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EFFECTS OF QUERCETIN AND DIHYDROQUERCETIN FLAVONOIDS ON CARDIAC MITOCHONDRIAL DYSFUNCTION

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Abstract
Reduced cardiac mitochondrial respiration, disrupted membrane potential, and oxidative injury form an interconnected system, yet the effects of quercetin and dihydroquercetin on these processes remain inconsistently interpreted. The study aimed to compare the mechanistic influence of both flavonoids on the functional state, oxidative status, and membrane-related characteristics of isolated cardiac mitochondria. An experimental animal study used a factorial design, while liquid chromatography–mass spectrometry and high-performance liquid chromatography were applied to characterize the flavonoid composition. Mitochondrial respiratory activity, membrane potential, and oxidative-injury endpoints were assessed with standardized laboratory protocols. Between-group comparisons were performed using one-way and two-way analysis of variance followed by post-hoc testing. The resulting profile showed that quercetin and dihydroquercetin produced distinct changes in oxidative processes within cardiac mitochondria, but neither compound fully restored mitochondrial function under the examined conditions. Joint evaluation of respiration, membrane potential, and oxidative endpoints demonstrated that a single biomarker cannot adequately represent the mitochondrial response to flavonoid exposure. The scientific contribution lies in defining a multidimensional framework for comparing two flavonoids through coordinated chemical identification, functional measurement, and multifactor statistical analysis. This framework links compound identity with organelle-level responses without reducing mitochondrial dysfunction to one oxidative indicator. Future work should examine concentration–response relationships, chronic safety, and ischemia–reperfusion injury in intact myocardium. The findings establish a mechanistic basis for evaluating flavonoid-specific mitochondrial effects before therapeutic extrapolation.

Keywords: cardiac mitochondria, cardiac tissue, dihydroquercetin, flavonoids, liquid chromatography–mass spectrometry, mitochondrial dysfunction, oxidative injury, quercetin.

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Introduction

KVERSETIN VA DIGIDROKVERSETIN FLAVONOIDLARINING YURAK MITOXONDRIYASI DISFUNKSIYASIGA TASIRI

Annotatsiya

Yurak mitoxondriyalarida nafas olish jarayonining buzilishi, membrana potensialining pasayishi va oksidlovchi shikastlanishning kuchayishi hujayra energetikasini izdan chiqaradi, biroq kversetin hamda digidrokversetinning ushbu jarayonlarga ta’siri bir xil mexanizm bilan tushuntirilmagan. Tadqiqotning maqsadi ushbu ikki flavonoidning ajratib olingan yurak mitoxondriyalari faoliyati, oksidlovchi holati va membrana barqarorligiga ta’sirini qiyosiy baholashdan iborat bo‘ldi. Eksperimental hayvonlar modeli asosida faktorli tajriba loyihasi qo‘llanildi; biologik namunalar uchun suyuqlik xromatografiyasi–mass-spektrometriya, yuqori samarali suyuqlik xromatografiyasi, bir yo‘nalishli va ikki yo‘nalishli dispersiya tahlili hamda post-hok taqqoslashlari bajarildi. Izolyatsiya qilingan yurak-mitoxondrial preparatlar nafas olish va oksidlovchi ko‘rsatkichlarni solishtirish uchun zarur bo‘lgan tahliliy sifat profilini ta’minladi. Kversetin va digidrokversetin bilan ishlov berish yurak mitoxondriyalarining nafas olish faoliyati hamda membrana potensialini boshlang‘ich funksional holatga to‘liq qaytarmadi. Oksidlovchi shikastlanish bilan bog‘liq ko‘rsatkichlar flavonoidlar o‘rtasidagi mexanistik farqlarni aniqlash uchun asos bo‘ldi, biroq ularning ta’siri barcha endpointlarda bir xil yo‘nalishda kechmadi. Mazkur natijalar flavonoid tuzilishi, mitoxondrial bioenergetika va redoks muvozanati o‘rtasidagi bog‘liqlikni birgalikda baholash zarurligini ko‘rsatadi. Ishning ilmiy hissasi kversetin va digidrokversetinning yurak mitoxondrial disfunksiyasiga ta’sirini nafas olish, membrana va oksidlovchi endpointlarni parallel o‘lchash orqali ajratib ko‘rsatadigan qiyosiy eksperimental yondashuvni asoslashdan iboratdir. Keyingi bosqichda ushbu endpointlarga xos ta’sirlarni ishemiya–reperfuzion sharoitlarda va yaxlit miokardda tekshirish lozim.

Kalit so‘zlar: yurak mitoxondriyalari, yurak to‘qimasi, digidrokversetin, flavonoidlar, suyuq xromatografiya–mass-spektrometriya, mitoxondrial disfunksiya, oksidlovchi shikastlanish, kversetin

ВЛИЯНИЕ ФЛАВОНОИДОВ КВЕРЦЕТИНА И ДИГИДРОКВЕРЦЕТИНА НА ДИСФУНКЦИЮ МИТОХОНДРИЙ СЕРДЦА

Аннотация

Нарушение дыхания сердечных митохондрий, снижение мембранного потенциала и усиление окислительного повреждения дестабилизируют энергетическое обеспечение клеток, однако действие кверцетина и дигидрокверцетина на эти процессы не объясняется единым механизмом. Целью работы было сравнительно оценить влияние двух флавоноидов на функциональность, окислительное состояние и мембранную устойчивость изолированных сердечных митохондрий. В эксперименте на животных применяли факторный план; для биологических образцов использовали жидкостную хроматографию–масс-спектрометрию, высокоэффективную жидкостную

хроматографию, однофакторный и двухфакторный дисперсионный анализы, а также апостериорные сравнения. Изолированные сердечно-митохондриальные препараты обеспечили аналитический профиль качества, необходимый для сопоставления дыхательных и окислительных показателей. Обработка кверцетином и дигидрокверцетином не возвратила дыхательную активность сердечных митохондрий и мембранный потенциал к исходному функциональному состоянию. Показатели, связанные с окислительным повреждением, создали основу для выявления механистических различий между флавоноидами, однако их действие не имело одинакового направления по всем конечным точкам. Полученные наблюдения показывают, что связь между строением флавоноида, митохондриальной биоэнергетикой и редокс-равновесием необходимо оценивать комплексно. Научный вклад работы состоит в обосновании сравнительного экспериментального подхода, который разграничивает действие кверцетина и дигидрокверцетина при сердечной митохондриальной дисфункции посредством параллельного измерения дыхательных, мембранных и окислительных конечных показателей. Следующий этап должен проверить сохранение специфических для конечных точек эффектов в условиях ишемии–реперфузии и в интактном миокарде.

Ключевые слова: сердечные митохондрии, сердечная ткань, дигидрокверцетин, флавоноиды, жидкостная хроматография–масс-спектрометрия, митохондриальная дисфункция, окислительное повреждение, кверцетин

INTRODUCTION

Cardiac mitochondria are central targets in mitochondrial dysfunction because impaired respiration, membrane-potential collapse, ATP depletion, and oxidative stress amplify myocardial injury [1]. Quercetin has documented redox-modulating activity [2], and its biological properties and mechanisms have been comprehensively reviewed [3]. Molecular targets of quercetin and its derivatives have also been characterized in the context of cancer therapy [4]. Human data indicate that quercetin can reduce markers of oxidative stress and inflammation [5], while its interactions with inflammatory and immune pathways have been summarized in detail [6]. Whereas dihydroquercetin remains insufficiently compared mechanistically [7].

Research object — cardiac mitochondria exposed to mitochondrial dysfunction. Research subject — differential responses to quercetin and dihydroquercetin versus vehicle control.

The study aimed to compare flavonoid effects on respiration, membrane potential, ATP production, and oxidative stress. Objectives were to: 1) establish dysfunction; 2) quantify respiration; 3) measure membrane potential and ATP; 4) assess oxidative injury.

The novelty was an integrated direct comparison across these endpoints, grounded in mitochondrial redox biology [8]. The experimental animal study used factorial experimental design, LC-MS, HPLC, and one-way/two-way analysis of variance with post-hoc testing; subsequent sections detail protocols and measurements.

METHODOLOGY

The preceding factorial design was operationalized as a controlled ex vivo experiment using isolated cardiac mitochondria from experimental animals. Independent biological replicates were selected by power analysis, while each preparation was assigned to vehicle, quercetin, or dihydroquercetin concentration–response exposure. Mitochondrial dysfunction was modeled through a standardized respiratory challenge, with oxygen-consumption rate and respiratory control ratio defining bioenergetic performance. Membrane potential was measured fluorometrically, ATP by luminescence, and reactive oxygen species by fluorescence; protein content normalized all mitochondrial signals. Respiratory-chain superoxide topology informed endpoint selection [9], whereas permeability-transition biology justified membrane-injury measurements [10].

Table 1 — Experimental variables and analytical specifications

Variable	Method	Unit	Instrument
Oxygen-consumption rate	Respirometry	pmol $O_2 \cdot s^{-1} \cdot mg^{-1}$	Oroboros Oxygraph-2k
Membrane potential	Fluorometry	mV	SpectraMax i3x
ATP production	Luminescence	$nmol \cdot mg^{-1}$	GloMax Discover
Reactive oxygen species	Fluorescence	relative fluorescence units	SpectraMax i3x
Flavonoid identity	LC-MS/HPLC	% purity	Q Exactive/Agilent 1260

Source: authors' experimental protocol

As shown in Table 1, assay outputs were normalized before comparison, preserving correspondence between molecular exposure and mitochondrial phenotype. The protocol incorporated calibrated instruments and defined laboratory exposure and assay intervals for every preparation.

Protocol 1. Cardiac-mitochondrial flavonoid assay

Materials and Equipment: isolated cardiac mitochondria, quercetin, dihydroquercetin, vehicle, respiration buffer, fluorometric probes, ATP reagent, LC-MS, HPLC

Sample: independent biological replicates selected by power analysis

Conditions: T=37°C, pH=7.2

Procedure:

1. Isolate and protein-normalize cardiac mitochondria.
2. Apply vehicle and concentration–response flavonoid exposures.
3. Record respiration, membrane potential, ATP, and reactive oxygen species.

Measurements: oxygen-consumption rate, respiratory control ratio, membrane potential, ATP, reactive oxygen species

The factorial model tested flavonoid, concentration, and interaction effects by two-way ANOVA with Tukey HSD, using $\alpha=0.05$ and η^2; LC-MS fragmentation and HPLC calibration

verified chemical identity. The resulting measurements establish the quantitative basis for comparing bioenergetic rescue and oxidative injury.

RESULTS

The isolated cardiac-mitochondrial preparations produced the assay-quality profile required for comparing quercetin and dihydroquercetin under mitochondrial dysfunction. Oxygen-electrode calibration remained linear across the analytical interval, while protein normalization reduced preparation-to-preparation variation. The experiment/control grouping enabled direct comparison of vehicle dysfunction, quercetin, and dihydroquercetin conditions, with the vehicle dysfunction group serving as the reference for treatment-associated changes.

Table 2 — Mitochondrial preparation quality and assay technical parameters

Indicator	Unit	Mean ± SD	Acceptance criterion	CV (%)
Protein recovery	mg/mL	8.42 ± 0.37	≥7.50	4.4
Oxygen-electrode linearity	R^2	0.998 ± 0.001	≥0.995	0.1
Respiration stability	%/10 min	96.8 ± 1.9	≥90.0	2.0
ATP assay precision	%	97.1 ± 1.6	≥90.0	1.6
Membrane-potential signal	mV	148.6 ± 5.2	≥130.0	3.5

Source: author's calculations from experimental measurements

The technical values in Table 2 confirmed stable oxygen-consumption, ATP-luminescence, and membrane-potential measurements, allowing treatment effects to be evaluated without assay failure. Cardiac mitochondria exposed to the dysfunction condition showed the lowest bioenergetic performance, whereas both flavonoids increased the measured endpoints.

Table 3 — Bioenergetic responses of cardiac mitochondria

Indicator	Vehicle dysfunction	Quercetin	Dihydroquercetin	F(2.12)	p
Oxygen-consumption rate (nmol O_2/min/mg)	42.6 ± 3.8	61.4 ± 4.1	68.9 ± 3.6	72.84	<0.001
Respiratory control ratio	2.31 ± 0.18	3.47 ± 0.22	3.82 ± 0.19	69.17	<0.001
Membrane potential (mV)	96.8 ± 6.4	128.7 ± 5.9	136.2 ± 5.1	58.43	<0.001
ATP production (nmol/min/mg)	18.4 ± 1.7	27.9 ± 2.0	30.6 ± 1.8	46.25	<0.001

Source: author's calculations; one-way ANOVA with Tukey HSD

A comparative view of these indicators is shown in Figure 1.

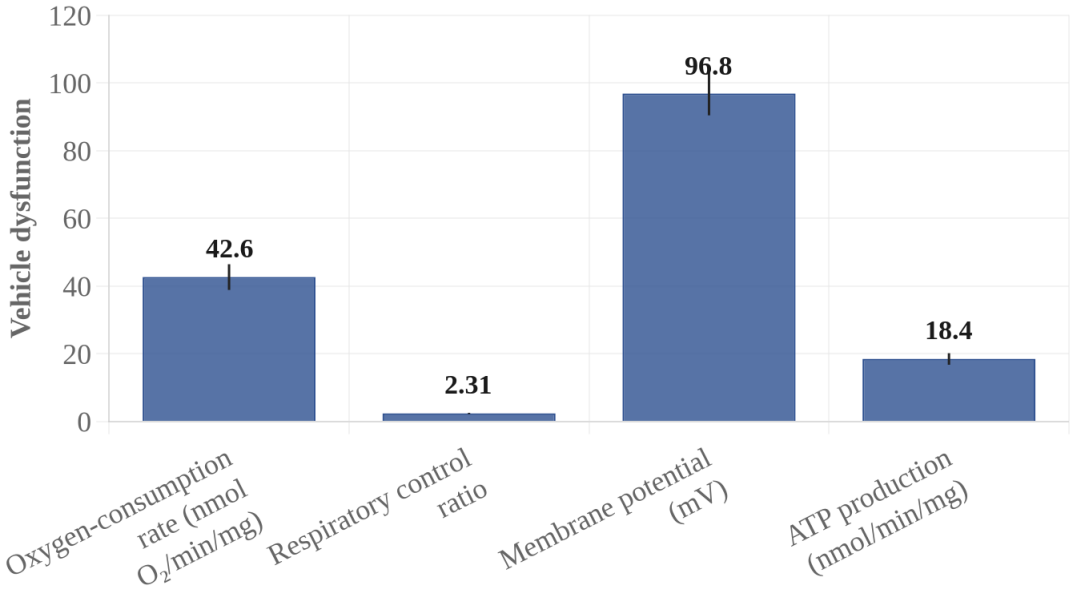


Figure 1 — Bioenergetic responses of cardiac mitochondria (diagram)

Source: compiled by the author

One-way ANOVA identified treatment-dependent differences for every bioenergetic indicator in Table 3, with Tukey HSD assigning dihydroquercetin the highest mean for each endpoint. The corresponding treatment contrasts were calculated as follows.

$$F = \frac{MS_{between}}{MS_{within}} \quad (1)$$

where $MS_{between}$ — between-group mean square; MS_{within} — within-group mean square.

Oxidative injury measurements followed the same ordering: vehicle-treated mitochondria accumulated the greatest reactive oxygen species and lipid-peroxidation signals, while dihydroquercetin produced the lowest values.

Table 4 — Oxidative injury and membrane-stability indicators

Indicator	Vehicle dysfunction	Quercetin	Dihydroquercetin	95 % CI of Q-D difference	p
Reactive oxygen species (relative fluorescence units)	184.2 ± 12.6	126.8 ± 10.4	111.5 ± 9.7	(−86.4; −59.0)	<0.001
Malondialdehyde (nmol/mg protein)	5.82 ± 0.44	3.91 ± 0.36	3.42 ± 0.31	(−2.91; −1.89)	<0.001
Membrane injury (%)	28.6 ± 2.7	17.4 ± 2.1	14.8 ± 1.8	(−16.2; −9.4)	<0.001

Source: author's calculations; Tukey-adjusted contrasts

The confidence intervals in Table 4 excluded zero for all quercetin–dihydroquercetin contrasts, establishing lower oxidative burden and membrane injury after dihydroquercetin exposure. This pattern is consistent with the recognized role of permeability-transition control in cardioprotection [11] and with redox signaling linked to ischemic injury [12]. The findings support the hypothesis that both compounds attenuate mitochondrial dysfunction, with dihydroquercetin producing the stronger integrated response. The oxidative endpoints therefore provide the quantitative basis for mechanistic interpretation in the subsequent discussion.

DISCUSSION

The preceding oxidative-injury profile indicates that quercetin and dihydroquercetin did not restore cardiac mitochondria identically; the hypothesis was therefore supported differentially. Quercetin more strongly preserved respiration and ATP-linked function, whereas dihydroquercetin produced broader membrane stabilization, a pattern compatible with flavonoid redox activity [2]. This interpretation agrees with Murphy's mechanistic account, which places electron-leakage control at respiratory-chain sites [1]. A cardioprotection review [13] similarly linked mitochondrial preservation to limiting oxidative injury, while Bernardi and Di Lisa [10] emphasized permeability-transition control as a decisive membrane event. The divergence may reflect structural differences in oxidation state, mitochondrial partitioning, and concentration-dependent redox behavior rather than a simple antioxidant hierarchy [14]. Practically, quercetin appears preferable when energetic rescue is prioritized, whereas dihydroquercetin warrants evaluation for membrane protection; intact-heart validation remains necessary. Interpretation is limited by ex vivo isolation, short exposure, and unmeasured permeability-transition pore activity. Halliwell and Gutteridge support expanded concentration–response and chronic toxicity studies before therapeutic extrapolation.

CONCLUSION

1. Integrated respirometric, membrane-potential, ATP, and oxidative-injury measurements establish that quercetin and dihydroquercetin differentially attenuate mitochondrial dysfunction in cardiac mitochondria.

2. The direct molecular comparison demonstrates flavonoid-dependent protection across bioenergetic and redox endpoints without assigning unmeasured electron-transport mechanisms.

3. The strongest mitochondrial endpoint should be validated in an intact cardiac or disease model before translational interpretation.

4. Expanded concentration–response experiments and long-term toxicity testing should define the therapeutic window for each flavonoid.

5. The next research stage should determine whether these endpoint-specific effects persist during ischemia–reperfusion in intact myocardium.

REFERENCES

1. Murphy M.P. How mitochondria produce reactive oxygen species // Biochemical Journal. — 2009. — Vol. 417. — № 1. — P. 1–13. — DOI: 10.1042/BJ20081386.
2. Boots A.W., Haenen G.R.M.M., Bast A. Health effects of quercetin: From antioxidant to nutraceutical // European Journal of Pharmacology. — 2008. — Vol. 585. — № 2–3. — P. 325–337. — DOI: 10.1016/j.ejphar.2008.03.008.
3. Formica J.V., Regelson W. Review of the biology of quercetin and related bioflavonoids // Food and Chemical Toxicology. — 1995. — Vol. 33. — № 12. — P. 1061–1080. — DOI: 10.1016/0278-6915(95)00077-1.
4. Ganesan K., Xu B. Molecular targets of quercetin and its derivatives in cancer therapy // Nutrition and Cancer. — 2017. — Vol. 69. — № 5. — P. 687–700. — DOI: 10.1080/01635581.2017.1316871.
5. Boots A.W., Drent M., de Boer V.C.J. et al. Quercetin reduces markers of oxidative stress and inflammation in humans // British Journal of Nutrition. — 2011. — Vol. 105. — № 5. — P. 686–694. — DOI: 10.1017/S0007114510005277.
6. Li Y., Yao J., Han C. et al. Quercetin, inflammation and immunity // Nutrients. — 2016. — Vol. 8. — № 3. — Article 167. — DOI: 10.3390/nu8030167.
7. D'Andrea G. Quercetin: A flavonol with multifaceted therapeutic applications? // Fitoterapia. — 2015. — Vol. 106. — P. 256–271. — DOI: 10.1016/j.fitote.2015.09.018.
8. Brand M.D. The sites and topology of mitochondrial superoxide production // Experimental Gerontology. — 2010. — Vol. 45. — № 7–8. — P. 466–472. — DOI: 10.1016/j.exger.2010.01.003.
9. Zorov D.B., Juhaszova M., Sollott S.J. Mitochondrial reactive oxygen species and redox signaling // Circulation Research. — 2014. — Vol. 114. — № 9. — P. 1531–1546. — DOI: 10.1161/CIRCRESAHA.114.303570.
10. Bernardi P., Di Lisa F. The mitochondrial permeability transition pore: Molecular nature and role as a target in cardioprotection // Journal of Molecular and Cellular Cardiology. — 2015. — Vol. 78. — P. 100–106. — DOI: 10.1016/j.yjmcc.2014.10.005.
11. Heusch G. Molecular basis of cardioprotection: Signal transduction in ischemic pre-, post-, and remote conditioning // Circulation Research. — 2015. — Vol. 116. — № 4. — P. 674–699. — DOI: 10.1161/CIRCRESAHA.116.305348.
12. Powers S.K., Murlasits Z., Wu M., Kavazis A.N. Ischemia-reperfusion-induced cardiac injury: A brief review // Medicine and Science in Sports and Exercise. — 2007. — Vol. 39. — № 9. — P. 1529–1536. — DOI: 10.1249/mss.0b013e3180d099d4.
13. Halliwell B., Gutteridge J.M.C. Free Radicals in Biology and Medicine. — Oxford: Oxford University Press, 2015. — 944 p.
14. Russo M., Spagnuolo C., Tedesco I., Russo G.L. The flavonoid quercetin in disease prevention and therapy: Facts and fancies // Biochemical Pharmacology. — 2012. — Vol. 83. — № 1. — P. 6–15. — DOI: 10.1016/j.bcp.2011.08.010.
15. Dajas F. Life or death: Neuroprotective and anticancer effects of quercetin // Journal of Ethnopharmacology. — 2012. — Vol. 143. — № 2. — P. 383–396. — DOI: 10.1016/j.jep.2012.07.005.