Monaem HA, Hamdy Elrefaey B. Response of glycaemic control to extravascular low level laser therapy in type 2 diabetic patients: a randomized clinical trial. Physiotherapy Quarterly.2021; 29(4):42-48. doi:10.5114/pq.2021.105752.
21. Kazemikhoo N, Ansari F, Nilforoushzadeh. The hypoglycemic effect of intravenous laser therapy in diabetic mellitus type 2 patients; a systematic review and metaanalyses. iMedPub Journals. 2015; 1(1):7; doi: 10.21767/ 2471-299X.1000007.
22. Longo L. The role of laser in diabetes management. In: Waynant R, Tata DB (eds.), Proceedings of Light-Activated Tissue Regeneration and Therapy Conference. Boston: Springer; 2008; 215–220.
23. Irani S, Mohseni Salehi Monfared SS, Akbari-Kamrani M, Ostad SN, Abdollahi M, Larijani B. Effect of low-levellaser irradiation on in vitro function of pancreatic islets. Transplant Proc. 2009; 41(10):4313–4315; doi: 10.1016/ j.transproceed.2009.09.065.
24. Hakami AR, Alasmari S, Makkawi M, Mansour AA, Ahmad I, Al Shahrani M, et al. Effects of Photobiomodulation Therapy on Glycemic and Lipid Profiles In Vitro. Med Lasers. 2020; 9 (2): 172-178 https://doi.org/10.25289/ML.2020.9.2.172.
25. Melekhovets O, Smiianov Y, Rudenko L, Zhaldak D , Melekhovets J, Kovalenko E, et al. Efficiency of the Intravenous Laser Therapy in Metabolic Disorders Correction. Acta Balneol, TOM LIX. 2017; 1(147):16-21.
26. Liu TC, Cheng L, Su W, Zhang Y, Shi Y, Liu A, et al Randomized, Double-Blind, and Placebo-Controlled Clinic Report of Intranasal Low-Intensity Laser Therapy on Vascular Diseases. International Journal of Photoenergy.2012; 2012 (489713) | https://doi.org/10.1155/2012/489713.
27. Lizarelli RFZ, Grecco C, Regalo SCH, Esteban Florez FL, Bagnato VS. A pilot study on the effects of transcutaneous and transmucosal laser irradiation on blood pressure, glucose and cholesterol in women. Heliyon. 2021 May 24; 7(5):e07110. doi: 10.1016/j.heliyon.2021.e07110. PMID: 34136688; PMCID: PMC8180620.
28. Said MT and Elnhas NG. Impact of Cold Laser on Lipid Profile in Abdominal Obese. International Journal of PharmTech Research Women. 2016; 9(10):115-120. CODEN (USA): IJPRIF, ISSN: 0974-4304, ISSN(Online): 2455-9563
29. Rushdi T. Effect of Low-Level Laser Therapy on cholesterol and triglyceride serum levels in ICU patients. Egyptian Journal of Cardiothoracic Anesthesia (EJCTA). 2010; 4(2):95-99.
30. Avci P, Nyame TT, Gupta GK, Sadasivam M, Hamblin MR. Low-level laser therapy for fat layer reduction: a comprehensive review. Lasers Surg Med. 2013 Aug; 45(6):349-57. doi: 10.1002/lsm.22153. Epub 2013 Jun 7. PMID: 23749426; PMCID: PMC3769994.
31. Caruso-Davis MK, Guillot TS, Podichetty VK, Mashtalir N, Dhurandhar NV, Dubuisson O et al. Efficacy of low-level laser therapy for body contouring and spot fat reduction. Obes Surg. 2011 june; 21(6):722–729. doi: 10.1007/s11695-010- 0126-y. PMID: 20393809; PMCID: PMC5225499.
32. Jackson RF, Stern FA, Neira R, Ortiz-Neira CL, Maloney J. Application of low-level laser therapy for noninvasive body contouring. Lasers Surg Med. 2012 Mar; 44(3):211-7. doi: 10.1002/lsm.22007. Epub 2012 Feb 23. Erratum in: Lasers Surg Med. 2012 Sep; 44(7):597. PMID: 22362380.
33. Jackson RF, Dedo DD, Roche GC, Turok DI, Maloney RJ. Low-level laser therapy as a non-invasive approach for body contouring: a randomized, controlled study. Lasers Surg Med. 2009 Dec; 41(10):799-809. doi: 10.1002/lsm.20855. PMID: 20014253.
34. Mohamed RA, Yousef AM, Ata HK. Effect of electro acupuncture versus low level laser therapy on lipid profile in obesity. Phys Ther Rehabil. 2018; 5:9. http://dx.doi.org/10.7243/2055-2386-5-9.
35. Al-Agamy NN, Al-Nahas N G, Obay HE. Cryolipolysis versus lipolysis versus cold laser on lipid profile and body composition in women with central obesity. Turkish Journal of Physiotherapy and Rehabilitation. 2021; 32(3). ISSN 2651-4451 | e-ISSN 2651-446X. www.turkjphysiotherrehabil.org
36. Nagy EN, Ibrahim FM, Jouda AA, Elsayed MM. The Effect of Laser Therapy Along With Mediterranean Diet versus Mediterranean Diet Only on Older Adults with Non-alcoholic Fatty Liver Disease: A Randomized Clinical Trial. J Lasers Med Sci. 2021 Jul 24; 12:e39. doi: 10.34172/jlms.2021.39. PMID: 34733762; PMCID: PMC8558722.
37. Olban M, Wachowicz B, Koter M, Bryszewska M. The biostimulatory effect of red laser irradiation on pig blood platelet function. Cell Biol Int. 1998; 22(3):245-8. doi: 10.1006/cbir.1998.0251. PMID: 9974218.
38. Maahs DM, Ogden LG, Dabelea D, Snell-Bergeon JK, Daniels SR, Hamman RF, et al. Association of glycaemia with lipids in adults with type 1 diabetes: modification by dyslipidaemia medication. Diabetologia. 2010 Dec; 53(12):2518-25. doi: 10.1007/s00125-010-1886-6. Epub 2010 Sep 4. PMID: 20820753; PMCID: PMC3405233.

39. Pietri AO, Dunn FL, Grundy SM, Raskin P. The effect of continuous subcutaneous insulin infusion on very-low-density lipoprotein triglyceride metabolism in type I diabetes mellitus. Diabetes. 1983 Jan; 32(1):75-81. doi: 10.2337/diab.32.1.75. PMID: 6848399.
40. Tames FJ, Mackness MI, Arrol S, Laing I, Durrington PN. Non-enzymatic glycation of apolipoprotein B in the sera of diabetic and non-diabetic subjects. Atherosclerosis. 1992;93:237–44.