Original Article

Antioxidant Potential of Cydonia oblonga in Isoproterenol-Induced Myocardial Infarction in rats

Azka Khan, Asima Ayyub, Maria Qamar, Shahnaz Akhtar, Umair Samee, Fiaz Ahmed

Abstract

Objective: An experimental study was carried out to find the antioxidant potential of methanolic leaf extract of Cydonia oblonga in Isoproterenol-Induced Myocardial Infarction in groups of rats.

Material and Methods: A total of 30 Wistar rats included in the study. Rats were divided into 5 groups comprising 6 animals per group. Group I was given normal saline while Group II was given normal saline followed by isoproterenol. Group III, Group IV and Group V received methanolic extract of C. oblonga 50 mg/kg, 100 mg/kg and Carvedilol 2 mg/kg respectively by oral route followed by isoproterenol. Blood samples were estimated for cardiac biomarkers (Troponin T, CK-MB and LDH). Anti-oxidative stress biomarkers (catalase, superoxide dismutase, glutathione peroxidase, malanodialdehyde) were also estimated using cardiac tissue.

Results: C. oblonga at doses of 50 mg/kg & 100 mg/kg significantly reduced the levels of cardiac markers Troponin T, CK-MB and Lactate dehydrogenase in treatment groups of rats. Significantly high values of anti-oxidants superoxide dismutase, catalase, and glutathione peroxidase were found only at high dose of extract of CO. Significantly decreased level of melanodialdehyde was found in treatment groups.

Conclusion: Study revealed that due to antioxidant characteristics, C. oblonga showed cardioprotective activity against myocardial infarction.

Keywords: C. oblonga, antioxidant, cardio-protective effect

How to cite: Khan A, Ayyub A, Qamar M, Akhtar S, Samee U, Ahmed F. Antioxidant Potential of Leaf Extract of Cydoniaoblonga in Isoproterenol-Induced Myocardial Infarction in Groups of Rat. *Esculapio - JSIMS 2024;20(02)254-257*

DOI: https://doi.org/10.51273/esc24.251320221

Introduction

Cardiovascular diseases (CVDs) are the principal cause of early death and disability in human beings with a rise in incidence globally. About 22.20 million cardiovascular disease related deaths are predictable to occur in up to year of 2030.[1,2] The underlying cause of most cardiovascular diseases is atherosclerosis, leading to conditions like heart attacks, strokes due to thromboembolism, vascular damage and arrhythmias.[3] Oxidative stress (OS) occurs when there's an imbalance between oxidative and antioxidative processes, leading to increased oxidation and results in inflammation[2,4] This oxidative stress contributes to cardiac dysfunction, encompassing myocardial infarction, ischemia /reperfusion, heart failure and athero-sclerosis.[5,6] Despite effective cardiac drugs, significant gaps still persist in treating cardiovascular diseases. Medicinal plants, with their safety profiles, offer potential benefits for addressing these issues7'8. The leaf extract of Cydonia oblonga, or quince, contains phenolic content, vitamin E, and fatty acids, while gallic acid, a polyphenolic metabolite, serves as an antioxidant with medicinal applications. CO exhibit

1,4. Department of Pharmacology, RLKU Medical College, Lahore
2. Department of Biochemistry, Akhtar Saeed Medical and Dental College
3. Department of Pharmacology, RLMC Medical College, Lahore
5. Department of Surgery, Central Park Medical College, Lahore

Correspondence:
Dr. Asima Ayyub, *Department of Biochemistry, Akhtar Saeed Medical and Dental College* asmaamin31@gmail.com

Submission Date: 15-02-2024
1st Revision Date: 13-04-2024
Acceptance Date: 06-06-2024

physiological benefits, potentially supplementing cardiovascular, pulmonary, and immunological defenses.[9]

Due to the reported anti-oxidative and anti-atherosclerotic properties of Cydonia oblonga, the experimental study was designed to find the antioxidant potential of methanolic leaf extract of Cydonia oblonga in Isoproterenol-Induced oxidative stress in groups of rats.

Material and Methods

The study was conducted after IRB approval from UHS Ethical Committee. Simple random sampling technique was used and total 30 male Wistar rats (weighed 225-250 g) were taken and kept in a suitable environment in Experimental Research Laboratory UHS, Lahore at temperature of 22-24°C with 45-65% humidity and 12 h/12 h dark/light cycle. All rats were given rat chow and water ad libitum. The study was performed at the Department of Pharmacology, University of Health Sciences, Lahore.

Isoproterenol (Sigma Aldrich) in the dose 85.0 mg /kg body weight /day was added in saline and was given intraperitoneally10 and Methanolic extract of Cydoniaoblonga (CO): 50 mg/kg body weight and 100 mg/kg body weight were dissolved in saline solution and was orally given11.Carvedilol (Sigma Aldrich) about was dissolved in saline solution and was orally given at dose of 2mg/kg body weight/ day 12.The leaves of CO were taken from Sawat-Pakistan and confirmed by botanist at Punjab university. The extract of CO was made with methanol (2 L). The concentrated mixture was dried and kept at 4°C. Induction of Myocardial Infarction in groups of rats by giving injection of isoproterenol (ISO) with a dose of 85mg/kg/day on 2 days (22nd and 23rd day of experiment)13. 30 Wistar rats were divided into five groups (6 rats in each group). Group I (Negative Control) received orally normal saline 10ml /kg body weight by oral for 23 days. Group II (Diseased Control) received orally normal saline 10 ml / kg body weight for 21 days followed by intraperitoneal injection of isoproterenol 85mg/kg body weight on day 22nd and 23rd. Group III (low dose CO) and Group IV (high Dose CO) received orally leaf extract of C. oblonga 50 and100 mg /per kg body weight for 21 days respectively followed by injection of ISO (85 mg/kg) on 22nd and 23rd days. Group V (Carvedilol) received orally Carvedilol 2mg /kg body weight for 21 days followed by injection of Isoproterenol (85mg/kg body weight) on 22nd and 23rd day. All animals were sacrificed at 24th hour, after the last treatment. The blood was taken via cardiac puncture, centrifuged; serum was separated and stored at -20oC for estimation of cardiac enzymes. The cardiac tissue was rinsed in ice-cold saline and homogenized in phosphate buffer saline (pH 7.4) for estimation of oxidative stress markers. This estimation utilized Elabscience Assay kit. Data

Table 1: *Levels of cardiac enzymes in all groups (n=06) of rats Values are expressed as Mean ± SD*

Parameters	Group I (Negative control)	Group II (Diseased control)	Group III (CO low dose)	Group IV (CO high dose)	Group V (Carvedilol) allopathic
Troponin T (ng/L)	330±65.49	516±45.06[a]	280±48.34[b]	169±68.66[b]	351±65[b]
CK-MB (U/L)	81±61.74	168.3±30.79[a]	112±5.4[b]	69±11.17[b]	93±5.3[b]
LDH (U/L)	85±2.26	180±33.57[a]	165±14.06[b]	66.25±9.2[b]	87.17±14.6[b]

[a] *shows a significant group difference with group I*
[b] *shows a significant group difference with group II*

Table 2: *Variation in levels of antioxidant and oxidants enzyme in study group animals (n=6) and controls Values are expressed as Mean ± SD*

Parameters	Group I (Negative control)	Group II (Diseased control)	Group III (CO low dose)	Group IV (CO high dose)	Group V (Carvedilol)
SOD (U/min/mgprot)	98.17±3.323	58.06±7.242[a]	88.85±6.719[b]	105.9±5.175[b]	97.16±3.056[b]
Catalase (U/mg prot)	66.85±1.89	33.77±12.41[a]	44.72±3.406[b]	54.53±2.905[b]	55.67±3.44[b]
GSH (nmol/g)	31.77±1.206	16.12±3.346[a]	36.32±1.014[b]	47.75±4.151[b]	40.16±4.702[b]
MDA (nmol/mg)	0.6471±0.563	7.88±0.520[a]	4.738±0.576[b]	1.048±0.241[b]	1.951±0.327[b]

[a] *shows a significant group difference with group I*
[b] *shows a significant group difference with group II*

was analyzed by SPSS 21. The variables were expressed as Mean ± Standard deviation. The statistical significance of data was estimated by One-way ANOVA. Mean differences between different groups was carried out by using Post hoc Tukey's test.

$P \leq 0.05$ was taken as significant.

Results

Levels of cardiac marker enzymes (troponin T, CK-MB and LDH) were significantly decreased ($P<0.001$) after taking carvedilol (group 5) as compared to controls (group 2). However, the levels of cardiac enzymes were significantly reduced ($P<0.001$) after taking low and high doses of CO as compared to group 2 and group 5. (diseased controls and carvedilol). This showed that both high and low doses of CO are more effective to reduce the level of cardiac enzymes as compared to allopathic drug carvedilol **(Table1).** Levels of antioxidants (SOD, Catalase and GSH) were found to be significantly increased ($P<0.05$) only at the dose of 100mg/kg body weight. On the other hand, level of oxidant or marker of lipid peroxidation MDA was significantly reduced ($P<0.05$) at the dose of 100 mg/kg only **(Table 2).**

Discussion

Our study concluded that Quince or Cydonia oblonga may reduce the levels of biomarkers (Troponin T, CK-MB & LDH) and have good therapeutic effect in cardiovascular problems. A review study included 12 researches based on cardiovascular effectiveness of quince. Study reported that all parts of quince (leaf, seed, and fruit) may be used to reduce risk factors related to cardiovascular disease. The factors are blood pressure, metabolism of glucose, obesity and level of lipids.[14] An experimental study was carried out in groups of rats. Study was conducted to explore the phytochemical and cardio protective potential of two different extractions. This study found the significant antioxidant and cardioprotective ability of CO observed with a dose of 50 mg phenolic extract of quince. It is evident that by using this dose, CO reduced the level of serum cardiac enzymes CK-MB, LDH &trop T and increased tissue parameters (SOD, CAT &GSH) and decrease MDA. It is concluded that cardio protective activity of the extract of quince may be due to its phyto-constituents that neutralize the cardiotoxicity and help to reinstate the cardiac injury in experimental animal.[15]

We also observed that CO with its high dose significantly increased level of antioxidant enzymes (SOD, Catalase, GSH) and decreased level of oxidant (MDA) in group of rats, suffering with cardiovascular issues. The antioxidant property of extract of CO was examined on cells of Ha CaT using the DCF-DA (fluorescent probe). Study found that production of ROS was markedly decreased by extract of CO. Study also found nontoxic effect of extract of CO on all tested doses and have antioxidant activity via controlling the ROS production in cells.[16] Another study also found that extract of CO showed antioxidant role mainly due to the polyphenols present in extract of CO.[17]

It is thought that polyphenol a constituent of extract of CO is a powerful antioxidant and help to slow down the oxidation of free radicals. The phytochemicals can forage a ROS via different mechanisms, counting the inhibition of different enzymes taking part in production of ROS and protection of antioxidant defenses.[18]

These results indicate higher antioxidant activity for certain parts of quince fruit, namely pulp and peel represent easy sources of natural antioxidants with powerful application in pharmaceutical/ nutritional fields, as therapeutic or preventive agents in cardiovascular and other diseases in which free radicals are frequently produced.

Conclusion

Cardioprotective effect of Cydoniaoblonga was observed (in both low and high doses) by reducing the levels of biomarker enzymes. Although it santioxidant potential was shown only at higher doses. However, further studies are needed to explore the key effects of CO consumption as cardiovascular preventive.

Conflict of interest : None

Funding Source: None

References

1. Roth GA, Mensah GA, Johnson CO, Addolorato G, Ammirati E, Baddour LM, et al. Global Burden of Cardiovascular Diseases Writing Group. Global Burden of Cardiovascular Diseases and Risk Factors, 1990-2019: Update From the GBD 2019 Study. J Am CollCardiol. 2020; 22;76(25):2982-3021. doi: 10.1016/j.jacc.2020.11.010.

2. Chang X, Zhang T, Zhang W, Zhao Z, Sun, J. Natural Drugs as a Treatment Strategy for Cardiovascular Disease through the Regulation of Oxidative Stress. Oxid Med Cell Longev. 2020;27;2020:5430407. doi: 10.1155/2020/5430407.

3. Flora GD, Nayak MK. A Brief Review of Cardiovascular Diseases, Associated Risk Factors and Current Treatment Regimes. Curr Pharm 2019;.25(38):4063-4084. doi: 10.2174/1381612825666190925163827.

4. Jelic MD, Mandic AD, Maricic SM, Srdjenovic BU. Oxidative stress and its role in cancer. J Cancer Res Ther. 2021 Jan-Mar;17(1):22-28. doi: 10.4103/jcrt.JCRT_862_16. PMID: 33723127.

5. D'Oria R, Schipani R, Leonardini A, Natalicchio A, Perrini S, Cignarelli A, et al. The Role of Oxidative Stress in Cardiac Disease: From Physiological Response to Injury Factor. Oxidative Medicine and Cellular Longevity 2020;2020, 29 pages. doi.org/10.1155/2020/5732956

6. Dubois-Deruy E, Peugnet V, Turkieh A, Pinet F. Oxidative Stress in Cardiovascular Diseases. Antioxidants (Basel). 2020;9(9):864. doi: 10.3390/antiox9090864.

7. Thomford N, Senthebane D, Rowe A, Munro D, Maroyi SA, Dzobo MK. Natural products for drug discovery in the 21st century: innovations for novel drug discovery. Int JMol Sci. 2018;19(6):p. 1578. doi: 10.3390/ijms19061578

8. Calixto JB. The role of natural products in modern drug discovery. Anais da Academia Brasileira de Ciencias. 2019;91(supplement 3) doi: 10.1590/0001-3765201920190105.

9. Ferreira DM, de Oliveira NM, Lopes L, Machado J, Oliveira MB. Potential Therapeutic Properties of the Leaf of CydoniaOblonga Mill. Based on Mineral and Organic Profiles. Plants (Basel). 2022;11(19):2638. doi: 10.3390/plants11192638.

10. Pan Y, Gao J, Gu R, Lin H, Wang J, Gu Y, et al. Effect of injection of different doses of isoproterenol on the hearts of mice. BMC CardiovascDisord 2022; 22:409. doi.org/10.1186/s12872-022-02852-x

11. Al-Zughbi I, Krayem M. Quince fruit Cydonia oblonga Mill nutritional composition, antioxidative properties, health benefits and consumers preferences towards some industrial quince products: A review. Food Chem. 2022 Nov 1;393:133362. doi: 10.1016/j.foodchem.2022.133362. Epub 2022 May 31. PMID: 35661598.

12. Khafagy ES, Abu Lila AS, Sallam NM, Sanad RA, Ahmed MM, Ghorab MM, et al. Preparation and Characterization of a Novel MucoadhesiveCarvedilolNanosponge: A Promising Platform for Buccal Anti-Hypertensive Delivery. Gels. 2022; 8(4):235. doi: 10.3390/gels8040235.

13. Ghasemi M, Turnbull T, Sebastian S, Kempson I. The MTT Assay: Utility, Limitations, Pitfalls, and Interpretation in Bulk and Single-Cell Analysis. Int J Mol 2021; Sci.22(23):12827. doi: 10.3390/ijms222312827.

14. Amerizadeh A, Vaseghi G, Esmaeilian N, Asgary S. Cardiovascular Effects of Cydoniaoblonga Miller (Quince). Evid Based Complement Alternat Med. 2022; 2022:3185442. doi: 10.1155/2022/3185442

15. Hanan E, Hasan N, Zahiruddin S, Ahmad S, Sharma V, Ahmad FJ. Utilizationof Quince(Cydoniaoblonga)Peel and Explorationof Its Metabolite Profiling and Cardioprotective Potential Against Doxorubicin-Induced Cardiotoxicityin Wistar Rats.m 2022; ACS Omega8:40036−40050

16. Gubitosa F, Fraternale D, De Bellis R,Gorassini A,Benayada L,Chiarantini L. Cydoniaoblonga Mill. Pulp Callus Inhibits Oxidative Stress and Inflammation in Injured Cells. Antioxidants 2023;12:1076. doi.org/10.3390/antiox12051076

17. Khan N,Maihemuti N,Nuer M,Abudurousuli K,Simayi J,Talihati Z, et al. Analysis of Major Polyphenolic Compounds of Cydoniaoblonga Miller (Quince) Fruit Extract by UPLC-MS/MS and Its Effect on Adipogenesis in 3T3-L1 Cells. Separations 2022; 9: 167. doi.org/10.3390/separations907016

18. De Bellis, Chiarantini L, Potenza L,Gorassini A,Verardo G, De Marco R, et al. High Production of Secondary Metabolites and Biological Activities of C. oblonga Mill. Pulp Fruit Callus. J. Funct. Foods 2022; 94:105133.

Authors Contribution

AK: Conceptualization of Project
AA: Data Collection
MQ: Literature Search
SA: Statistical Analysis
US: Drafting, Revision
FA: Writing of Manuscript