

Oxidopamine and oxidative stress: Recent advances in experimental physiology and pharmacology

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Abstract

Oxidopamine (6-hydroxydopamine, 6-OHDA) is a toxin commonly used for the creation of experimental animal models of Parkinson's disease, attention-deficit hyperactivity disorder, and Lesch-Nyhan syndrome. Its exact mechanism of action is not completely understood, although there are many indications that it is related to the generation of reactive oxygen species (ROS), primarily in dopaminergic neurons. In certain experimental conditions, oxidopamine may also cause programmed cell death via various signaling pathways. Oxidopamine may also have a significant impact on chromatin structure and nuclear structural organization in some cells. Today, many researchers use oxidopamine-associated oxidative damage to evaluate different antioxidant-based pharmacologically active compounds as drug candidates for various neurological and non-neurological diseases. Additional research is needed to clarify the exact biochemical pathways associated with oxidopamine toxicity, related ROS generation and apoptosis. In this short review, we focus on the recent research in experimental physiology and pharmacology, related to the cellular and animal experimental models of oxidopamine - mediated toxicity.

Keywords: 6-hydroxydopamine; Apoptosis; Reactive oxygen species; Toxicology.

Perinatal complications related to inherited thrombophilia: review of evidence in different regions of the world

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Abstract

The term thrombophilia describes disorders associated with an increased predisposition of developing venous thromboembolism (VTE). It may be acquired, like in those with antiphospholipid syndrome or inherited. The aim of this review was to compare the complications and outcomes of pregnancies in women with inherited thrombophilia between different populations, including the population of our country where the results of the research are scarce. The review of literature included all papers indexed on PubMed and Medline in the last 20 years, with different study design, including other reviews of literature, systematic reviews with meta-analysis and several case-control studies and population-based cohort studies. We aimed to cover as many geographic regions as possible with the aim to show the differences in the different parts of the world and including our country. Our analysis showed that types of thrombophilia differ in different geographic regions. Also, the differences exist between one particular type of thrombophilia in different regions. Nevertheless, no matter what the differences are between prevalence, all authors investigated the association between inherited thrombophilia and poor pregnancy outcome and managed to find some kind of association. The case with our own country is similar. Although we lack in studies with this issue and the design of published studies is not powerful enough, we may conclude that in our samples, women with thrombophilia are in potential risk of several poor pregnancy outcomes. Further and better analyses are necessary to prove this hypothesis not only on the level of study sample but also on general population. Given the fact that thrombophilia certainly affects the pregnancy and its outcome, the urge to perform screening tests in every woman suspected to have this kind of disorder and with respect to differences that exist in different world regions is inevitable.

Keywords: Inherited thrombophilia; poor outcome; pregnancy; pregnancy loss.

FKBPL and SIRT-1 Are Downregulated by Diabetes in Pregnancy Impacting on Angiogenesis and Endothelial Function

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Abstract

Diabetes in pregnancy is associated with adverse pregnancy outcomes including preterm birth. Although the mechanisms leading to these pregnancy complications are still poorly understood, aberrant angiogenesis and endothelial dysfunction play a key role. FKBPL and SIRT-1 are critical regulators of angiogenesis, however, their roles in pregnancies affected by diabetes have not been examined before in detail. Hence, this study aimed to investigate the role of FKBPL and SIRT-1 in pre-gestational (type 1 diabetes mellitus, T1D) and gestational diabetes mellitus (GDM). Placental protein expression of important angiogenesis proteins, FKBPL, SIRT-1, PIGF and VEGF-R1, was determined from pregnant women with GDM or T1D, and in the first trimester trophoblast cells exposed to high glucose (25 mM) and varying oxygen concentrations [21%, 6.5%, 2.5% (ACH-3Ps)]. Endothelial cell function was assessed in high glucose conditions (30 mM) and following FKBPL overexpression. Placental FKBPL protein expression was downregulated in T1D (FKBPL; $p < 0.05$) whereas PIGF/VEGF-R1 were upregulated ($p < 0.05$); correlations adjusted for gestational age were also significant. In the presence of GDM, only SIRT-1 was significantly downregulated ($p < 0.05$) even when adjusted for gestational age ($r = -0.92$, $p = 0.001$). Both FKBPL and SIRT-1 protein expression was reduced in ACH-3P cells in high glucose conditions associated with 6.5%/2.5% oxygen concentrations compared to experimental normoxia (21%; $p < 0.05$). FKBPL overexpression in endothelial cells (HUVECs) exacerbated reduction in tubule formation compared to empty vector control, in high glucose conditions (junctions; $p < 0.01$, branches; $p < 0.05$). In conclusion, FKBPL and/or SIRT-1 downregulation in response to diabetic pregnancies may have a key role in the development of vascular dysfunction and associated complications affected by impaired placental angiogenesis.

Keywords: Diabetes; FKBPL; GDM; SIRT-1; Trophoblasts; angiogenesis; endothelial cells; pregnancy.

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Sensitivity and specificity of anthropometric measures during early pregnancy for prediction of development of gestational diabetes mellitus

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Distribution of normal and pathological OGTTs among pregnant population and non-pregnant women with PCOS – the cross-sectional study

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Abstract

Both pregnancy, as physiological, and polycystic ovary syndrome (PCOS), as a pathological condition, carry the risk for developing glucose metabolism abnormalities. In this retrospective cross-sectional study, we hypothesized that pregnancy as a physiological condition carries a higher likelihood for abnormal oral glucose tolerance test (OGTT) results than PCOS as a pathological condition. We have compared the prevalence and likelihood ratios for abnormal OGTT results between non-pregnant women with PCOS (Group A) and pregnant women at 24 to 28 weeks of gestation (Group B). Participants of both study groups underwent glucose tolerance testing with 75 g glucose OGTT. During the study period, 7411 women were tested, 3932 women encompassed Group A, and 3479 women comprised Group B. The numbers of yearly tested pregnant women and the corresponding proportion of tested women among all study participants have decreased during the study period, from 766 to 131 and 89.1% to 20.5%, respectively. Group A had a significantly lower prevalence (4.4%) of pathological OGTT results compared to Group B (8.1%). This has resulted in a 45.427 likelihood ratio ($P < .001$) for abnormal OGTT results in pregnant women compared to non-pregnant women with PCOS. We might conclude that pregnancy could have a more challenging influence on glucose metabolism and that carries higher risks for abnormal glucose metabolism than PCOS. The awareness of obstetricians regarding physiological changes during pregnancy that predisposes abnormal glucose metabolism is decreasing over time and the compliance concerning OGTT testing of pregnant women is decreasing too.

Uptake of Human Papillomavirus Vaccine and Intention to Vaccinate among Healthy Pregnant Women in Serbia: A Cross-Sectional Study on Awareness, Knowledge, and Attitudes

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Abstract

We aimed to assess awareness, knowledge, and attitudes of healthy pregnant women towards human papillomavirus (HPV), to estimate factors associated with a positive attitude towards HPV immunization and to assess the uptake of the vaccine among their children. A cross-sectional study was conducted at the University Clinic of Gynecology and Obstetrics, Belgrade, Serbia among pregnant women attending their regular gynecological check-ups at the 12th gestational week. Knowledge about HPV and HPV vaccine was assessed using a specifically designed 12-item and 5-item questionnaires. Out of total 265 included women, 79.3% had heard of HPV, and 37.5% knew that HPV vaccine exists. HPV vaccine knowledge score was associated with higher odds for a positive attitude towards vaccination of both female (OR = 4.10, 95% CI 1.50-11.29) and male (OR = 3.71, 95% CI 1.52-9.01) child. The number of children (OR = 1.32, 95% CI 1.04-1.67) and high vaccine knowledge score (OR = 1.64 95% CI 1.13-2.39) were independent predictors associated with willingness to vaccinate child against HPV. The gynecologist was the preferable point of reference for information seeking about the HPV vaccine. Despite relatively high HPV awareness and knowledge among pregnant women in Serbia, about one-third of them are HPV vaccine aware, and are willing to vaccinate their children against HPV.

Keywords: attitudes; human papillomavirus; knowledge; pregnancy; vaccine.

The association between IUGR and maternal inherited thrombophilias: A case-control study

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Abstract

One of the risk factors for vascular obstetric complications, such as intrauterine growth restriction (IUGR), is inherited thrombophilias. Nevertheless, routine screening for thrombophilias is not endorsed in pregnant women due to their low prevalence and conflicting results of published studies regarding the usefulness of screening in these patients. The cause of IUGR remains unknown in almost 1 quarter of cases. There are no published studies evaluating the association of inherited thrombophilias and IUGR in patients with IUGR of unknown origin. Understanding and preventing IUGR is an important public health concern, as IUGR has been associated with fetal mortality and neonatal morbidity, as well as adverse long-standing consequences. This study aimed to evaluate the prevalence of inherited thrombophilias in IUGR of unknown cause and to test the association between the inherited thrombophilias and IUGR of unknown cause. This study included 33 cases of IUGR of unknown cause tested for inherited thrombophilias and 66 controls individually matched for age, ethnicity, and smoking status. Patients with plasminogen activator inhibitor 1 (PAI-1) and methylenetetrahydrofolate reductase (MTHFR) had significantly higher odds for IUGR of unknown cause ($P < .001$ and $P = .002$, respectively) with OR 13.546 (CI 95% 3.79-48.37) and 8.139 (CI 95% 2.20-30.10), respectively. A positive association between other inherited thrombophilias (homozygous 20210 prothrombin gene mutation and homozygous factor V Leiden) and IUGR of unknown cause was also found, $P = .096$, OR 6.106 (CI 95% 0.72-51.30), although it was not statistically significant ($P = .096$, OR = 6.106, CI 95% 0.72-51.30). Our results indicate that PAI-1 and MTHFR thrombophilias represent risk factors for IUGR of otherwise unidentified cause.

Factors Associated with the Leisure–Time Physical Activity (LTPA) during the First Trimester of the Pregnancy: The Cross–Sectional Study among Pregnant Women in Serbia

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Abstract

Background: The benefits of physical activity during pregnancy include lower maternal weight gain, a lower likelihood of gestational diabetes, low back pain, preeclampsia, preterm delivery, caesarian delivery, and macrosomia. This study aimed to examine the factors associated with insufficient leisure-time physical activity (LTPA) during the first trimester. **Methods:** A cross-sectional study was conducted at the Clinic for Obstetrics and Gynecology of Clinical Center of Serbia, Belgrade, between January and June of 2018. The final analyses included 162/175 pregnant women. The questionnaire was used to obtain social characteristics, pregnancy, and lifestyle characteristics (Pregnancy Risk Assessment Monitoring System-PRAMS), pre-pregnancy LTPA (International Physical Activity Questionnaire-IPAQ), and LTPA during the first trimester (Pregnancy Physical Activity Questionnaire-PPAQ). Women were classified into two groups of sufficient and insufficient LTPA during the first trimester based on the recommendations of the World Health Organization. Multivariate logistic regression analysis was applied. **Results:** A total of 27.2% of the women had insufficient LTPA during pregnancy. Insufficient LTPA during pregnancy was associated with <12 years of education (OR: 2.3, 95% CI: 1.05-5.04), self-rated financial status as poor (OR: 0.34, 95% CI: 0.14-0.79), and hours spent walking before pregnancy (OR: 0.87, 95% CI: 0.77-0.99). **Conclusions:** Our results can help direct health care professionals advice for women who are planning pregnancy towards walking as it seems to be sustained during pregnancy.

Keywords: factors; physical activity; pregnancy; walking.

Combined hereditary thrombophilias are responsible for poor placental vascularization development and low molecular weight heparins (LMWH) prevent adverse pregnancy outcomes in these patients

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Abstract

Background: Even though thrombophilias are associated with negative pregnancy outcomes (PO), there is not a consensus of when thrombophilias should be screened for, or how they affect placental vascularization during pregnancy. Therefore, the main aim of this study was to discover inherited thrombophilias (IHT) in the first trimester in women with otherwise no indications for thrombophilia screening, based on their vascularization parameters. LMWH treatment in improvement of placental vascularization and PO was also assessed. Finally, the classification of thrombophilias based on observed obstetric risks was proposed.

Methods: Women were included in study based on their poor gestational sac and later utero-placental juncture vascularization signal and screening for inherited thrombophilias. LMWH were then initiated and Resistance index of Uterine artery (RIAU) was followed alongside PO (preterm birth, preeclampsia, placental abruption, intrauterine growth reduction). Study group consisted of women with combined inherited thrombophilias. Control group consisted of patients with inherited thrombophilias who have received LMWH therapy since pregnancy beginning.

Findings: Out of 219 women, 93 had IHT, and 43 had combined IHT. All pregnancies both in both groups ended up with live births. Vaginal birth was more present in the control group ($p < .001$), and all women in study group delivered by CS. Premature birth was present in 8.4% of patients in control group, and in 32.55% of the patients in the study ($p < .001$). PE wasn't noted, and only 1 case of PA in control group. In the control group, 6.5% patients had IUGR, and 32.55% in the study group ($p < .05$). Based on RIAU and PO, thrombophilia categories were established: S (severe), MO (moderate), MI (mild) and L (low). Higher risk thrombophilias had higher RIAU later in the pregnancy, earlier pregnancy termination and Intrauterine Growth Reduction (IUGR).

Comparison of 2 approaches in management of pregnant women with inherited thrombophilias: Prospective analytical cohort study

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Abstract

Previous adverse pregnancy outcomes (APO) in women with hereditary thrombophilia have emerged as new indications for prophylactic use of low-molecular-weight heparin (LMWH) during pregnancy. Recent meta-analysis conducted to establish if LMWH may prevent recurrent placenta-mediated pregnancy complications point to important therapeutic effect but these findings are absolutely not universal. Furthermore, previous studies regarding LMWH prophylaxis for APO in women with inherited thrombophilia were performed in high risk patients with previous adverse health outcomes in medical, family and/or obstetric history. Therefore, the aim of this study was to investigate the effects of LMWH prophylaxis on pregnancy outcomes in women with inherited thrombophilias regardless of the presence of previous adverse health outcomes in medical, family, and obstetric history. Prospective analytical cohort study included all referred women with inherited thrombophilia between 11 and 15 weeks of gestation and followed-up to delivery. Patients were allocated in group with LMWH prophylaxis (study group) and control group without LMWH prophylaxis. The groups were compared for laboratory parameters and Doppler flows of umbilical artery at 28 to 30th, 32nd to 34th and 36th to 38th gestational weeks (gw), and for obstetric and perinatal outcomes. The study group included 221 women and control group included 137 women. Mean resistance index of the umbilical artery Ri in 28 to 30, 32 to 34, and 36 to 38 gw were significantly higher in the control group compared to study group (0.71 ± 0.02 vs 0.69 ± 0.02 ; 0.67 ± 0.03 vs 0.64 ± 0.02 ; and 0.67 ± 0.05 vs 0.54 ± 0.08 , respectively). Intrauterine fetal death (IUFD) and miscarriages were statistically significantly more frequent in control group compared to the patients in study ($P < .001$). The frequencies of fetal growth restriction (FGR) and APO were significantly higher in the control group compared to the study group ($P = .008$ and $P < .001$, respectively). In a multivariate regression model with APO as a dependent variable, only Ri was detected as a significant protective factor for APO, after adjusting for age and LMWH prophylaxis ($P < .001$). We have demonstrated better perinatal outcomes in women with LMWH

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Association between physiological oscillations in self-esteem, narcissism and internet addiction: A cross-sectional study

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Abstract

Internet addiction is a novel and relatively uninvestigated form of dependence that is fairly common in adolescent population. Previous research has indicated that it may be associated with other mental health problems, such as dysthymic mood and narcissistic behavior. In our study, we tested the existence and strength of relationship between Internet addiction, self-esteem and narcissism in a student population. On a sample of 244 students, we also investigated social networking activities, such as number of self-portrait photographs ("selfies"), and their potential connection with self-esteem and narcissism. Each participant completed a questionnaire consisting of Young Internet Addiction Test, Rosenberg Self-Esteem scale, and Narcissistic Personality Inventory. There was a statistically significant negative correlation between internet addiction score and self-esteem. Internet addiction increased as self-esteem decreased and vice versa. On the other hand, there was a positive correlation between internet addiction and narcissism. NPI score and number of self-portrait photographs (selfies) on Facebook were also in a positive relationship. Conversely, NPI score increased as the self-esteem decreased. The results of the study are in accordance with our previous findings on Internet use and mental health, confirming that Internet addiction is a potentially a serious public health problem.

Keywords: Dependence; Facebook; Mental health; Personality; Selfie.

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Postnatal Developmental Changes in Fractal Complexity of Giemsa–Stained Chromatin in Mice Spleen Follicular Cells

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Abstract

Although there are numerous recent works focusing on fractal properties of DNA and chromatin, many issues regarding changes in chromatin fractality during physiological aging remain unclear. In this study, we present results indicating that in mice, there is an age-related reduction of chromatin fractal complexity in a population of spleen follicular cells (SFCs). Spleen tissue was obtained from 16 mice and fixated in Carnoy solution. The youngest animal was newborn, and each animal was exactly 1 month older than the previous. We performed fractal analysis of SFC chromatin structure, stained using Giemsa technique. Fractal analysis was done in a plugin algorithm of ImageJ software. We also performed gray-level co-occurrence matrix (GLCM) analysis of all chromatin structures with the calculation of parameters such as angular second moment and inverse difference moment. Giemsa-stained SFC chromatin exhibited an age-dependent reduction of fractal dimension with statistically significant ($p < 0.01$) linear trend. Moreover, there was a statistically significant increase of SFC chromatin lacunarity. The chromatin GLCM parameters did not significantly change. To our knowledge, this is the first study to perform fractal and GLCM analyses of SFC chromatin and to investigate potential changes of fractal parameters during postnatal development.

Keywords: aging; lymphocyte; micrograph; microscopy; spleen.

Relationship between mid-trimester ultrasound fetal liver length measurements and gestational diabetes mellitus

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Abstract

Background: The aim of the present study was to investigate the relationship between mid-trimester ultrasound fetal liver length (FLL) and gestational diabetes mellitus (GDM) in a high-risk population.

Methods: A prospective study was performed in 331 women with singleton pregnancies who were at high risk of GDM and were undergoing a mid-trimester ultrasound examination. The ultrasound scan at 23 weeks gestation was followed by a 100-g oral glucose tolerance test (OGTT) at 24 weeks gestation. Correlations between FLL and OGTT results at different time points were tested. Receiver operating characteristic (ROC) analysis of FLL as a potential prognostic factor for GDM was also performed.

Results: In GDM patients, there was a significant positive correlation ($P < 0.01$) between FLL and OGTT glycemia immediately before and 60, 120, and 180 min after glucose intake. Mean FLL in GDM was significantly higher than in healthy subjects (41.04 vs 31.09 mm, respectively; $P < 0.001$). When tested as a potential prognostic factor for GDM, fetal liver measurements showed excellent diagnostic performance. The ROC analysis established a cut-off value of FLL of 39 mm for the prediction GDM, with sensitivity of 71.76%, specificity 97.56%, positive predictive value 91.0%, and negative predictive value 90.9%. The usefulness of FLL measurements was supported by a high area under the ROC curve (90.5%).

Conclusion: In conclusion, there is a strong correlation between FLL and OGTT results, with FLL possibly serving as a valid marker for the prediction of GDM in high-risk populations.

> [ScientificWorldJournal](#). 2015;2015:673196. doi: 10.1155/2015/673196. Epub 2015 Feb 15.

Cross-cultural adaptation and validation of the Serbian version of the ICS SF male questionnaire

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Abstract

Introduction: The objective of this study was to cross-culturally adapt and validate ICS male SF questionnaire to Serbian language.

Materials and methods: This study included 91 male patients with lower urinary tract symptoms and 24 men with similar age and with confirmed absence of LUTS. ICS male SF questionnaire was translated from English to Serbian language and then back-translated to English.

Results: Internal consistency was high in both dimensions, voiding (Cronbach's alpha = 0.916) and incontinence (Cronbach's alpha = 0.763). Comparison of the average scores between patients and controls revealed significant differences in both dimensions: voiding (med = 8 versus med = 0; $P < 0.001$) and incontinence (med = 3 versus med = 0; $P < 0.001$). Interclass correlation revealed high test-retest validity in both dimensions, voiding ICC = 0.992 ($P < 0.001$) and incontinence ICC = 0.989 ($P < 0.001$). Correlation analysis revealed high agreement between ICS male SF voiding dimension and IPSS questionnaire ($\rho = 0.943$; $P < 0.001$).

Conclusion: The Serbian version of male ICS SF questionnaire showed acceptable reliability and validity. The ICS male SF questionnaire could be used in routine practice as an easy and comprehensive tool for assessment of LUTS.

Maternal and Fetal Outcomes among Pregnant Women with Diabetes

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Abstract

The aim of this study was to examine the differences in pregnancy complications, delivery characteristics, and neonatal outcomes between women with type 1 diabetes mellitus (T1DM), type 2 diabetes mellitus (T2DM), and gestational diabetes mellitus (GDM). This study included all pregnant women with diabetes in pregnancy in Belgrade, Serbia, between 2010 and 2020. The total sample consisted of 6737 patients. In total, 1318 (19.6%) patients had T1DM, 138 (2.0%) had T2DM, and 5281 patients (78.4%) had GDM. Multivariate logistic regression with the type of diabetes as an outcome variable showed that patients with T1DM had a lower likelihood of vaginal delivery (OR: 0.73, 95% CI: 0.64-0.83), gestational hypertension (OR: 0.47, 95% CI: 0.36-0.62), higher likelihood of chronic hypertension (OR: 1.88, 95% CI: 1.55-2.29), and a higher likelihood of gestational age at delivery before 37 weeks (OR: 1.38, 95% CI: 1.18-1.63) compared to women with GDM. Multivariate logistic regression showed that patients with T2DM had a lower likelihood of gestational hypertension compared to women with GDM (OR: 0.37, 95% CI: 0.15-0.92). Our results indicate that the highest percentage of diabetes in pregnancy is GDM, and the existence of differences in pregnancy complications, childbirth characteristics, and neonatal outcomes are predominantly between women with GDM and women with T1DM.

Keywords: diabetes in pregnancy; gestational diabetes; pre-gestational diabetes.

Gray-Level Co-occurrence Matrix Analysis for the Detection of Discrete, Ethanol-Induced, Structural Changes in Cell Nuclei: An Artificial Intelligence Approach

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Abstract

Gray-level co-occurrence matrix (GLCM) analysis is a contemporary and innovative computational method for the assessment of textural patterns, applicable in almost any area of microscopy. The aim of our research was to perform the GLCM analysis of cell nuclei in *Saccharomyces cerevisiae* yeast cells after the induction of sublethal cell damage with ethyl alcohol, and to evaluate the performance of various machine learning (ML) models regarding their ability to separate damaged from intact cells. For each cell nucleus, five GLCM parameters were calculated: angular second moment, inverse difference moment, GLCM contrast, GLCM correlation, and textural variance. Based on the obtained GLCM data, we applied three ML approaches: neural network, random trees, and binomial logistic regression. Statistically significant differences in GLCM features were observed between treated and untreated cells. The multilayer perceptron neural network had the highest classification accuracy. The model also showed a relatively high level of sensitivity and specificity, as well as an excellent discriminatory power in the separation of treated from untreated cells. To the best of our knowledge, this is the first study to demonstrate that it is possible to create a relatively sensitive GLCM-based ML model for the detection of alcohol-induced damage in *Saccharomyces cerevisiae* cell nuclei.

Keywords: cell; microscopy; morphology; nucleus; texture.