

EFFECT OF MELATONIN ON CARBOHYDRATE AND LIPID METABOLISM IN RATS UNDER ALLOXAN DIABETES COMBINED WITH CONSTANT ILLUMINATION

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Diabetes mellitus combined with circadian desynchronosis caused by constant illumination represents an increasingly prevalent comorbid condition that compounds metabolic disturbances beyond those of diabetes alone. Melatonin, the principal pineal hormone and potent antioxidant, is chronically suppressed under continuous light exposure, removing a key metabolic regulatory signal. This study investigated the effect of exogenous melatonin on carbohydrate and lipid metabolism in rats with alloxan-induced diabetes under equinox photoperiod and constant illumination. The study was performed on 40 male Wistar rats allocated to five groups: intact control, alloxan diabetes (AD), AD + melatonin (5 mg/kg, intragastrically, 14 days), AD combined with constant light (1500 lux, 24 h/day), and AD+ constant light + melatonin. Plasma glucose, HbA1c, total lipids, cholesterol, triglycerides, LDL-cholesterol, HDL-cholesterol, non-esterified fatty acids, and phospholipids were measured on day 15. Alloxan diabetes produced marked hyperglycemia, elevated HbA1c, dyslipidemia characterized by increased total lipids, cholesterol, triglycerides, LDL-cholesterol, and non-esterified fatty acids, and reduced phospholipids. Constant illumination potentiated all disturbances and raised the LDL/HDL atherogenic ratio to its highest value. Melatonin normalized glycaemia, restored total lipids, cholesterol, triglycerides, and phospholipids to control values in both diabetic groups, and substantially reduced LDL-cholesterol and non-esterified fatty acids, with a modest residual deviation in the photoperiod-disrupted group. These findings confirm that constant illumination significantly aggravates alloxan-induced metabolic disruption and support the therapeutic potential of melatonin as a hypoglycemic and hypolipidemic agent in diabetes mellitus associated with circadian desynchronosis.

Key words: melatonin, alloxan diabetes, constant illumination, carbohydrate metabolism, lipid metabolism, hyperglycemia, dyslipidemia, circadian desynchronosis.

Connection of the publication with planned research work.

The results of this work are fragment of the research project at Bukovinian State Medical University “Morpho-functional restructuring of the structures of the nervous and endocrine systems in different periods of postnatal ontogeny and biochemical mechanisms of signal molecules metabolism, state of oxidative and antioxidant systems under conditions of experimental pathologies, and the influence of glutathione and melatonin”, state registration number 0124U002513.

Introduction.

Diabetes mellitus (DM) is one of the most prevalent chronic metabolic diseases worldwide, affecting more than 537 million adults and projected to reach 600 million by 2030 according to the International Diabetes Federation [1]. The pathological basis of both type 1 and type 2 DM involves profound disturbances in glucose homeostasis and secondary dysregulation of lipid and protein metabolism, collectively driving the development of macro- and microvascular complications [2, 3].

A growing body of evidence links circadian rhythm disruption to the pathogenesis and exacerbation of metabolic disorders, including DM [4]. Modern society is characterised by widespread exposure to artificial light at night – a phenomenon designated as “light pollution” – which chronically suppresses the night secretion of melatonin by the pineal gland [5]. Melatonin (N-acetyl-5-methoxytryptamine) orchestrates circadian time-keeping, exerts pleiotropic antioxidant, anti-inflammatory, and metabolic regulatory effects [6], and has been shown to participate in the regulation of insulin secretion, glucose transport, and lipid oxidation [7].

Experimental alloxan-induced diabetes is a model that reproduces the metabolic syndrome of insulin-deficient type 1 DM through selective necrosis of pancreatic β -cells mediated by reactive oxygen species (ROS) [8]. Constant illumination, by chronically inhibiting melatonin synthesis, compounds the oxidative and metabolic burden, thereby worsening the diabetic phenotype [9]. The combined model therefore provides a clinically relevant platform to study the corrective potential of exogenous melatonin.

Although the antioxidant properties of melatonin are extensively documented, its capacity to restore carbohydrate and lipid homeostasis under the dual challenge of alloxan toxicity and photoperiod disruption has received limited systematic attention.

The aim of the study.

To characterize the metabolic profile of rats in this combined model and to evaluate the hypoglycaemic and hypolipidaemic efficacy of exogenous melatonin.

Object and research methods.

The study was conducted on 40 sexually mature male non-inbred white rats (body weight 150–180 g) maintained under controlled conditions (temperature 18–22°C, relative humidity 50–55%) with free access to standard chow and water. All procedures complied with EU Directive 2010/63/EU on the protection of animals used for scientific purposes and were approved by the local bioethics committee (Bukovinian State Medical University, Chernivtsi).

Animals were randomly assigned to five groups (n=8 each):

Group 1 – intact control (equinox photoperiod, 12 h light/12 h dark);

Group 2 – alloxan diabetes (AD) under equinox conditions;

Group 3 – AD + melatonin (AD+MT);

Group 4 – AD + constant light (AD+CL);

Group 5 – AD + CL + melatonin (AD+CL+MT).

To induce alloxan diabetes a 5% solution of alloxan monohydrate (Synbias, Ukraine) was administered intraperitoneally as a single dose of 150 mg/kg body weight in 0.9% NaCl after a 24-hour fast [8]. Control animals received an equivalent volume of 0.9% NaCl. Blood glucose was measured from the tail vein using a OneTouch Select glucometer (LifeScan, USA) on day 3 post-injection; animals with fasting glycaemia ≥ 10 mmol/L were included in the diabetic groups. Approximately 40% of alloxan-treated animals did not survive to day 3 due to acute renal toxicity, consistent with the known nephrotoxic action of alloxan.

Constant illumination was achieved by housing animals under fluorescent daylight lamps (1500 lux) for 24 hours per day throughout the 14-day experimental period, modelling the suppression of endogenous melatonin secretion observed under light-at-night exposure [5].

Melatonin (Sigma, USA) was dissolved in 0.5% ethanol/0.9% NaCl and administered intragastrically at a dose of 5 mg/kg body weight at 20:00 h daily for 14 days, coinciding with the physiological circadian peak of melatonin secretion. The dose was selected based on published evidence of its antioxidant efficacy in experimental free-radical pathologies [6].

Animals were sacrificed by decapitation under light ether anaesthesia on day 15. Blood was collected into EDTA-anticoagulated tubes (1 mg/mL). Plasma was separated by centrifugation (3000 rpm, 10 min) and used for all biochemical analyses.

Plasma glucose, glycated haemoglobin (HbA1c), lipid profile parameters total lipids, total cholesterol, triglycerides (TG), LDL-cholesterol (LDL-C), HDL-cholesterol (HDL-C), non-esterified fatty acids (NEFA), and phospholipids - were measured using certified commercial reagent kits (NPP Filisit-Diagnostica, Dnipro, Ukraine) by spectrophotometric methods.

Data are expressed as $M \pm m$. Statistical analysis was performed using STATISTICA 12 (StatSoft, USA) and MS Excel 2013. Normality of distribution was confirmed by the Shapiro-Wilk test. Between-group differences were assessed by Student's t-test and the non-parametric Mann-Whitney U-test. Differences were considered statistically significant at $p \leq 0.05$.

Research results and their discussion.

On day 14 of the experiment, alloxan administration produced severe hyperglycaemia in both diabetic groups (**table 1**). In rats maintained under equinox conditions (AD group), fasting blood glucose increased by 117% compared to the control (11.5 ± 0.84 vs. 5.3 ± 0.44 mmol/L, $p \leq 0.05$). The combination of alloxan diabetes with constant illumination (AD+CL group) exerted an additive deleterious effect, with plasma glucose exceeding the control value by 179% (14.8 ± 1.18 mmol/L, $p \leq 0.05$). The more pronounced hyperglycaemia in the AD+CL group is consistent with the known inhibitory role of melatonin on gluconeogenesis and its stimulatory effects on glycolysis in the liver; chronic suppression of endogenous melatonin by

continuous light thus removes an important hypoglycaemic regulatory mechanism [7, 10].

HbA1c, a marker of prolonged glycaemic exposure and a predictor of diabetic microvascular complications, was 2.53-fold elevated in the AD group ($12.2 \pm 1.21\%$, $p \leq 0.05$) and 2.94-fold elevated in the AD+CL group ($14.2 \pm 1.20\%$, $p \leq 0.05$) relative to the intact control ($4.82 \pm 0.63\%$). The significantly higher HbA1c in the AD+CL group compared to the AD group ($p \leq 0.05$) corroborates the potentiation of glycaemia by the photoperiod disruption.

Melatonin treatment (5 mg/kg for 14 days) significantly attenuated hyperglycaemia in both diabetic groups. In the AD+MT group, fasting glycaemia was reduced by 32% compared to untreated AD animals and exceeded the control by only 48% (7.83 ± 0.73 mmol/L). In the AD+CL+MT group, glucose remained 64% above the control (8.72 ± 0.79 mmol/L), reflecting a 41% reduction relative to the untreated AD+CL group. HbA1c in both treated groups showed a significant downward trend (AD+MT: $9.2 \pm 0.86\%$, -25% vs. AD; AD+CL+MT: $9.73 \pm 0.92\%$, -31% vs. AD+CL; both $p \leq 0.05$). The persistent HbA1c elevation likely reflects the cumulative glycaemic exposure prior to treatment onset, given the long erythrocyte half-life of this biomarker.

The mechanism underlying the hypoglycaemic action of melatonin is multifaceted. It encompasses modulation of hepatic glucose metabolism (activation of glycolysis, suppression of gluconeogenesis, and stimulation of the pentose phosphate pathway), activation of insulin receptor kinase, and the potential for partial regeneration of Langerhans islet β -cells [9, 10]. Furthermore, by reducing lipid peroxidation of erythrocyte and cellular membranes, melatonin may restore the insulin-binding capacity of peripheral receptors, facilitating GLUT-4-mediated glucose uptake [11].

Both diabetic models were associated with pronounced dyslipidaemia, consistent with the metabolic consequences of absolute or relative insulin deficiency (**table 2**). In the AD group, total plasma lipids increased by 86% (4.88 ± 0.35 vs. 2.62 ± 0.24 g/L, $p \leq 0.05$), and a further 127% increase was observed in the AD+CL group (5.94 ± 0.50 g/L, $p \leq 0.05$). This elevation reflects enhanced mobilisation of lipids from adipose depots due to unopposed hormone-sensitive lipase activity in the absence of adequate insulin signalling, compounded by the loss of melatonin-mediated suppression of stress-induced lipolysis under constant light [7, 12].

Plasma triglycerides (TG) were elevated by 58% and 45% in the AD and AD+CL groups, respectively (1.86 ± 0.19 and 1.71 ± 0.13 mmol/L vs. 1.18 ± 0.09 mmol/L in controls; $p \leq 0.05$ for both). The increase in TG reflects impaired lipoprotein lipase activity - normally stimulated by insulin - in combination with increased hepatic VLDL synthesis driven by the excess acetyl-CoA generated from accelerated β -oxidation of fatty acids.

Table 1 – Glucose and glycated haemoglobin (HbA1c) in rat blood under alloxan diabetes, constant illumination, and melatonin administration ($M \pm m$; $n=8$)

Indicator	Control	AD	AD+MT	AD+CL	AD+CL+MT
Glucose, mmol/L	5.3 ± 0.44	$11.5 \pm 0.84^*$	$7.83 \pm 0.73^{*+}$	$14.8 \pm 1.18^{*+}$	$8.72 \pm 0.79^{*+}$
HbA1c, %	4.82 ± 0.63	$12.2 \pm 1.21^*$	$9.2 \pm 0.86^{*+}$	$14.2 \pm 1.20^{*+}$	$9.73 \pm 0.92^{*+}$

Notes: AD – alloxan diabetes, CL – constant light, MT – melatonin (5 mg/kg/day), * – $p \leq 0.05$ vs. control, + – $p \leq 0.05$ vs. corresponding untreated diabetic group, + – $p \leq 0.05$ vs. AD group under equinox conditions.

Table 2 – Lipid profile in rat plasma under alloxan diabetes, constant illumination, and melatonin administration ($M \pm m$; $n=8$)

Indicator	Control	AD	AD+MT	AD+CL	AD+CL+MT
Total lipids, g/L	2.62±0.24	4.88±0.35*	3.04±0.48†	5.94±0.50*‡	3.30±0.41†
Total cholesterol, mmol/L	2.38±0.19	3.83±0.35*	2.84±0.34†	3.74±0.44*	2.77±0.30†
Triglycerides, mmol/L	1.18±0.09	1.86±0.19*	1.10±0.12†	1.71±0.13*	1.34±0.18†
LDL-C, mmol/L	1.43±0.16	2.76±0.29*	1.76±0.27†	3.04±0.35*‡	2.04±0.29*†
HDL-C, mmol/L	1.17±0.09	1.08±0.18	1.28±0.16	1.02±0.17	1.12±0.11
NEFA, mmol/L	0.80±0.05	1.73±0.19*	1.13±0.14*†	1.90±0.22*‡	1.38±0.16*†
Phospholipids, g/L	3.32±0.45	1.91±0.57*	2.61±0.47†	1.49±0.57*‡	3.12±0.41†
LDL/HDL ratio	1.22	2.56	1.37	2.98	1.82

Notes: AD – alloxan diabetes, CL – constant light, MT – melatonin (5 mg/kg/day), LDL-C – LDL cholesterol, HDL-C – HDL cholesterol, NEFA – non-esterified fatty acids, * – $p \leq 0.05$ vs. control, † – $p \leq 0.05$ vs. corresponding untreated diabetic group, ‡ – $p \leq 0.05$ vs. AD group under equinox conditions.

Total cholesterol was significantly elevated in both diabetic groups (+61% in AD and +57% in AD+CL; $p \leq 0.05$ vs. control). Alloxan-mediated ROS generation disrupts plasma membrane structure, releasing membrane cholesterol into the circulation and impairing its esterification, resulting in elevated free cholesterol in plasma [2, 13].

LDL-C, the principal carrier of atherogenic cholesterol, increased by 93% in the AD group (2.76±0.29 mmol/L) and by 112% in the AD+CL group (3.04±0.35 mmol/L), both significantly exceeding the control value (1.43±0.16 mmol/L, $p \leq 0.05$). HDL-C showed no statistically significant changes in either untreated diabetic group. Consequently, the LDL-C/HDL-C atherogenic ratio rose from 1.22 in the control to 2.56 in the AD group and 2.98 in the AD+CL group, reflecting a substantially increased cardiovascular risk in the combined model.

NEFA were elevated by 106% in the AD group (1.73±0.19 mmol/L) and by 126% in the AD+CL group (1.90±0.22 mmol/L) relative to the control (0.80±0.05 mmol/L; $p \leq 0.05$ for both). Chronically elevated circulating NEFA impair insulin signalling through intracellular accumulation of lipid intermediates (diacylglycerol, ceramides, acyl-CoA), thereby exacerbating insulin resistance and reinforcing the lipotoxic cycle [3].

Phospholipids, integral structural components of biological membranes, were markedly reduced in both diabetic groups: by 42.5% in the AD group (1.91±0.57 g/L) and by 55% in the AD+CL group (1.49±0.57 g/L), compared to the control (3.32±0.45 g/L; $p \leq 0.05$ for both). The greater depletion in the AD+CL group suggests enhanced oxidative degradation of membrane phospholipids under conditions of combined oxidative stress and circadian dysregulation, as well as their increased utilisation as energy substrates in the insulin-deficient state [13].

Melatonin administration resulted in substantial normalization of the lipid profile in both treated groups. In the AD+MT group, total lipids, total cholesterol, TG, and phospholipids returned to values that did not significantly differ from the control (table 2). LDL-C decreased to 1.76±0.27 mmol/L (not significantly different from control; $p > 0.05$), and NEFA declined to 1.13±0.14 mmol/L (still 41% above control, but 35% below the untreated AD value; $p \leq 0.05$). The LDL-C/HDL-C ratio was restored to 1.37, approaching the control value of 1.22.

In the AD+CL+MT group, the corrective effect of melatonin was also significant, though less complete than in the equinox-treated group, reflecting the greater severity of the combined metabolic disruption. Total lip-

ids, cholesterol, TG, and phospholipids were normalised ($p > 0.05$ vs. control), while LDL-C (2.04±0.29 mmol/L) and NEFA (1.38±0.16 mmol/L) remained significantly above the control ($p \leq 0.05$) but were substantially reduced compared to untreated AD+CL animals (–33% and –27%, respectively; $p \leq 0.05$). The LDL-C/HDL-C ratio decreased from 2.98 (AD+CL) to 1.82 (AD+CL+MT).

The hypolipidaemic action of melatonin is attributable to multiple complementary mechanisms. By attenuating oxidative stress, melatonin stabilises hepatocyte membranes, preserving normal hepatic lipid metabolism including cholesterol esterification and lipoprotein assembly [14]. Melatonin enhances fatty acid oxidation in skeletal muscle, suppresses gluconeogenesis and hepatic VLDL production, and, via MT1/MT2 receptor signalling, participates in the circadian regulation of lipid gene expression [9, 12]. Additionally, by improving glycaemic control, melatonin indirectly reduces hypertriglyceridaemia, as elevated VLDL-TG production in diabetes is largely driven by hyperglycaemia-associated insulin resistance [2, 3].

The potentiation of alloxan-induced metabolic disturbances by constant illumination observed in the present study underscores the integral role of the melatonin-dependent circadian system in metabolic homeostasis. Chronic suppression of endogenous melatonin by light at night removes a major antioxidant and metabolic regulatory signal, amplifying the toxicity of alloxan-generated ROS and worsening insulin deficiency. This is consistent with clinical epidemiological data linking shift work and light-at-night exposure to increased incidence and severity of type 2 DM and metabolic syndrome [4, 5].

Conclusions.

1. Alloxan-induced diabetes under equinox conditions on day 14 of the experiment was accompanied by pronounced hyperglycaemia, a significant increase in HbA1c, and dyslipidaemia characterised by elevated total lipids, total cholesterol, triglycerides, LDL-cholesterol, and non-esterified fatty acids, alongside a reduction in plasma phospholipids.

2. The combination of alloxan diabetes with constant illumination potentiated all metabolic disturbances observed under equinox conditions, resulting in a more pronounced increase in blood glucose, HbA1c, total lipids, LDL-cholesterol, and non-esterified fatty acids, a greater decrease in phospholipids, and a more unfavourable atherogenic index compared to animals maintained under a standard photoperiod.

3. Melatonin administration (5 mg/kg/day, intragastrically, for 14 days) exerted pronounced hypoglycaemic and hypolipidaemic effects in both diabetic groups, significantly reducing fasting glycaemia and largely normalising total lipids, total cholesterol, triglycerides, and phospholipids in plasma. The correction of LDL-cholesterol and non-esterified fatty acids was partial but statistically significant, particularly in animals exposed to constant illumination.

4. The findings support the therapeutic potential of melatonin as a corrective agent targeting carbohydrate and lipid metabolism disturbances in experimental diabetes mellitus, and indicate that its efficacy is main-

tained – though attenuated – under conditions of circadian desynchronosis induced by constant illumination, suggesting that restoration of melatonin signalling may constitute an important component in the comprehensive management of diabetes mellitus associated with photoperiod disruption.

Prospects for further research.

They include dose optimisation of melatonin, elucidation of the underlying MT1/MT2 receptor-mediated molecular mechanisms, and evaluation of its potential synergism with conventional antidiabetic agents in long-term models of diabetes mellitus combined with circadian desynchronosis.

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ВПЛИВ МЕЛАТОНІНУ НА ПОКАЗНИКИ ВУГЛЕВОДНОГО ТА ЛІПІДНОГО ОБМІНУ ЩУРІВ ЗА УМОВ АЛОКСА-НОВОГО ДІАБЕТУ В ПОЄДНАННІ ІЗ ПОСТІЙНИМ ОСВІТЛЕННЯМ

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Резюме. Цукровий діабет (ЦД) у поєднанні з порушенням циркадіанних ритмів, спричиненим постійним освітленням, являє собою клінічно актуальну та дедалі поширенішу коморбідну патологію. Мелатонін, основний гормон епіфіза, є потужним антиоксидантом і регулятором метаболізму, ендогенний синтез якого суттєво пригнічується в умовах безперервного впливу світла. Питання можливості екзогенного мелатоніну коригувати поєднані метаболічні порушення за даної експериментальної моделі, залишається недостатньо вивченим.

Метою дослідження було вивчити вплив екзогенного мелатоніну на показники вуглеводного та ліпідного обміну крові щурів з алоксан-індукованим діабетом за умов рівнодення та постійного освітлення.

Дослідження проведено на 40 щурах-самцях лінії Wistar, розподілених на 5 груп (n=8): інтактний контроль; алоксановий діабет (АД); АД + мелатонін (5 мг/кг, внутрішньошлунково, 14 діб); АД в поєднанні з постійним освітленням (ПО, 1500 лк, 24 год/добу); АД+ПО + мелатонін. Алоксану моногідрат (150 мг/кг, в/очеревинно) вводили після 24-годинного голодування. На 15-ту добу в плазмі крові визначали рівень глюкози, глікози-льованого гемоглобіну (HbA1c), загальних ліпідів, загального холестерину, триацилгліцеролів, ліпопротеїнів низької щільності (ЛПНЩ), ліпопротеїнів високої щільності (ЛПВЩ), неетерифікованих жирних кислот (НЕЖК) та фосфоліпідів із використанням стандартизованих колориметричних і ферментативних методів.

Встановлено, що алоксановий діабет за умов рівнодення спричинив значну гіперглікемію, підвищення HbA1c (у 2,53 рази), загальних ліпідів (на 86%), холестерину (на 61%), триацилгліцеролів (на 58%), ЛПНЩ (на 93%), НЕЖК (на 106%) та зниження фосфоліпідів (на 42,5%). Постійне освітлення потенціювало всі виявлені порушення: зростання глюкози на 179%, HbA1c – у 2,94 рази, загальних ліпідів – на 127%, ЛПНЩ – на 112%, НЕЖК – на 126%, зниження фосфоліпідів – на 55%; атерогенний коефіцієнт ЛПНЩ/ЛПВЩ зріс від 1,22 (контроль) до 2,98. Введення мелатоніну нормалізувало рівень глікемії натще, відновило вміст загальних ліпідів, холестерину, триацилгліцеролів і фосфоліпідів до контрольних значень в обох діабетичних групах та знизило рівні НЕЖК і ЛПНЩ до контрольних величин, з більш вираженим залишковим відхиленням у групі АД+ПО+МТ.

Отже, постійне освітлення суттєво поглиблює спричинені алоксаном порушення вуглеводного та ліпідного гомеостазу у щурів. Екзогенний мелатонін (5 мг/кг, 14 діб) проявив виражені гіпоглікемічний та гіполіпідеміч-

ний ефекти, значною мірою нормалізуючи метаболічний профіль як у стандартній, так і моделі діабету, поєднаний із порушенням фотоперіоду. Отримані результати обґрунтовують можливість застосування мелатоніну як коригуючого засобу при цукровому діабеті, асоційованому з циркадіанним десинхронізом.

Ключові слова: мелатонін, алоксановий діабет, постійне освітлення, вуглеводний обмін, ліпідний обмін, гіперглікемія, дисліпідемія, циркадіанний десинхронізм.

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Abstract. Diabetes mellitus (DM) combined with circadian rhythm disruption caused by constant illumination represents a clinically relevant and increasingly prevalent comorbid condition. Melatonin, the principal pineal hormone, is a potent antioxidant and metabolic regulator whose endogenous synthesis is severely suppressed under conditions of continuous light exposure. The extent to which exogenous melatonin can correct the compounded metabolic disturbances in this combined model remains insufficiently studied.

The aim of the study was to investigate the effect of exogenous melatonin on indices of carbohydrate and lipid metabolism in the blood of rats with alloxan-induced diabetes under conditions of equinox photoperiod and constant illumination.

The study was conducted on 40 male Wistar rats distributed into 5 groups (n=8): intact control; alloxan diabetes (AD); AD + melatonin (5 mg/kg, intragastrically for 14 days); AD combined with constant light (CL, 1500 lux, 24 h/day); AD+CL + melatonin. Alloxan monohydrate (150 mg/kg, i.p.) was administered after 24-hour fasting. Plasma glucose, glycated haemoglobin (HbA1c), total lipids, total cholesterol, triglycerides, LDL-cholesterol, HDL-cholesterol, non-esterified fatty acids (NEFA), and phospholipids were measured using validated colorimetric and enzymatic methods on day 15.

It was revealed that alloxan diabetes under equinox conditions produced significant hyperglycaemia, elevated HbA1c (2.53 times), total lipids (by 86%), cholesterol (by 61%), triglycerides (by 58%), LDL-C (by 93%), NEFA (by 106%), and reduced phospholipids (by 42.5%). Constant light potentiated all abnormalities: elevation of glucose by 179%, HbA1c 2.94 times, total lipids by 127%, LDL-C by 112%, NEFA by 126%, and phospholipids reduction by 55%; the LDL/HDL atherogenic ratio rose from 1.22 (control) to 2.98. Melatonin administration normalised fasting glycaemia, restored total lipids, cholesterol, triglycerides, and phospholipids to control values in both diabetic groups, and reduced NEFA and LDL-C toward control levels, with a more pronounced residual deviation in the AD+CL+MT group.

Thus, constant illumination significantly aggravates alloxan-induced disruption of carbohydrate and lipid homeostasis in rats. Exogenous melatonin (5 mg/kg, 14 days) demonstrates pronounced hypoglycaemic and hypolipidaemic effects, largely normalising the metabolic profile in both the standard and the photoperiod-disrupted diabetic models. These findings support the potential use of melatonin as a corrective agent in diabetes mellitus associated with circadian desynchronisation.

Key words: melatonin, alloxan diabetes, constant illumination, carbohydrate metabolism, lipid metabolism, hyperglycemia, dyslipidemia, circadian desynchronisation.

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Conflict of interest:

The authors declare no conflict of interest.

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A – Work concept and design, B – Data collection and analysis, C – Responsibility for statistical analysis, D – Writing the article, E – Critical review, F – Final approval of the article.

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