INOSR APPLIED SCIENCES 13(2):33-38, 2025
ISSN: 2705-165X
©INOSR PUBLICATIONS
INOSR13.2.000
International Network Organization for Scientific Research
https://doi.org/10.59298/INOSRAS/2025/13.2.3338

Mitochondrial Dysregulation in Drug-Induced Cardiotoxicity: Redox Imbalance, Bioenergetics, and Cell Death Pathways

Kungu Erisa

Faculty of Pharmacy Kampala International University Uganda

Email: erisa.kungu@studwc.kiu.ac.ug

ABSTRACT

Mitochondria are central regulators of cardiomyocyte viability, bioenergetics, and oxidative homeostasis. Drug-induced cardiotoxicity remains a significant clinical challenge, particularly with the rising use of chemotherapeutics, antiretrovirals, and targeted biologics. These agents often exert cardiotoxic effects by disrupting mitochondrial dynamics, impairing oxidative phosphorylation, generating reactive oxygen species (ROS), and triggering apoptosis or necrosis. This review provides a comprehensive overview of mitochondrial dysregulation as a core mechanism of drug-induced cardiotoxicity. We examine the molecular pathways linking mitochondrial redox imbalance to impaired ATP synthesis, cardiomyocyte dysfunction, and cell death. Furthermore, we explore how mitochondrial fission/fusion imbalances, calcium overload, and permeability transition pore (mPTP) opening contribute to structural and functional cardiac damage. The cardiotoxic mechanisms of doxorubicin, trastuzumab, tyrosine kinase inhibitors, and other pharmacologic agents are discussed with emphasis on their mitochondrial targets. We also review emerging cardioprotective strategies targeting mitochondrial dysfunction, including antioxidant therapies, mPTP inhibitors, and mitochondrial biogenesis enhancers. Understanding these mechanisms is vital for developing predictive biomarkers, refining drug safety, and advancing personalized cardioprotective interventions.

Keywords: Mitochondrial dysfunction, Cardiotoxicity, Reactive oxygen species, Bioenergetics, Apoptosis

INTRODUCTION

Drug-induced cardiotoxicity has emerged as a formidable challenge in modern pharmacotherapy, particularly in oncology, infectious disease treatment, and chronic disease management [1]. While the therapeutic efficacy of agents such as anthracyclines, targeted biologics, antiretroviral drugs, and tyrosine kinase inhibitors is well established, their unintended effects on cardiac tissue remain a major concern [2]. These adverse effects are frequently mediated by perturbations in mitochondrial function, a consequence of the heart's unique dependence on oxidative phosphorylation to meet its high energy demands [2]. The myocardium is a metabolically active tissue that requires a constant and abundant supply of adenosine triphosphate (ATP) to maintain ionic gradients, contractile function, and signal transduction [3]. Mitochondria, which constitute approximately 30 percent of the myocardial cell volume, are therefore central to cardiac performance. However, this reliance renders cardiomyocytes particularly vulnerable to mitochondrial insults, including those caused by xenobiotics. A growing body of evidence implicates mitochondrial dysfunction as a key determinant in the pathogenesis of drug-induced cardiomyopathy, arrhythmogenesis, and heart failure [4]. Mitochondrial damage leads to a cascade of events including excess reactive oxygen species (ROS) production, impaired oxidative phosphorylation, calcium dyshomeostasis, and the initiation of intrinsic apoptotic pathways [5]. These changes culminate in bioenergetic failure and cardiomyocyte death, which are hallmark features of cardiotoxicity [5]. Furthermore, these processes often evolve in the absence of early clinical symptoms, making it imperative to understand the underlying mechanisms for timely diagnosis and intervention. This review aims to provide a detailed exploration of the mechanisms by which pharmacological agents disrupt mitochondrial function, focusing specifically on redox imbalance, bioenergetic disruption, and cell death signaling.

By identifying shared and drug-specific pathways of injury, this paper also highlights emerging therapeutic strategies to counteract mitochondrial-mediated cardiotoxicity and improve clinical outcomes.

Mitochondrial Biology in the Heart

The heart is an organ of immense metabolic demand, consuming more than six kilograms of ATP daily, most of which is generated by mitochondrial oxidative phosphorylation [6]. Cardiac mitochondria are responsible for supplying the continuous energy required for excitation-contraction coupling, ion transport, and biosynthetic reactions [7]. The functional integrity of mitochondria is maintained by a complex network of interrelated processes, including mitochondrial dynamics, calcium signaling, and redox balance. Mitochondrial dynamics refer to the processes of fusion and fission that regulate mitochondrial morphology, distribution, and quality control. Fusion helps maintain mitochondrial function by diluting damaged components through content mixing, whereas fission facilitates the removal of dysfunctional mitochondria via mitophagy [8]. Disruption of this dynamic balance has been observed in cardiac pathologies and drug-induced mitochondrial stress, leading to fragmented mitochondria and reduced energy production [8]. Another critical aspect of mitochondrial physiology is calcium handling. Mitochondria buffer cytosolic calcium and utilize it to regulate key enzymes in the tricarboxylic acid (TCA) cycle [9]. However, excessive calcium uptake can cause mitochondrial permeability transition pore (mPTP) opening, leading to membrane potential collapse and the release of pro-apoptotic factors [9]. Reactive oxygen species (ROS), including superoxide anion and hydrogen peroxide, are natural byproducts of the electron transport chain. Under physiological conditions, mitochondrial antioxidant enzymes such as superoxide dismutase (SOD), glutathione peroxidase, and catalase maintain ROS at non-toxic levels [10]. When mitochondrial integrity is compromised, excessive ROS generation overwhelms these defenses, resulting in oxidative damage to lipids, proteins, and DNA [11]. This oxidative stress is a common denominator in cardiotoxicity induced by various drugs. Mitochondria also communicate with the nucleus through retrograde signaling pathways that influence the expression of genes involved in metabolism, stress response, and survival. These processes are orchestrated by key transcriptional regulators such as peroxisome proliferator-activated receptor gamma coactivator 1-alpha (PGC-1α), nuclear respiratory factors (NRFs), and mitochondrial transcription factor A (TFAM) [12]. Dysregulation of these signaling pathways underlies several forms of acquired mitochondrial dysfunction in drug-treated cardiac tissue.

Redox Imbalance and ROS Generation in Cardiotoxicity

Redox homeostasis is vital for the preservation of cardiomyocyte structure and function. Many cardiotoxic drugs impair this balance by promoting mitochondrial ROS generation, either through direct interference with the electron transport chain (ETC) or by inducing mitochondrial DNA (mtDNA) damage that impairs ETC protein synthesis [13]. Among the most well-characterized examples is doxorubicin, an anthracycline widely used in oncology. Doxorubicin undergoes redox cycling within mitochondria, producing semiquinone radicals that react with molecular oxygen to yield superoxide [14]. This initiates a vicious cycle of mitochondrial lipid peroxidation, protein oxidation, and further impairment of respiratory chain complexes [14]. ROS-mediated damage in cardiomyocytes extends beyond simple oxidative stress. Oxidative modification of ion channels and contractile proteins compromises cellular excitability and contractility, contributing to arrhythmias and systolic dysfunction [15]. DNA damage by ROS can trigger p53 activation and downstream apoptotic signaling [16]. Inflammatory responses are also activated, exacerbating myocardial injury. Other drugs, such as trastuzumab, interfere with cardioprotective signaling pathways like the neuregulin-1/ErbB axis, indirectly enhancing susceptibility to mitochondrial oxidative stress [17]. Tyrosine kinase inhibitors and proteasome inhibitors have been shown to increase ROS levels by affecting mitochondrial respiration or blocking antioxidant responses [18].

Importantly, the mitochondrial generation of ROS is tightly linked to bioenergetics. When ETC complexes are partially inhibited, electrons accumulate and leak to oxygen, forming superoxide [19]. This compromises proton gradient formation, ATP synthesis, and overall cellular energy supply. Furthermore, excessive ROS can induce opening of the mPTP, causing depolarization and eventual collapse of mitochondrial function [20]. Overall, redox imbalance represents an early and sustained mechanism of cardiomyocyte injury in drug-induced cardiotoxicity. Targeting mitochondrial sources of ROS, reinforcing endogenous antioxidant defenses, and preserving ETC integrity represent promising avenues for mitigating this damage and preventing clinical deterioration.

Impaired Bioenergetics and ATP Depletion

Bioenergetic integrity is essential for maintaining the contractile function, electrical conductance, and survival of cardiomyocytes. Drugs that impair mitochondrial function commonly do so by inhibiting components of the electron transport chain (ETC) or by uncoupling oxidative phosphorylation, ultimately leading to a significant reduction in ATP synthesis [21]. The resultant energy deficit compromises the activity of ATP-dependent ion channels and pumps, impairs calcium homeostasis, and weakens contractile performance, all of which are detrimental to cardiac function. One of the most well-documented examples is sunitinib, a tyrosine kinase inhibitor widely used in oncology. Sunitinib disrupts mitochondrial respiration by impairing the activity of ETC complexes, particularly Complex I and II, leading to decreased ATP production and accumulation of metabolic intermediates [22]. Clinically, this manifests as left ventricular dysfunction and, in some cases, overt heart failure [22]. Another agent, zidovudine

(AZT), an antiretroviral drug, impairs mitochondrial bioenergetics by inhibiting mitochondrial DNA polymerase gamma [23]. This reduces the replication and expression of mitochondrial DNA, leading to a depletion of ETC proteins and subsequent respiratory chain dysfunction. Compensatory mechanisms are activated in response to ATP depletion, notably the upregulation of AMP-activated protein kinase (AMPK), which senses energy deficiency and attempts to restore balance by promoting catabolic pathways and mitochondrial biogenesis [24]. However, chronic AMPK activation is insufficient to counteract sustained mitochondrial dysfunction and may itself become maladaptive, contributing to pathological cardiac remodeling [25]. Thus, the failure of bioenergetic homeostasis is a central mechanism in drug-induced cardiotoxicity that warrants targeted therapeutic intervention.

Mitochondrial-Mediated Cell Death Pathways

Mitochondria serve not only as the powerhouses of the cell but also as critical regulators of cell death. Their involvement in both apoptotic and necrotic signaling pathways renders them central to the pathophysiology of cardiotoxicity induced by pharmacological agents. In the intrinsic apoptotic pathway, mitochondrial outer membrane permeabilization leads to the release of pro-apoptotic factors such as cytochrome c into the cytosol [26]. Cytochrome c binds to apoptotic protease activating factor-1 (Apaf-1) and procaspase-9 to form the apoptosome, initiating a cascade that activates downstream caspases and culminates in DNA fragmentation and programmed cell death [27]. This process has been clearly demonstrated in doxorubicin-induced cardiotoxicity, where excessive ROS and mitochondrial damage trigger robust apoptotic responses in cardiac cells [28]. Necrotic cell death, in contrast, is largely mediated by the opening of the mitochondrial permeability transition pore (mPTP), a high-conductance channel that disrupts membrane potential and leads to osmotic swelling and rupture of the mitochondrial membrane [29]. This catastrophic event results in the uncontrolled release of mitochondrial contents and induces inflammatory responses in surrounding tissue. Unlike apoptosis, necrosis is not energy-dependent and often reflects severe mitochondrial failure [30]. Another contributing mechanism is the dysregulation of mitophagy, the selective autophagic clearance of damaged mitochondria [31]. Inadequate or dysfunctional mitophagy allows the accumulation of depolarized mitochondria, further exacerbating ROS production and propagating cell injury [31]. Disruption in the balance between mitochondrial biogenesis and mitophagy has been observed in various models of drug-induced cardiac injury, suggesting a need for therapeutic strategies that restore mitochondrial quality control [32].

Drug-Specific Mitochondrial Toxicities

The mitochondrial mechanisms of cardiotoxicity vary across different drug classes. Doxorubicin, for example, exerts its cardiotoxic effect by intercalating into mitochondrial DNA, inhibiting topoisomerase II beta, and promoting excessive ROS generation through redox cycling [33]. These processes culminate in mitochondrial swelling, ETC dysfunction, and both apoptotic and necrotic cell death. Trastuzumab, a monoclonal antibody targeting the HER2 receptor, does not generate ROS directly but interferes with neuregulin-1/ErbB signaling, a key cardioprotective pathway that maintains mitochondrial function [34]. This sensitizes cardiomyocytes to stress-induced mitochondrial dysfunction, particularly when administered in combination with anthracyclines. Sunitinib and sorafenib, both tyrosine kinase inhibitors, directly impair mitochondrial respiration and ATP synthesis [35]. These agents are also associated with the downregulation of PGC-1 alpha and impaired mitochondrial biogenesis, further contributing to energy depletion [36] Zidovudine, through its inhibition of mitochondrial DNA replication, leads to mitochondrial depletion and impaired respiratory function [37]. This results in energy failure and myocyte injury, particularly in long-term HIV patients. These drug-specific mitochondrial insults highlight the need for personalized monitoring and prevention strategies based on the pharmacodynamic and mitochondrial profiles of individual agents.

Therapeutic Targets and Cardioprotective Strategies

Therapeutic strategies targeting mitochondrial dysfunction offer promising avenues for preventing and mitigating cardiotoxicity. Antioxidants are among the most investigated options. Dexrazoxane, an iron chelator and FDA-approved cardioprotective agent, reduces ROS formation in doxorubicin-treated patients [38]. Novel mitochondria-targeted antioxidants such as MitoQ and SS-31 have shown potential in preclinical studies, effectively reducing mitochondrial ROS and improving cardiac outcomes [39] Another approach involves enhancing mitochondrial biogenesis through activation of the PGC-1 alpha pathway [40]. Natural compounds like resveratrol have demonstrated efficacy in restoring mitochondrial number and function in models of drug-induced cardiotoxicity [41] Inhibition of the mPTP with agents such as cyclosporin A has also been explored. By preventing pore opening, cyclosporin A preserves mitochondrial membrane potential and reduces necrotic cell death [42] Non-pharmacological interventions, including aerobic exercise and dietary modification, have shown promise in improving mitochondrial dynamics, enhancing antioxidant defenses, and promoting mitophagy [43]. These interventions may serve as adjuncts to pharmacological therapy in high-risk patients.

Clinical Implications and Biomarker Development

Current biomarkers for cardiotoxicity, such as cardiac troponins and natriuretic peptides, lack specificity for mitochondrial injury and often reflect irreversible damage [44]. There is increasing interest in identifying more

sensitive and mechanistically informative biomarkers. Circulating mitochondrial DNA (mtDNA), indicative of mitochondrial damage and release, is emerging as a potential early biomarker of cardiotoxic stress [45]. Other candidates include oxidized lipids, such as malondialdehyde and 4-hydroxynonenal, which reflect oxidative stress burden [46]. Imaging modalities such as 99mTc-MIBI SPECT are also under investigation for assessing mitochondrial function in vivo, offering the possibility of non-invasive monitoring [47] Developing robust biomarker panels will be essential for stratifying risk, monitoring subclinical toxicity, and tailoring cardioprotective interventions.

Future Perspectives

The future of cardiotoxicity management lies in precision medicine approaches that integrate mitochondrial phenotyping, pharmacogenomics, and advanced imaging. Stratifying patients based on mitochondrial vulnerability could enable early identification of those at highest risk. Incorporating omics-based platforms, such as transcriptomics and metabolomics, may uncover novel therapeutic targets and pathways involved in mitochondrial resilience. Combination therapies that maintain anticancer efficacy while safeguarding mitochondrial integrity represent an important direction. Furthermore, continued development of mitochondria-targeted agents and exploration of lifestyle-based interventions will enhance the therapeutic arsenal. Ultimately, a deeper understanding of mitochondrial pathobiology in drug-induced cardiotoxicity will drive the evolution of safer therapies and improve long-term cardiovascular outcomes in vulnerable patient populations.

CONCLUSION

Mitochondrial dysregulation is a critical and convergent mechanism in drug-induced cardiotoxicity. Understanding the redox, bioenergetic, and cell death pathways involved offers avenues for precision cardio protection. Future therapies must balance pharmacologic efficacy with mitochondrial preservation to ensure both oncologic success and cardiovascular safety.

REFERENCES

1. Costanzo V, Ratre YK, Andretta E, Acharya R, Bhaskar LVKS, Verma HK. A comprehensive review of cancer drug–induced cardiotoxicity in blood cancer patients: current perspectives and therapeutic strategies. Current Treatment Options in Oncology. 2024;25(4):465–95. doi:10.1007/s11864-023-01175-z
2. Dong J, Chen H. Cardiotoxicity of anticancer therapeutics. Frontiers in Cardiovascular Medicine. 2018;5:9. doi:10.3389/fcvm.2018.00009
3. Dunn J, Grider MH. Physiology, adenosine triphosphate. StatPearls – NCBI Bookshelf. 2023. Available from: https://www.ncbi.nlm.nih.gov/books/NBK553175/
4. Liu M, Lv J, Pan Z, Wang D, Zhao L, Guo X. Mitochondrial dysfunction in heart failure and its therapeutic implications. Frontiers in Cardiovascular Medicine. 2022;9:945142. doi:10.3389/fcvm.2022.945142
5. Kowalczyk P, Sulejczak D, Kleczkowska P, Bukowska-Ośko I, Kucia M, Popiel M, et al. Mitochondrial oxidative stress—a causative factor and therapeutic target in many diseases. International Journal of Molecular Sciences. 2021;22(24):13384. doi:10.3390/ijms222413384
6. Schwarz K, Siddiqi N, Singh S, Neil CJ, Dawson DK, Frenneaux MP. The breathing heart—mitochondrial respiratory chain dysfunction in cardiac disease. International Journal of Cardiology. 2013;171(2):134–43. doi:10.1016/j.ijcard.2013.12.014
7. Maack C, O'Rourke B. Excitation–contraction coupling and mitochondrial energetics. Basic Research in Cardiology. 2007;102(5):369–92. doi:10.1007/s00395-007-0666-z
8. Lei Y, Gan M, Qiu Y, Chen Q, Wang X, Liao T, et al. The role of mitochondrial dynamics and mitophagy in skeletal muscle atrophy: from molecular mechanisms to therapeutic insights. Cellular & Molecular Biology Letters. 2024;29:1. doi:10.1186/s11658-024-00572-y
9. Endlicher R, Drahota Z, Štefková K, Červinková Z, Kučera O. The mitochondrial permeability transition pore—current knowledge of its structure, function, and regulation, and optimized methods for evaluating its functional state. Cells. 2023;12(9):1273. doi:10.3390/cells12091273
10. Endlicher R, Drahota Z, Štefková K, Červinková Z, Kučera O. The mitochondrial permeability transition pore—current knowledge of its structure, function, and regulation, and optimized methods for evaluating its functional state. Cells. 2023;12(9):1273. doi:10.3390/cells12091273
11. Kowalczyk P, Sulejczak D, Kleczkowska P, Bukowska-Ośko I, Kucia M, Popiel M, et al. Mitochondrial oxidative stress—a causative factor and therapeutic target in many diseases. International Journal of Molecular Sciences. 2021;22(24):13384. doi:10.3390/ijms222413384
12. Shelbayeh OA, Arroum T, Morris S, Busch KB. PGC-1α is a master regulator of mitochondrial lifecycle and ROS stress response. Antioxidants. 2023;12(5):1075. doi:10.3390/antiox12051075
13. Rocca C, De Francesco EM, Pasqua T, Granieri MC, De Bartolo A, Cantafio MEG, et al. Mitochondrial determinants of anti-cancer drug-induced cardiotoxicity. Biomedicines. 2022;10(3):520. doi:10.3390/biomedicines10030520

14. Wallace KB, Sardão VA, Oliveira PJ. Mitochondrial determinants of doxorubicin-induced cardiomyopathy. Circulation Research. 2020;126(7):926–41. doi:10.1161/CIRCRESAHA.119.314681
15. Lei M, Salvage SC, Jackson AP, Huang CLH. Cardiac arrhythmogenesis: roles of ion channels and their functional modification. Frontiers in Physiology. 2024;15:134276. doi:10.3389/fphys.2024.134276
16. Shi T, Dansen TB. Reactive oxygen species induced p53 activation: DNA damage, redox signaling, or both? Antioxidants and Redox Signaling. 2020;33(12):839–59. doi:10.1089/ars.2020.8074
17. Morelli MB, Bongiovanni C, Da Pra S, Miano C, Sacchi F, Lauriola M, et al. Cardiotoxicity of anticancer drugs: molecular mechanisms and strategies for cardioprotection. Frontiers in Cardiovascular Medicine. 2022;9:847012. doi:10.3389/fcvm.2022.847012
18. Allegra A, Mirabile G, Caserta S, Stagno F, Russo S, Pioggia G, et al. Oxidative stress and chronic myeloid leukemia: a balance between ROS-mediated pro- and anti-apoptotic effects of tyrosine kinase inhibitors. Antioxidants. 2024;13(4):461. doi:10.3390/antiox13040461
19. Nolfi-Donegan D, Braganza A, Shiva S. Mitochondrial electron transport chain: oxidative phosphorylation, oxidant production, and methods of measurement. Redox Biology. 2020;37:101674. doi:10.1016/j.redox.2020.101674
20. Zorov DB, Juhaszova M, Sollott SJ. Mitochondrial reactive oxygen species (ROS) and ROS-induced ROS release. Physiological Reviews. 2014;94(3):909–50. doi:10.1152/physrev.00026.2013
21. Kuretu A, Arineitwe C, Mothibe M, Ngubane P, Khathi A, Sibiya N. Drug-induced mitochondrial toxicity: risks of developing glucose handling impairments. Frontiers in Endocrinology. 2023;14:112392. doi:10.3389/fendo.2023.1123928
22. Gorini S, De Angelis A, Berrino L, Malara N, Rosano G, Ferraro E. Chemotherapeutic drugs and mitochondrial dysfunction: focus on doxorubicin, trastuzumab, and sunitinib. Oxidative Medicine and Cellular Longevity. 2018;2018:758273. doi:10.1155/2018/7582730
23. Scruggs ER, Naylor AJD. Mechanisms of zidovudine-induced mitochondrial toxicity and myopathy. Pharmacology. 2008;82(2):83–8. doi:10.1159/000134943
24. Garcia D, Shaw RJ. AMPK: mechanisms of cellular energy sensing and restoration of metabolic balance. Molecular Cell. 2017;66(6):789–800. doi:10.1016/j.molcel.2017.05.032
25. Gélinas R, Mailleux F, Dontaine J, Bultot L, Demeulder B, Ginion A, et al. AMPK activation counteracts cardiac hypertrophy by reducing O-GlcNAcylation. Nature Communications. 2018;9:1. doi:10.1038/s41467-017-02795-4
26. Gupta S, Kass GEN, Szegezdi E, Joseph B. The mitochondrial death pathway: a promising therapeutic target in diseases. Journal of Cellular and Molecular Medicine. 2009;13(6):1004–33. doi:10.1111/j.1582-4934.2009.00697.x
27. Kaiser WJ, Upton JW, Mocarski ES. Viral modulation of programmed necrosis. Current Opinion in Virology. 2013;3(3):296–306. doi:10.1016/j.coviro.2013.05.019
28. Rawat PS, Jaiswal A, Khurana A, Bhatti JS, Navik U. Doxorubicin-induced cardiotoxicity: an update on the molecular mechanism and novel therapeutic strategies for effective management. Biomedicine & Pharmacotherapy. 2021;139:111708. doi:10.1016/j.biopha.2021.111708
29. Robichaux DJ, Harata M, Murphy E, Karch J. Mitochondrial permeability transition pore-dependent necrosis. Journal of Molecular and Cellular Cardiology. 2022;174:47–55. doi:10.1016/j.yjmcc.2022.11.003
30. Khalid N, Azimpouran M. Necrosis pathology. StatPearls – NCBI Bookshelf. 2023. Available from: https://www.ncbi.nlm.nih.gov/books/NBK557627
31. Zong Y, Li H, Liao P, Chen L, Pan Y, Zheng Y, et al. Mitochondrial dysfunction: mechanisms and advances in therapy. Signal Transduction and Targeted Therapy. 2024;9:1. doi:10.1038/s41392-024-01839-8
32. Gottlieb RA, Thomas A. Mitophagy and mitochondrial quality control mechanisms in the heart. Current Pathobiology Reports. 2017;5(2):161–9. doi:10.1007/s40139-017-0133-y
33. Kciuk M, Gielecińska A, Mujwar S, Kołat D, Kałuzińska-Kołat Ż, Celik I, et al. Doxorubicin—an agent with multiple mechanisms of anticancer activity. Cells. 2023;12(4):659. doi:10.3390/cells12040659
34. Méndez-Valdés G, Gómez-Hevia F, Bragato MC, Lillo-Moya J, Rojas-Solé C, Saso L, et al. Antioxidant protection against trastuzumab cardiotoxicity in breast cancer therapy. Antioxidants. 2023;12(2):457. doi:10.3390/antiox12020457
35. Varga ZV, Ferdinandy P, Liaudet L, Pacher P. Drug-induced mitochondrial dysfunction and cardiotoxicity. AJP Heart and Circulatory Physiology. 2015;309(9):H1453–67. doi:10.1152/ajpheart.00554.2015
36. Rodríguez-Hernández MA, De La Cruz-Ojeda P, López-Grueso MJ, Navarro-Villarán E, Requejo-Aguilar R, Castejón-Vega B, et al. Integrated molecular signaling involving mitochondrial dysfunction and alteration of cell metabolism induced by tyrosine kinase inhibitors in cancer. Redox Biology. 2020;36:101510. doi:10.1016/j.redox.2020.101510

37. Lynx MD, LaClair DD, McKee EE. Effects of zidovudine and stavudine on mitochondrial DNA of differentiating 3T3-F442a cells are not associated with imbalanced deoxynucleotide pools. Antimicrobial Agents and Chemotherapy. 2008;53(3):1252–5. doi:10.1128/AAC.01115-08
38. Krone RJ, Merchant A, Mitchell JD. Cardioprotection using doxorubicin: the role of dexrazoxane. In: Pharmaceutical Science. 2024. doi:10.5772/intechopen.1004240
39. Jiang Q, Yin J, Chen J, Ma X, Wu M, Liu G, et al. Mitochondria-targeted antioxidants: a step towards disease treatment. Oxidative Medicine and Cellular Longevity. 2020;2020:8837893. doi:10.1155/2020/8837893
40. Fernandez-Marcos PJ, Auwerx J. Regulation of PGC-1α, a nodal regulator of mitochondrial biogenesis. American Journal of Clinical Nutrition. 2011;93(4 Suppl):884S–90S. doi:10.3945/ajcn.110.001917
41. Wang Z, Zhu Y, Yao Y, Zhang W, Wang B, Wang J, et al. Natural products targeting regulated cell deaths for adriamycin-induced cardiotoxicity. Cell Death Discovery. 2025;11(1). doi:10.1038/s41420-025-02389-w
42. Mendoza A, Patel P, Robichaux D, Ramirez D, Karch J. Inhibition of the MPTP and lipid peroxidation is additively protective against I/R injury. Circulation Research. 2024;134(10):1292–305. doi:10.1161/CIRCRESAHA.123.323882
43. Chen W, Zhao H, Li Y. Mitochondrial dynamics in health and disease: mechanisms and potential targets. Signal Transduction and Targeted Therapy. 2023;8(1). doi:10.1038/s41392-023-01547-9
44. Attanasio U, Di Sarro E, Tricarico L, Di Lisi D, Armentaro G, Miceli S, et al. Cardiovascular biomarkers in cardio-oncology: antineoplastic drug cardiotoxicity and beyond. Biomolecules. 2024;14(2):199. doi:10.3390/biom14020199
45. Trumpff C, Michelson J, Lagranha CJ, Taleon V, Karan KR, Sturm G, et al. Stress and circulating cell-free mitochondrial DNA: a systematic review of human studies, physiological considerations, and technical recommendations. Mitochondrion. 2021;59:225–45. doi:10.1016/j.mito.2021.04.002
46. Cordiano R, Di Gioacchino M, Mangifesta R, Panzera C, Gangemi S, Minciullo PL. Malondialdehyde as a potential oxidative stress marker for allergy-oriented diseases: an update. Molecules. 2023;28(16):5979. doi:10.3390/molecules28165979
47. Matsuo S, Nakajima K, Kinuya S. Evaluation of cardiac mitochondrial function by a nuclear imaging technique using technetium-99m-MIBI uptake kinetics. DOAJ. 2013;1(1):39–43. Available from: https://doaj.org/article/1be33eb5e6104064a8127dbdaef4f88d

CITE AS: Kungu Erisa (2025). Mitochondrial Dysregulation in Drug-Induced Cardiotoxicity: Redox Imbalance, Bioenergetics, and Cell Death Pathways. INOSR APPLIED SCIENCES 13(2):33-38. https://doi.org/10.59298/INOSRAS/2025/13.2.3338