Anthocyanin rich extract from Red cabbage (*Brassica oleracea*) reduces oxidative stress and prevents apoptosis in stressed rat cardiomyocytes.

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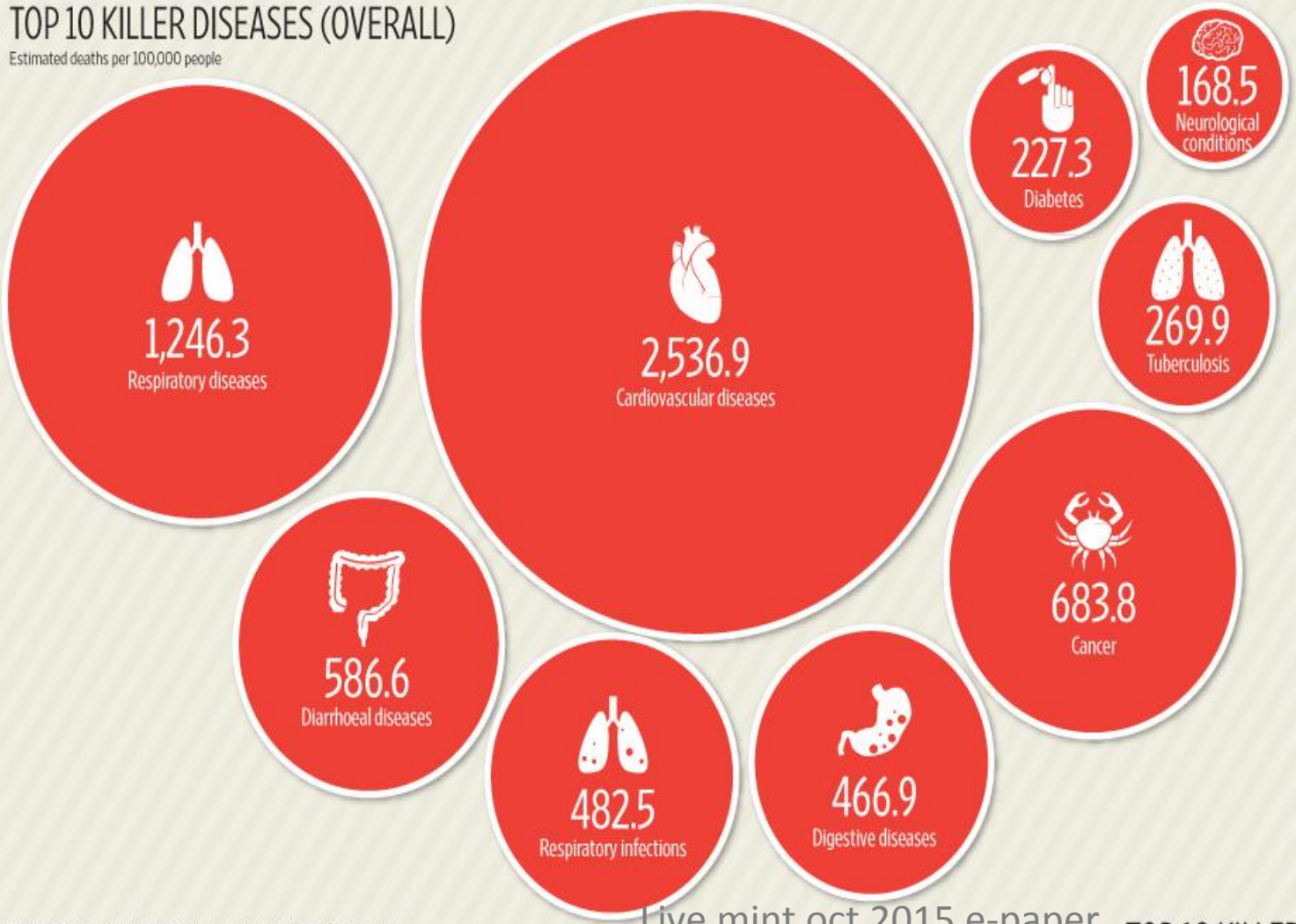
WHAT'S KILLING INDIANS

Heart diseases are the leading cause of death in India, as it is the case in most other countries. But unlike the rest of the world, respiratory diseases are the second biggest killer in the country, which is home to some of the most polluted cities in the world, according to recent reports. The health and family welfare ministry has projected that India will have more than 60 million people with coronary heart diseases by 2015, and 40 million people suffering from diabetes. Meanwhile, a recent report revealed that India has emerged as the world's largest consumer of antibiotics. The use of antibiotics in India grew 62% between 2000 and 2010. Mint reviews the top 10 killer diseases in India, and the drugs most consumed by Indians.

Data compiled by Nikita Mehta/Mint

TOP 10 KILLER DISEASES (OVERALL)

Estimated deaths per 100,000 people

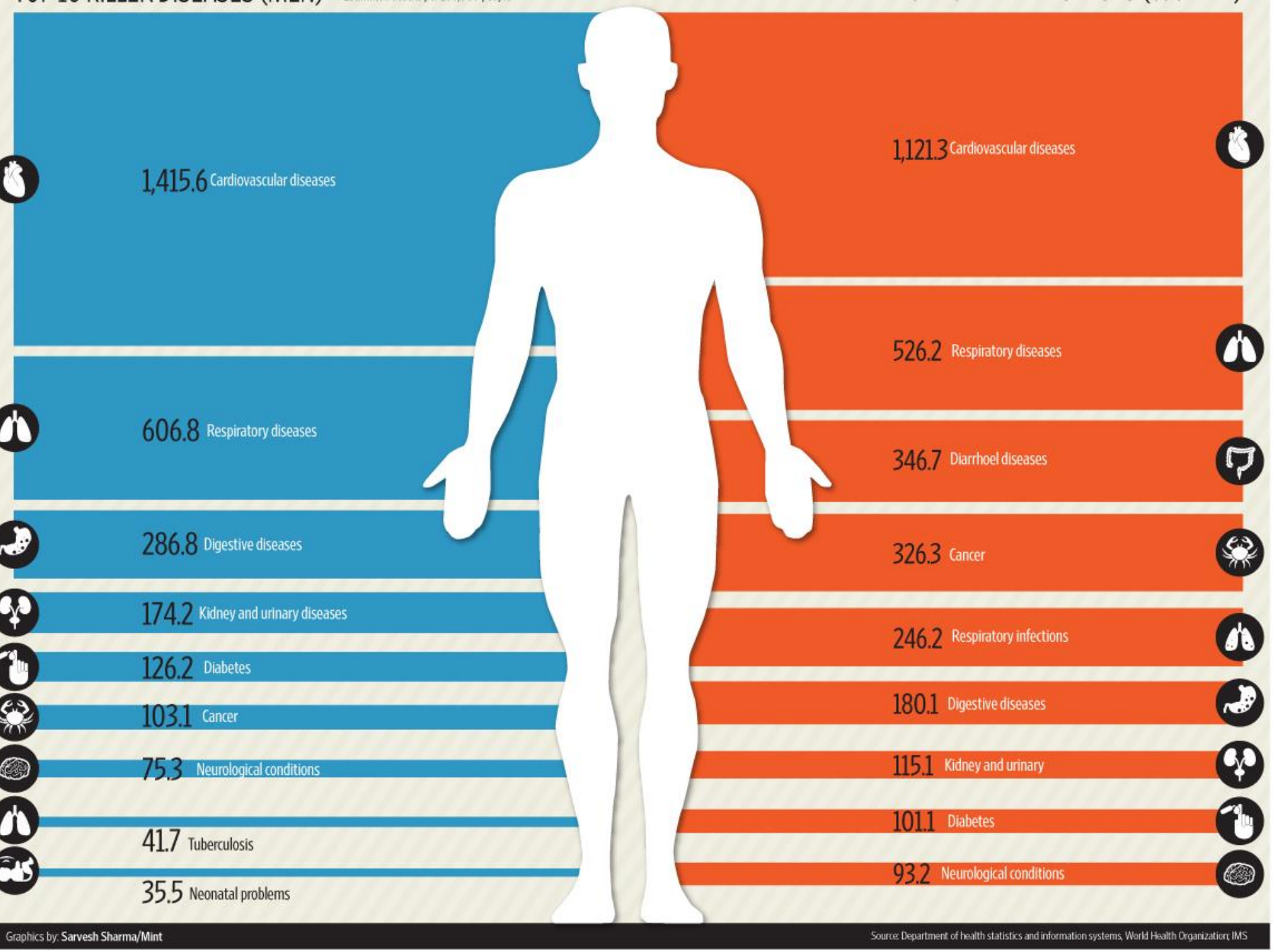


TOP SELLING DRUGS IN INDIA

1	**Augmentin**	Bacterial infections
2	**Corex**	Cough
3	**Phensedyl Cough**	Cough
4	**Voveran**	Inflammatory disorders
5	**Human Mixtard 30/70**	Insulin
6	**Monocef**	Typhoid
7	**Liv-52**	Ayurvedic liver supplement
8	**Betadine**	Antiseptic
9	**Dexorange**	Vitamin deficiency

TOP 10 KILLER DISEASES (MEN) Estimated deaths per 100,000 people

TOP 10 KILLER DISEASES (WOMEN)


1,415.6 Cardiovascular diseases
606.8 Respiratory diseases
286.8 Digestive diseases
174.2 Kidney and urinary diseases
126.2 Diabetes
103.1 Cancer
75.3 Neurological conditions
41.7 Tuberculosis
35.5 Neonatal problems
1,121.3 Cardiovascular diseases
526.2 Respiratory diseases
346.7 Diarrhoel diseases
326.3 Cancer
246.2 Respiratory infections
180.1 Digestive diseases
115.1 Kidney and urinary
101.1 Diabetes
93.2 Neurological conditions
Graphics by: Sarvesh Sharma/Mint
Source: Department of health statistics and information systems, World Health Organization; IMS

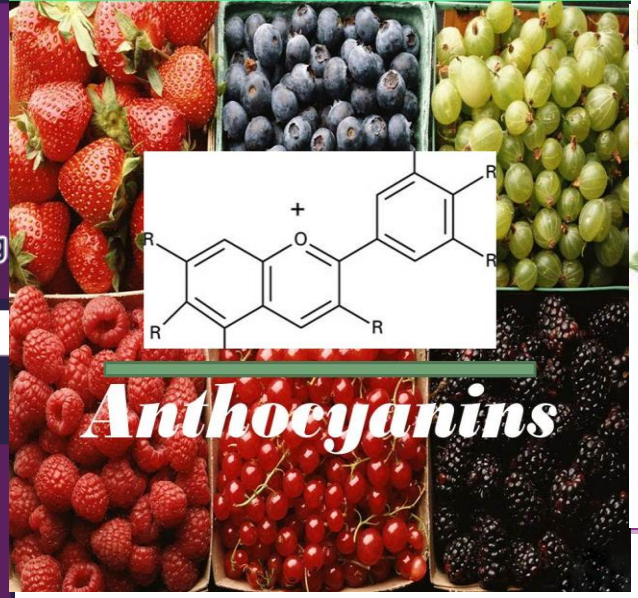
Anthocyanins and Health

Anthocyanins are a class of pigments that occur naturally in plants. Anthocyanins are responsible for the rich colors in red and purple berries, purple corn, red grapes, eggplant, blood oranges and other red, purple or violet plants.

naturalhealthzone.org

Recommended Dietary Allowances (RDA) would be 12.5 grams every day.

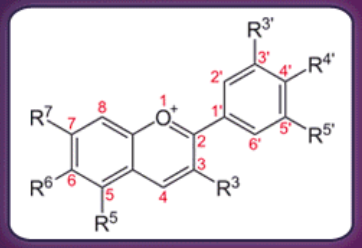
Anthocyanins are strongly suggested by a number of studies to improve sharpness of vision. It has even been suggested by researchers that they may help reduce the risk of cataracts and macular degeneration.



Health Benefits:

Laboratory evidence has suggested that they may be beneficial against:

- ☑ cancer
- ☑ inflammation
- ☑ heart disease
- ☑ diabetes
- ☑ bacterial infections
- ☑ age-related neurodegenerative disease
- ☑ other neurological diseases

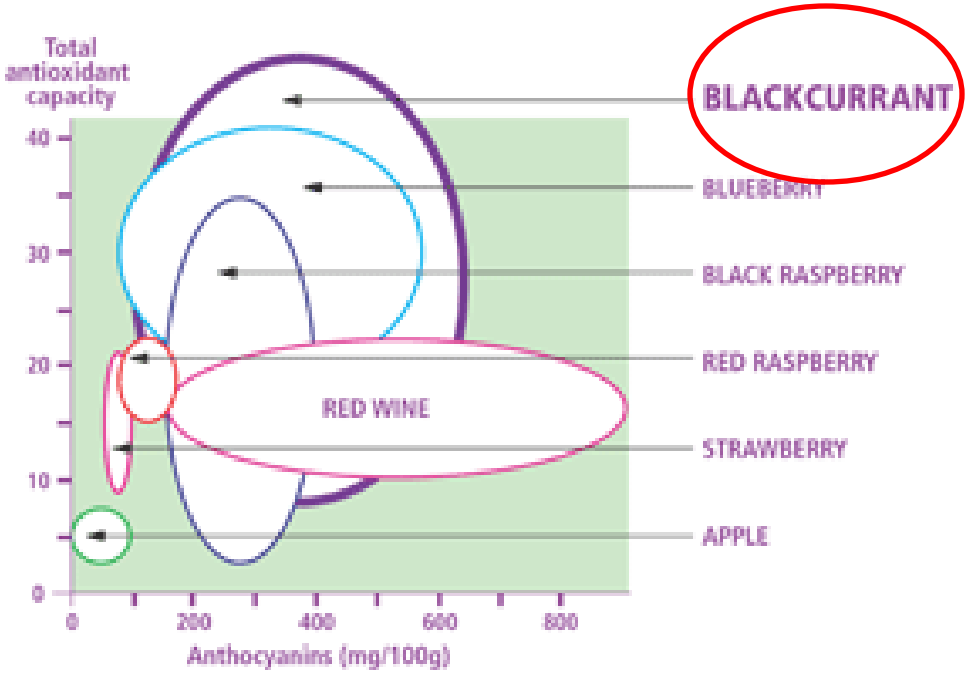


Anthocyanin-rich mixtures and extracts were used in old times to treat many conditions including

- ✓ hypertension
- ✓ liver disorders
- ✓ dysentery
- ✓ diarrhoea
- ✓ urinary problems
- ✓ kidney stones
- ✓ urinary tract infections
- ✓ colds
- ✓ flu

Foods Highest In Anthocyanins:

ANTHOCYANIN CONTENT OF FRUIT



Dr Derek Stuart, Scottish Crop Research Institute

……. Anthocyanins…..not only have imperative role in plants but are extensively researched for their protective role against a myriad of human diseases.

nature International weekly journal of science

News

Nature **135**, 732-736 (04 May 1935) | doi:10.1038/135732a0

Chemistry of the Anthocyanins

R. ROBINSON

Top

THE classical paper of Willstatter and Everest (1913),, on the isolation of the pigment of blue cornflowers, heralded a dramatic transformation of the state of our knowledge of the blue and red colouring matters of flowers and blossoms, and the present position is that we not only know the molecular structure of the more important and widespread anthocyanins, but also that many o
With the simultaneou
carotenoids, the poly
the more obvious cha
have been taken up,
still, it is true, but on
them. Willstatter owe
the anthocyanins, alt
and these salts can b
many ammonium salt
precipitation with a n

nature International weekly journal of science

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News

Nature **137**, 172-173 (01 February 1936) | doi:10.1038/137172a0

Formation of Anthocyanins in Plants

R. Robinson

Top

DISTINCT lines of investigation converge on the problem of the formation of antho-cyanins in plants, our information being derived from studies in plant physiology, in genetics and in the organic chemistry of the pigments and related members of the flavan group. Anthocyanins are frequently produced when photo-synthetic activity at the site of eventual pigmentation is diminished through seasonal changes or various kinds of injuries to the plant (mechanical, fungus disease, etc.). Under such conditions, carbohydrates and other synthetic products tend to accumulate as the result of interference with the translocation currents. Abundant nutriment favours anthocyanin formation, which can, in many cases, be accelerated by artificial feeding with sugars.

nature biotechnology

Letter

Nature Biotechnology **26**, 1301 - 1308 (2008)
Published online: 26 October 2008 | doi:10.1038/nbt.1506

Enrichment of tomato fruit with health-promoting anthocyanins by expression of select transcription factors

Eugenio Butelli[1], Lucilla Titta[2], Marco Giorgio[2], Hans-Peter Mock[3], Andrea Matros[3], Silke Peterek[3], Elio G W M Schijlen[4], Robert D Hall[5], Arnaud G Bovy[4], Jie Luo[1] & Cathie Martin[1]

Dietary consumption of anthocyanins, a class of pigments produced by higher plants, has been associated with protection against a broad range of human diseases. However, anthocyanin levels in the most commonly eaten fruits and vegetables may be inadequate to confer optimal benefits. When we expressed two transcription factors from snapdragon in tomato, the fruit of the plants accumulated anthocyanins at levels substantially higher than previously reported for efforts to engineer anthocyanin accumulation in tomato and at concentrations comparable to the anthocyanin levels found in blackberries and blueberries. Expression of the two transgenes enhanced the hydrophilic antioxidant capacity of tomato fruit threefold and resulted in fruit

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PLOS | ONE

Flavonoids, Flavonoid Subclasses and Breast Cancer Risk: A Meta-Analysis of Epidemiologic Studies

Chang Hui[1], Xie Qi[1], Zhang Qianyong[1], Peng Xiaoli[2], Zhu Jundong[1]*, Mi Mantian[1]*

1 Research Center for Nutrition and Food Safety, Third Military Medical University, Chongqing Key Laboratory of Nutrition and Food Safety, Chongqing, China, **2** Department of Pub

Abstract

Background epidemiolog between flav

Objective: W risk of breas

Design: We 1st, 2012, usi or random-e

Results: Twe studies, and categories o intake of flav low intake c flavanones (s (summary RI control stud significant re

Conclusions flavonoids, is

Citation: Hui C, Q Studies. PLoS ONE

OPEN ACCESS Freely available online

PLOS | ONE

Anthocyanin-Rich Purple Corn Extract Inhibit Diabetes-Associated Glomerular Angiogenesis

Min-Kyung Kang[1], Soon Sung Lim[1], Jae-Yong Lee[2], Kyung Mok Yeo[3], Young-Hee Kang[1]*

1 Department of Food and Nutrition and Center for Aging and Healthcare, Hallym University, Chuncheon, Korea, **2** Department of Biochemistry, School of Medicine, Hallym University, Chunche

Abstract

Diabetic nephrop Abnormal angiog renal fibrosis and activities. This stu angiogenesis und cells exposed to factor (VEGF) and the endothelial m Endothelial tube employing db/db by attenuating th mouse kidneys, diminished the m induction and ac demonstrate that the Angpt-Tie-2 therapeutic agen

Citation: Kang M-K, Lim ONE 8(11): e79823. doi:1

Editor: David Long, UCl

Received June 14, 2013

OPEN ACCESS Freely available online

PLOS | ONE

Blueberry and Mulberry Juice Prevent Obesity Development in C57BL/6 Mice

Tao Wu[1,2], Qiong Tang[1], Zichun Gao[1], Zhuoping Yu[1], Haizhao Song[1], Xiaodong Zheng[1,2]*, Wei Chen[1,2]*

1 College of Biosystems Engineering and Food Science, Zhejiang University, Hangzhou, Zhejiang, China, **2** Fuli Institute of Food Science, Zhejiang University, Hangzhou, Zhejiang, China

Abstract

Objectives: To establish whether blueberry (*Vaccinium ashei*) and mulberry (*Morus australis* Poir) juice, anthocyanin rich fruit juice, may help counteract obesity.

Design: **And Methods**: Four-week-old C57BL/6 mice were fed a high-fat diet (HFD) with or without blueberry and mulberry juice for 12 weeks. Body weight, serum and hepatic lipids, liver and adipose tissues morphology, insulin and leptin were assessed.

Results: Mice fed HFD exhibited increased body weight, insulin resistance, serum and hepatic lipids. In comparison, blueberry and mulberry juice inhibited body weight gain, decreased the serum cholesterol, reduced the resistance to insulin, attenuated lipid accumulation and decreased the leptin secretin.

Conclusion: These results indicate that blueberry and mulberry juice may help counteract obesity.

Natural News
America's truth news bureau, read by 7+ million and growing

Red Cabbage Found to Contain 36 Anti-Cancer Anthocyanins

Tuesday, October 14, 2008 by: David Gutierrez, staff writer
Tags: red cabbage, health news, Natural News

Plantae

Angiosperms

Eudicots

Brassicales

Brassicaceae

Brassica

B. oleracea (var. capitata f. rubra)

ANTHOCYANIN RICH RED CABBAGE (*Brassica oleracea*) extract (ARCE)

BJP British Journal of Pharmacology

DOI:10.1111/bph.12676
www.brjpharmacol.org

RESEARCH PAPER

The pharmacokinetics of anthocyanins and their metabolites in humans

R M de Ferrars[1]*, C Czank[1]*†, Q Zhang[2], N P Botting[2]‡, P A Kroon[3], A Cassidy[1] and C D Kay[1]

[1]*Department of Nutrition, Norwich Medical School, University of East Anglia, Norwich, UK,* [2]*Department of Chemistry, St Andrews University, St Andrews, Fife, Scotland, UK, and* [3]*Institute of Food Research, Norwich Research Park, Norwich, UK*

Correspondence
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*These authors contributed equally to this work.

†Present address: Linear Clinical Research, Nedlands, WA, Australia.

‡Passed away on 4 June 2011.

Keywords
anthocyanins; metabolites; hippuric acid; ferulic acid; vanillic acid

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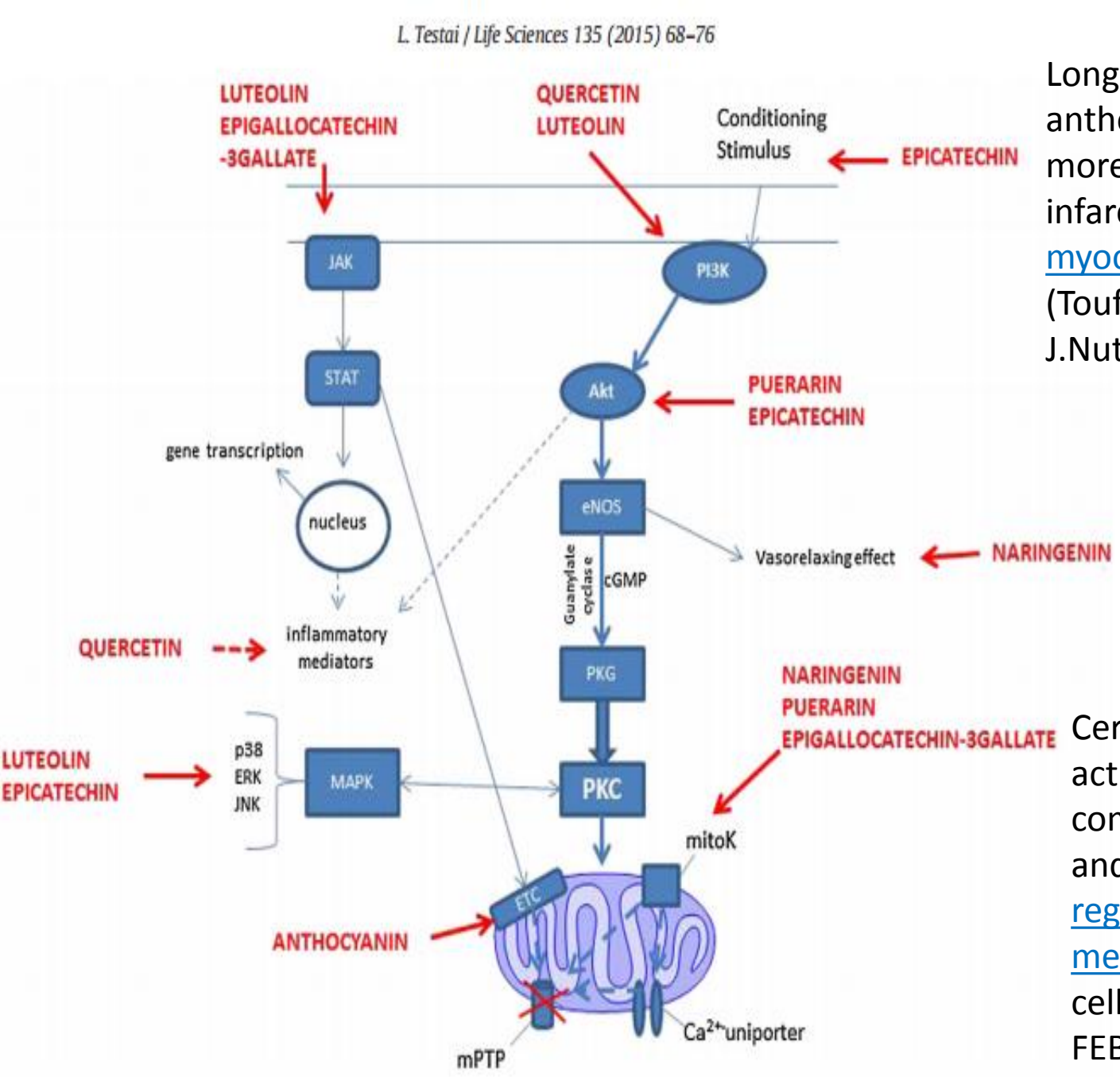
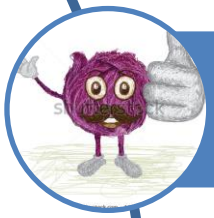


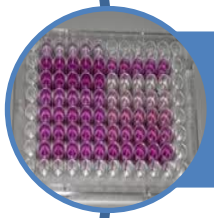
Long-term consumption anthocyanins makes the heart more resistant to myocardial infarction due to increased myocardial glutathione levels (Toufektsian et al., 2008) J.Nutrition.

Certain anthocyanins can act as electron acceptors at complex I of mitochondria and bypass ischemia and regulate energy metabolism in mammalian cells (Skemiene et al, 2015) FEBS Journal.

Preparation and characterization of ARCE



Safety evaluation



Cytotoxicity Assay

Cardioprotective potential of ARCE

Studies with stressed rat cardiomyocytes

Anthocyanin Rich red Cabbage Extract (ARCE)

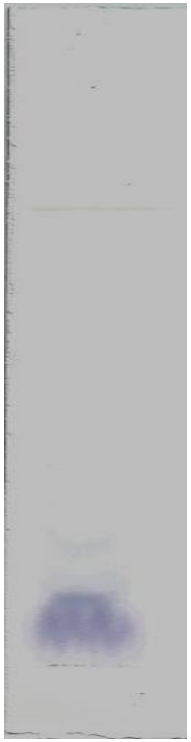
- Shredded and dried at 50 deg.

- Extraction with Methanol: Water : HCL (50:50:1) solvent system

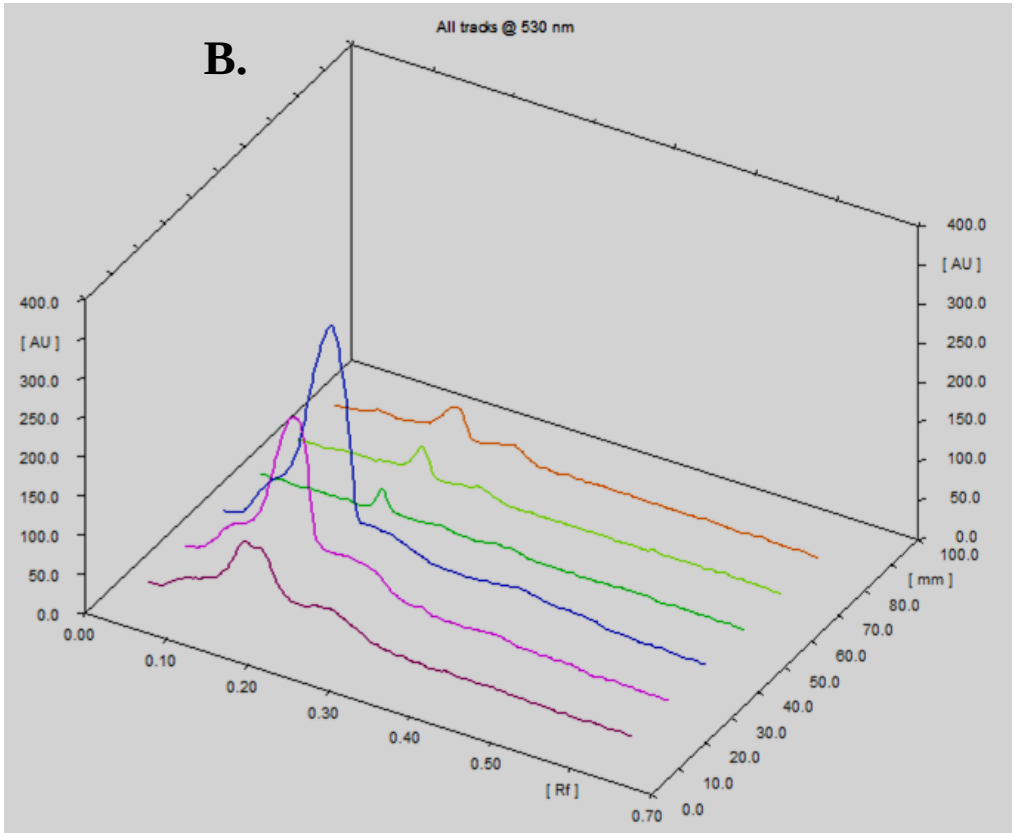
- Evaporated till dryness in rotatory evaporator at 40̊C

ANTHOCYANIN RICH RED CABBAGE EXTRACT (ARCE)

A.



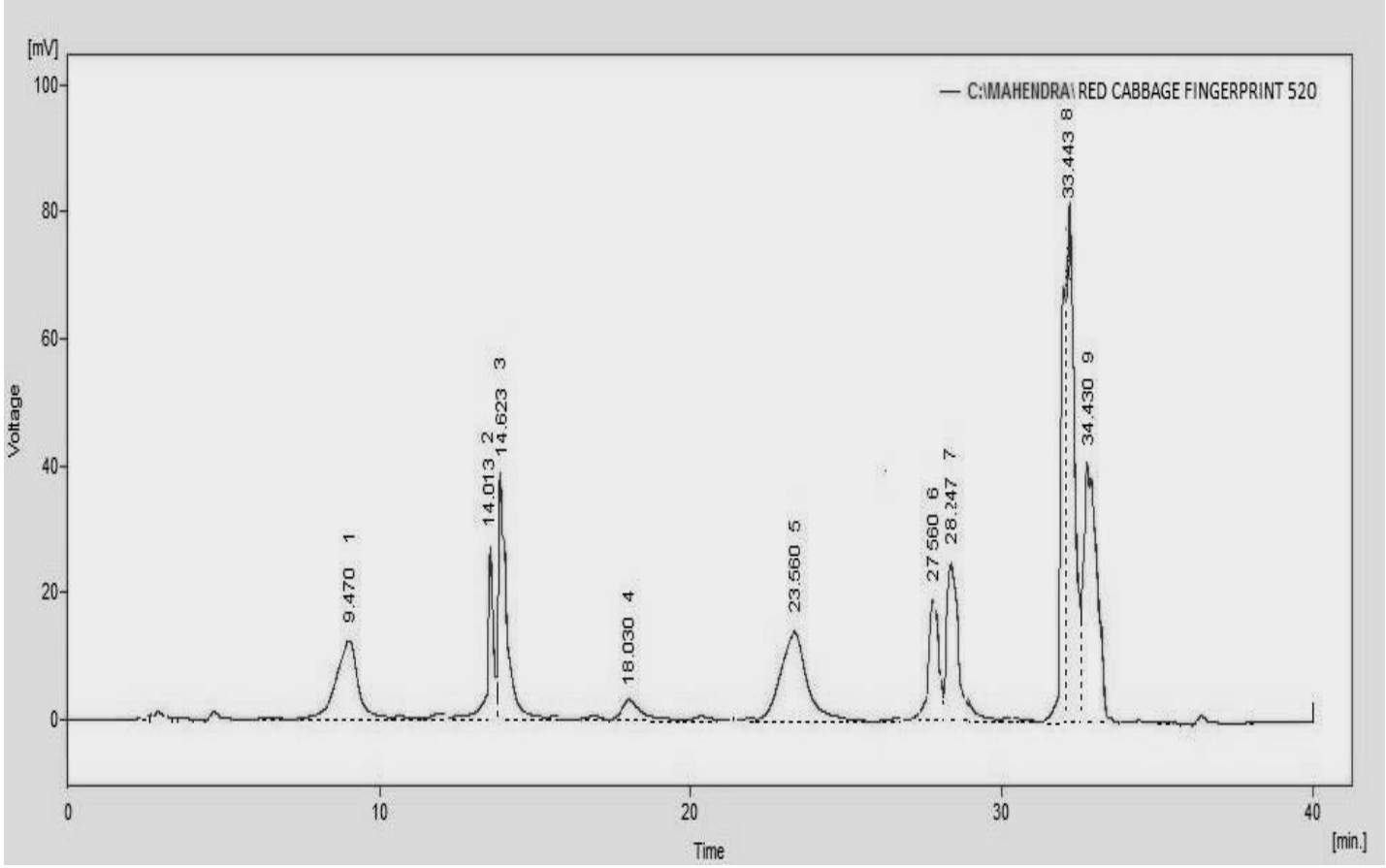
B.



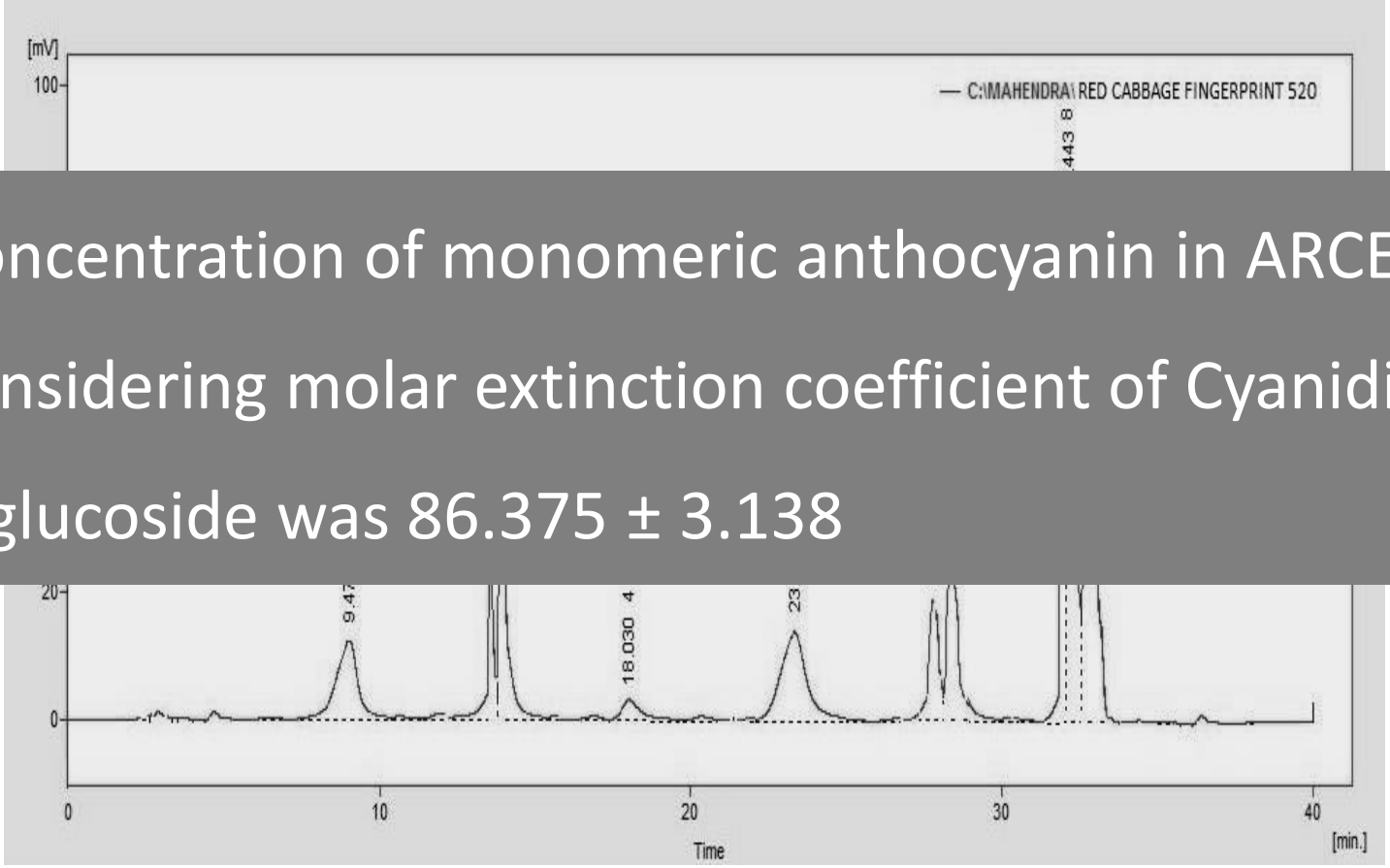
A. TLC chromatogram of Anthocyanin rich extract of Red Cabbage.

B. 3D densitogram of HPTLC measured at 530 nm in CAMAG Linomat5. First three lanes are of extract dissolved in methanol and remaining three lanes are of extract dissolved in acidified methanol.

HPLC fingerprinting of ARCE.



HPLC fingerprinting of ARCE.



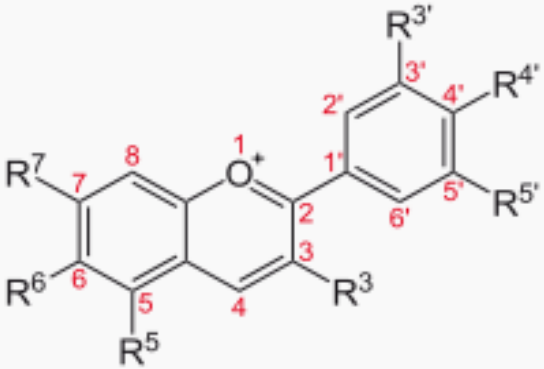
Concentration of monomeric anthocyanin in ARCE considering molar extinction coefficient of Cyanidin -3,5-diglucoside was 86.375 ± 3.138

Anthocyanins present in functional foods is member of flavonoid family are glycosylated poly-hydroxyl and poly-methoxy derivatives of flavinium salts.

The anti-oxidant property of anthocyanin is particularly from the hydroxyl moieties of the c-ring.

Natural electron deficiency of anthocyanins makes it reactive towards oxygen radicals.

Selected anthocyanidins and their substitutions

Basic structure	Anthocyanidin	R_3'	R_4'	R_5'	R_3	R_5	R_6	R_7
	Aurantinidin	-H	-OH	-H	-OH	-OH	-OH	-OH
	Cyanidin	-OH	-OH	-H	-OH	-OH	-H	-OH
	Delphinidin	-OH	-OH	-OH	-OH	-OH	-H	-OH
	Europinidin	$-OCH_3$	-OH	-OH	-OH	$-OCH_3$	-H	-OH
	Pelargonidin	-H	-OH	-H	-OH	-OH	-H	-OH
	Malvidin	$-OCH_3$	-OH	$-OCH_3$	-OH	-OH	-H	-OH
	Peonidin	$-OCH_3$	-OH	-H	-OH	-OH	-H	-OH
	Petunidin	-OH	-OH	$-OCH_3$	-OH	-OH	-H	-OH
	Rosinidin	$-OCH_3$	-OH	-H	-OH	-OH	-H	$-OCH_3$

Acute oral toxicity in mice

•Limit test procedure as per the OECD test guidelines. Experimental protocol was executed according to CPCSEA India guidelines and approved by the animal ethical committee of the Department of Zoology, The M.S. University of Baroda, Vadodara (Approval No.827/ac/04/CPCSEA)

•Thirty two *Swiss* albino mice of either sex were divided into four groups (n=8) and were orally administered with a single dose of 1000, 2000, 3000, 4000 or 5000 mg/kg body weight of ARCE extract.

•Animals were observed for possible behavioral changes such as

- Tremors
- Convulsions
- Sleep
- Altered feeding
- Salivation
- Diarrhoea till 72 hr post treatment

Acute toxicity studies

•No mortality was recorded in acute toxicity study with ARCE extract up to a dose of 5000mg/kg body weight till 72 h.

•No abnormalities in behavior could be monitored on extract administration .

Sub chronic oral toxicity in mice

•The sub chronic oral toxicity study was conducted according to OECD Test 407 (OECD, 1995). Experimental protocol was executed according to CPCSEA India guidelines and approved by the animal ethical committee of the Department of Zoology, The M.S. University of Baroda, Vadodara (Approval No.827/ac/04/CPCSEA)

•Thirty two *Swiss* albino mice of either sex were divided into four groups (n=8) and maintained for 28 days for this experiment.

•Group I was orally fed with carboxy methyl cellulose (CMC; 0.5 %) that served as control whereas, Groups 2, 3 and 4 were orally administered with 1000, 2000 and 3000 mg/kg of ARCE extract respectively.

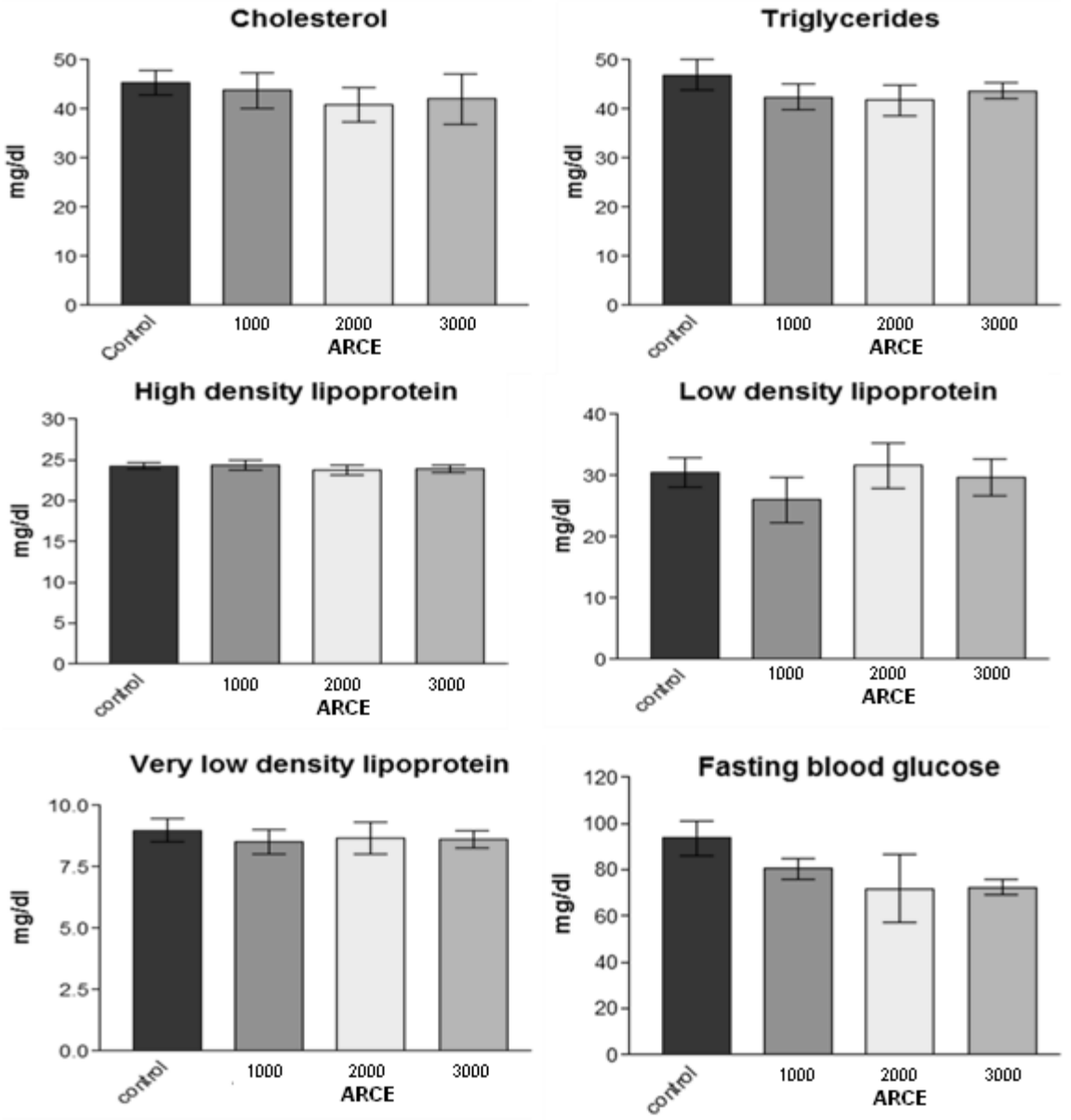
•After **28 days of treatment**, blood was collected from overnight fasted mice.

LD_{50} of ARCE extract

•Since no mortality was recorded even after administration of 5000mg/kg of ARCE extract the LD_{50} of ARCE extract could not be established.

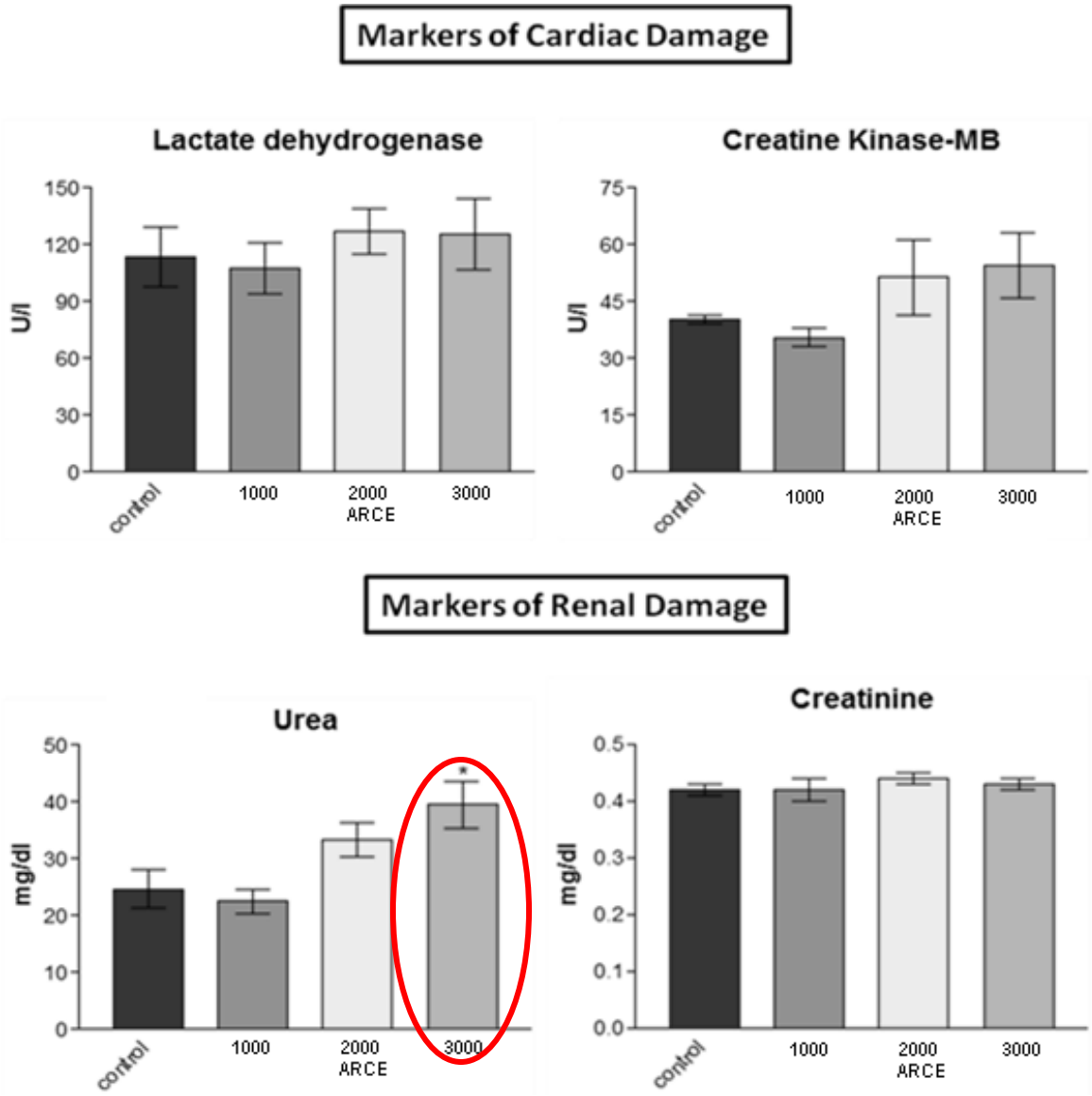
•The present observations indicates that, the LD_{50} of ARCE extract is likely to be higher than 5000mg/kg BW.

Subchronic administration of ARCE in *Swiss* albino mice and plasma metabolic indices



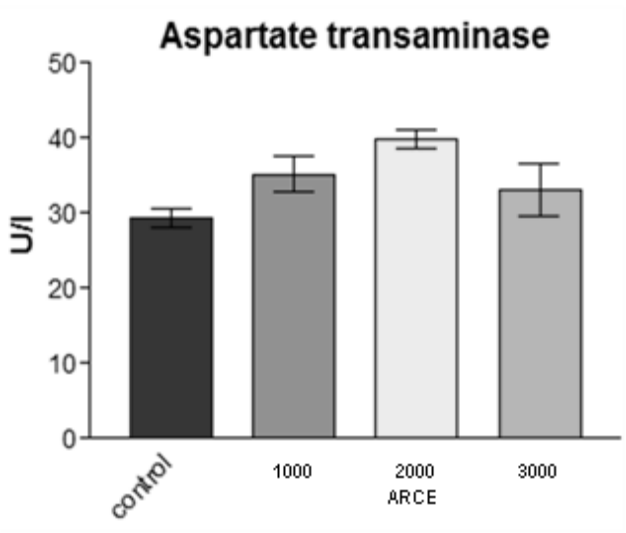
Results are expressed as Mean ± S.E.M for n=8. *p<0.05 compared to CON.

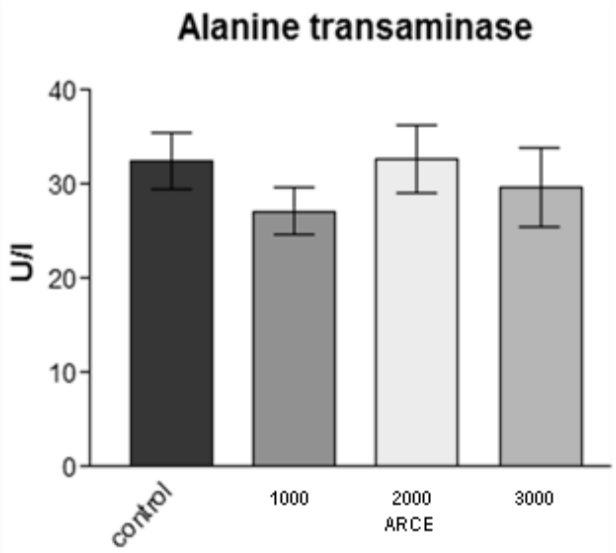
Subchronic (28 days) administration of ARCE on plasma markers of cardiac and renal function in *Swiss* albino mice.

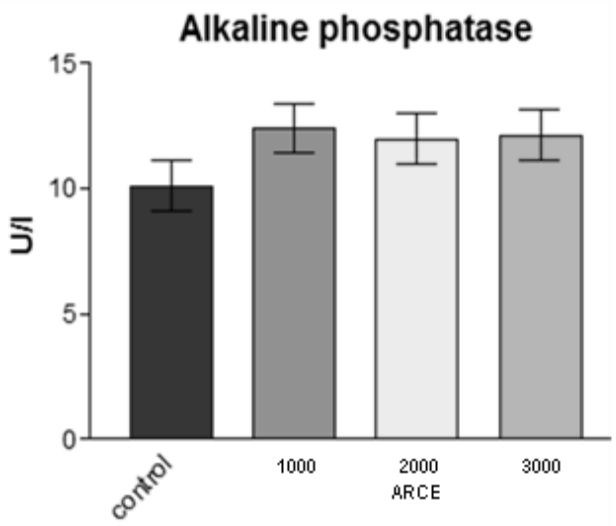


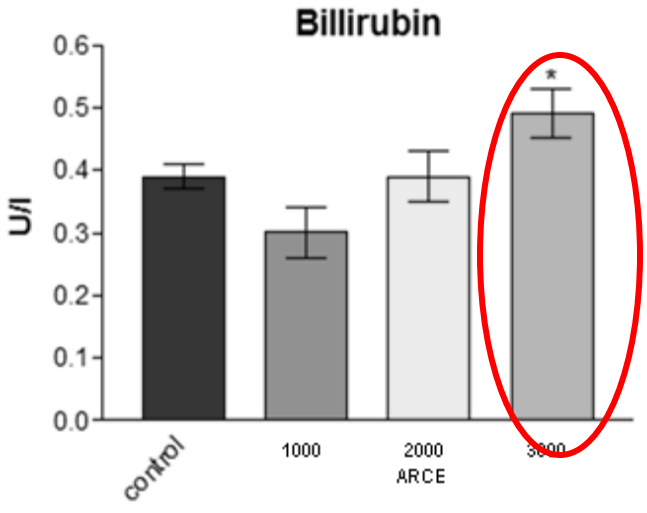
Results are expressed as Mean ± S.E.M for n=8. *p<0.05 compared to CON.

Subchronic administration of ARCE on plasma indices of hepatic function in *Swiss* albino mice.









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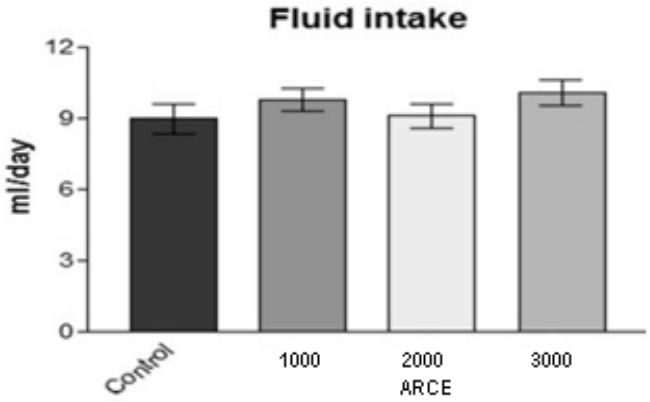
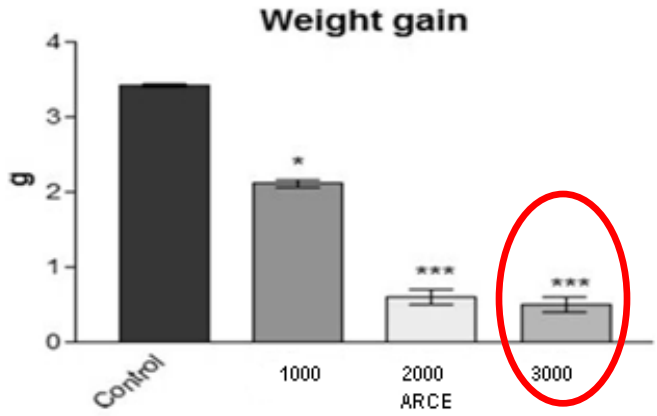
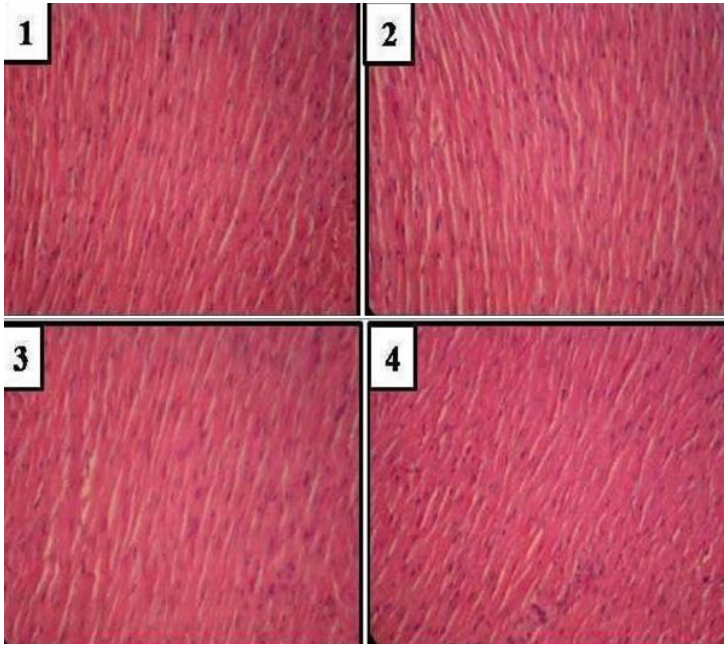
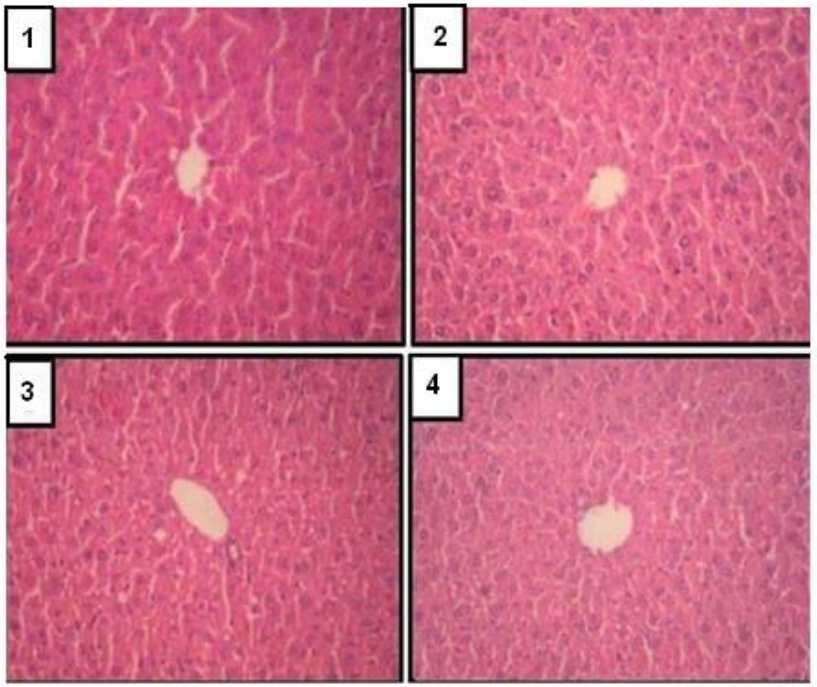


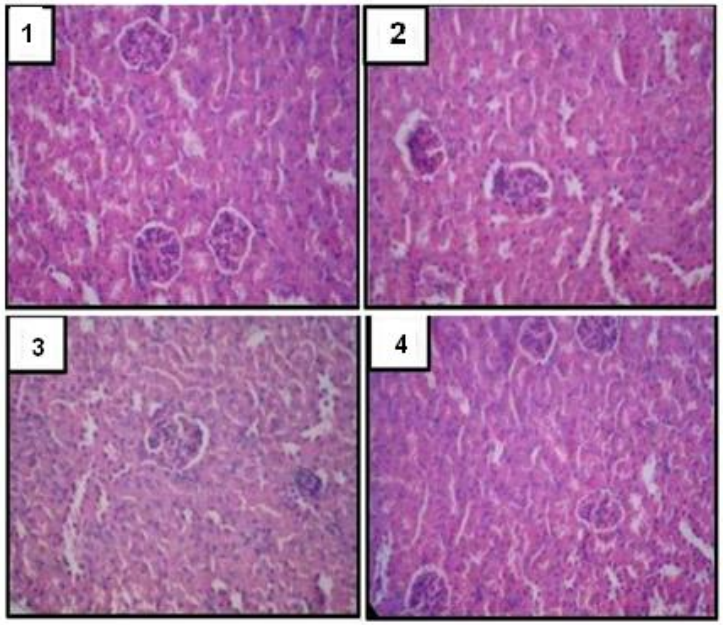


Subchronic administration of ARCE extract on bodyweight, food and fluid intake of *Swiss* albino mice

Results are expressed as Mean ± S.E.M for n=8. *p<0.05 compared to CON.







Photomicrographs of Heart, liver and kidney of control (1) and 1000, 2000 and 3000mg/kg ARCE treated mice (2, 3, 4)

- Significant reduction in bodyweight gain, food intake, red blood cell count and hemoglobin content along with higher alkaline phosphatase, billirubin and urea levels were observed in mice treated with 3000 mg/kg bodyweight after 28 days.

•NOAEL of the ARCE extract was found to be 2000mg/kg BW. Hence, consumption of ARCE extract for various medicinal purposes is safe.

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Safety Evaluations on Ethanolic Extract of Red Cabbage (*Brassica oleracea* L.) in Mice

Menaka C. Thounaojam, Ravirajsinh N. Jadeja, Jayanta M. Sankhari, Ranjitsinh V. Devkar, and A.V. Ramachandran

Abstract: The present study has carried out safety evaluations on an ethanolic extract of red cabbage (RC) leaves in terms of acute and subchronic oral toxicity tests as per Organisation for Economic Cooperation and Development (OECD) guidelines in Swiss albino mice. Single-dose administration of RC extract (1000, 2000, 3000, 4000, or 5000 mg/kg body weight) to Swiss albino mice did not manifest toxicity or any significant adverse behavioral alterations. Chronic administration of RC extract (1000, 2000, and 3000 mg/kg body weight) for 28 d also did not register any significant alterations in fluid intake, organ weights, plasma lipid profile, plasma creatine kinase-MB, lactate dehydrogenase, aspartate transaminase, alanine transaminase, creatinine, electrolytes, and calcium levels, and the total blood count showed a nonsignificant change. However, significant reduction in body-weight gain, food intake, red blood cell count, and hemoglobin content along with higher alkaline phosphatase, bilirubin, and urea levels was observed in mice treated with 3000 mg/kg body weight for 28 d. Since there was no mortality up to a dose of 5000 mg/kg body weight, 50%

MS 20101000 Submitted 9/4/2010, Accepted 10/19/2010. *Authors are with Div. of Phytotherapeutics and Metabolic Endocrinology, Faculty of Science, The M. S. Univ. of Baroda, Vadodara-390002, Gujarat, India. Direct inquiries to author Devkar (Email: phyto_met@yahoo.com).*

doi: 10.1111/j.1750-3841.2010.01962.x

Journal of Food Science

Assessment of anti-atherosclerotic and cardioprotective potentials

- Male Sprague Dawley rats weighing 300 ± 20 (Obtained from Sun pharmaceutical advanced research centre, Vadodara, India .

- Experimental protocol was executed according to CPCSEA India guidelines and approved by the animal ethical committee of the Department of Zoology, The M.S. University of Baroda, Vadodara (Approval No.827/ac/04/CPCSEA)

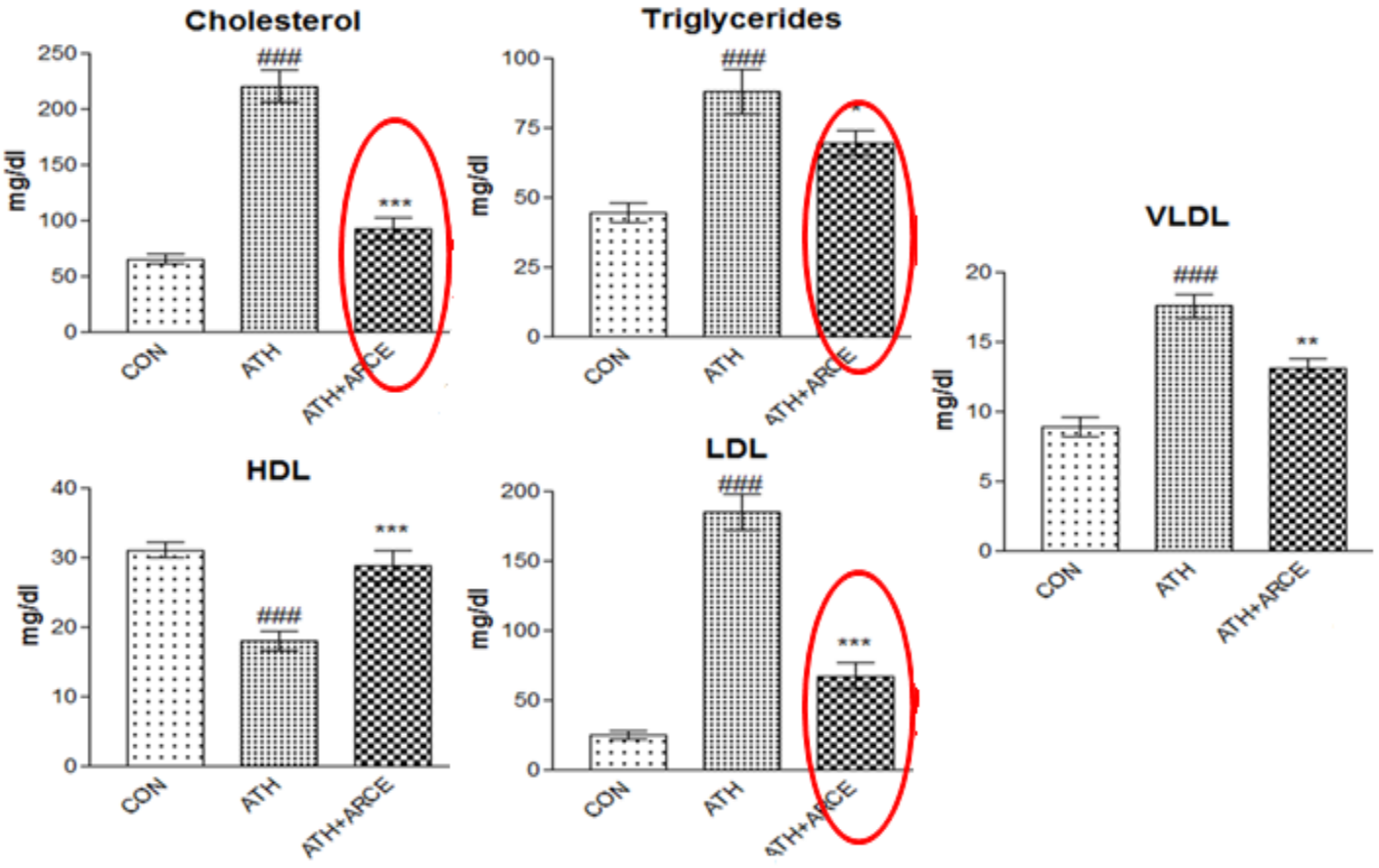
A total of thirty two rats were divided into 4 groups of 8 animals each.

•Group I served as control (CON) and was fed with standard laboratory chow and orally administered with 0.5 % CMC for 8 weeks.

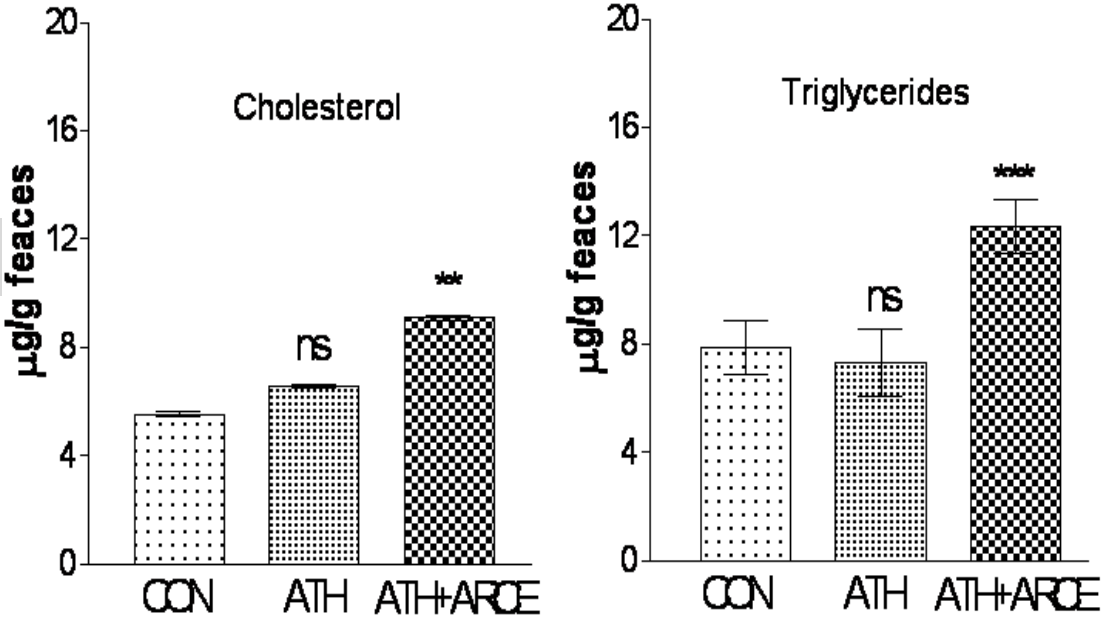
•Group II (ATH)
as per Cai et al., 2005 – Briefly, Vit D3 + HCD.

•Group III (ATH+ARCE) was orally administered with 100 mg/kg while, group II received equal volume of vehicle (0.5% carboxy methyl cellulose).

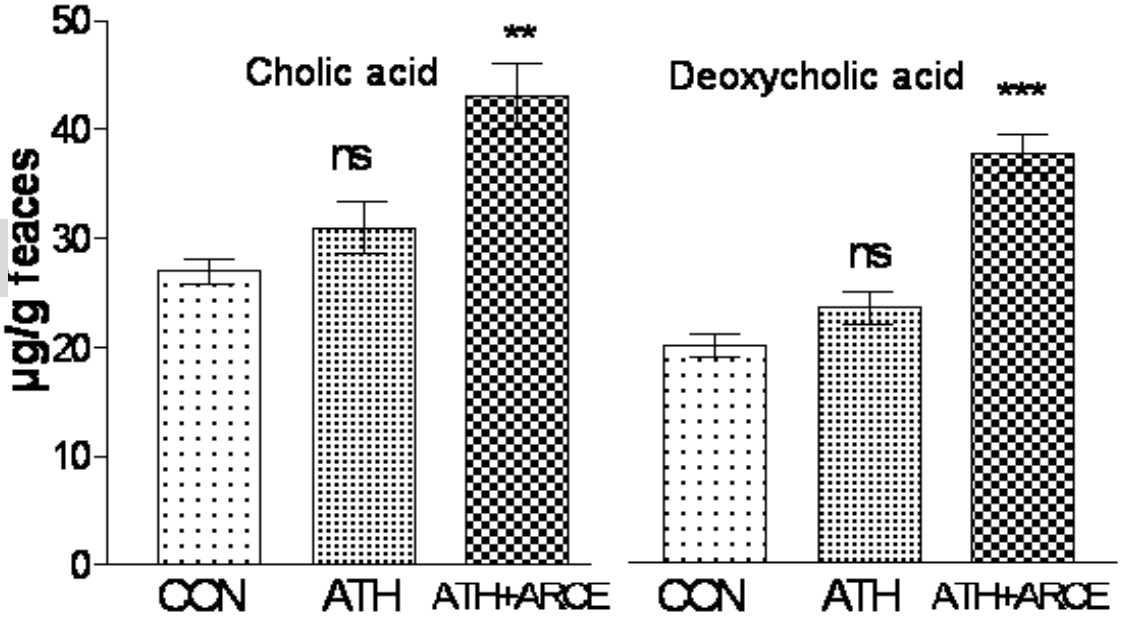
Plasma lipid profile



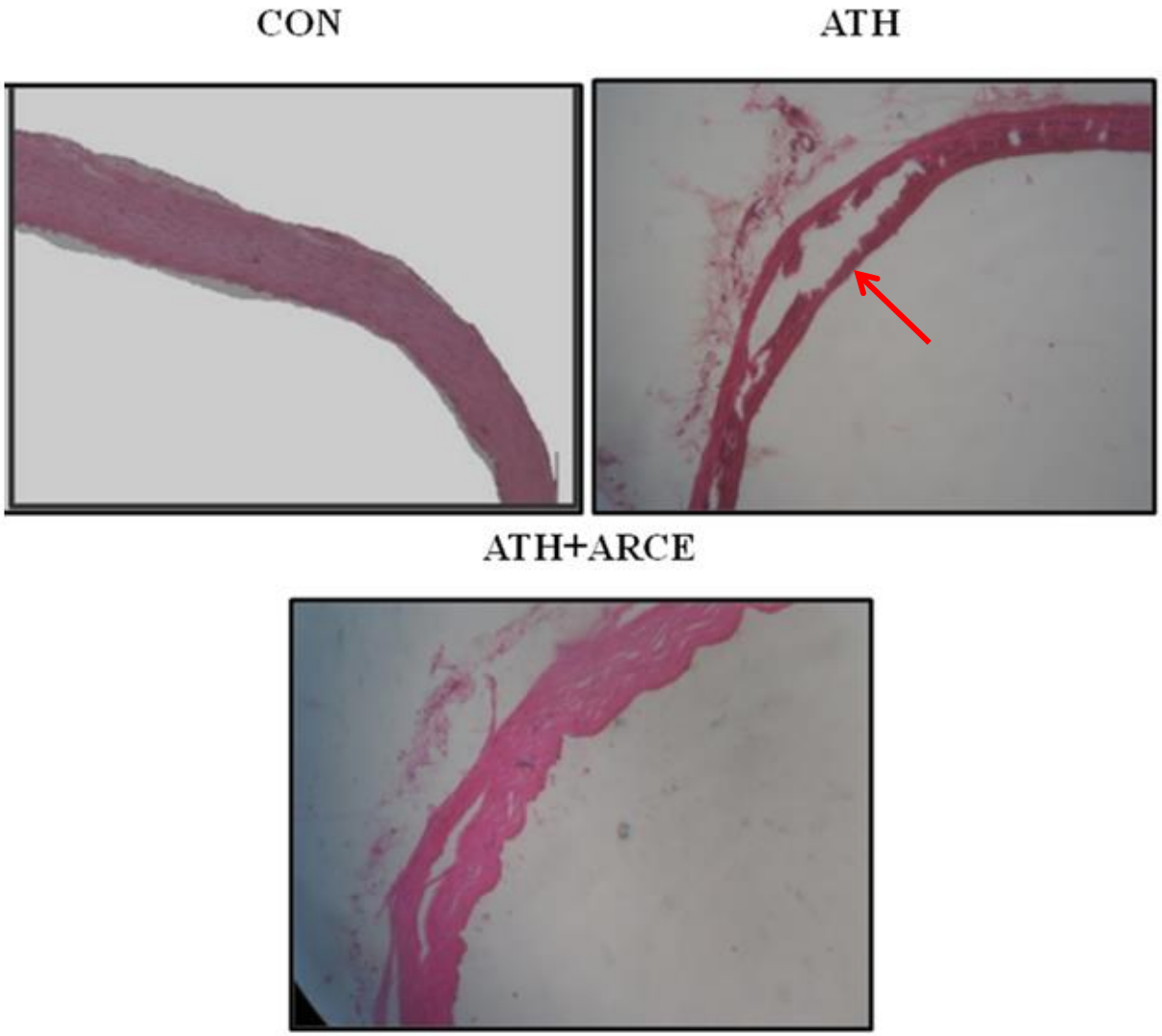
Fecal lipid profile



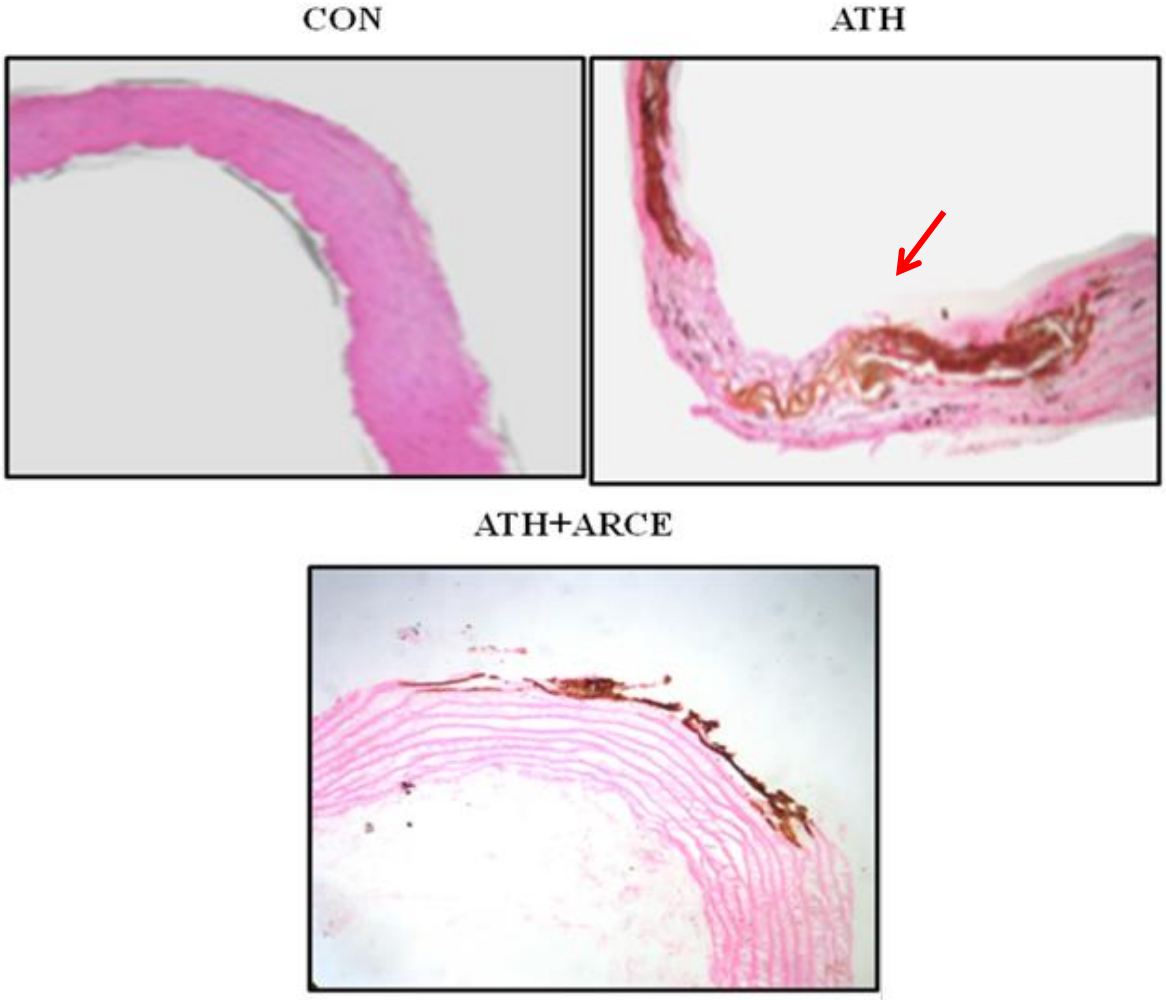
Fecal bile acid contents



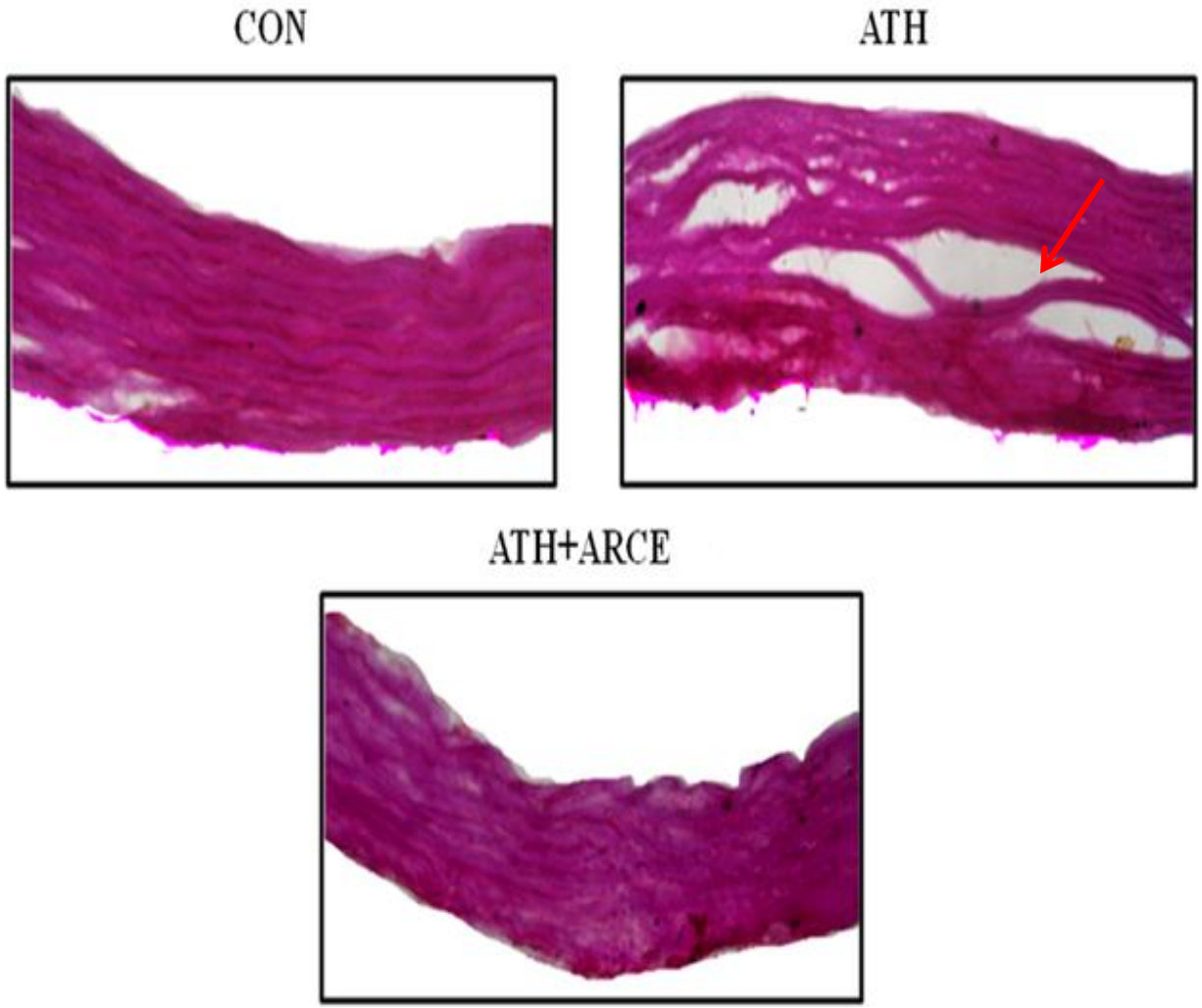
Thoracic aorta of control, ATH, ATH+ARCE rats stained with HXE.



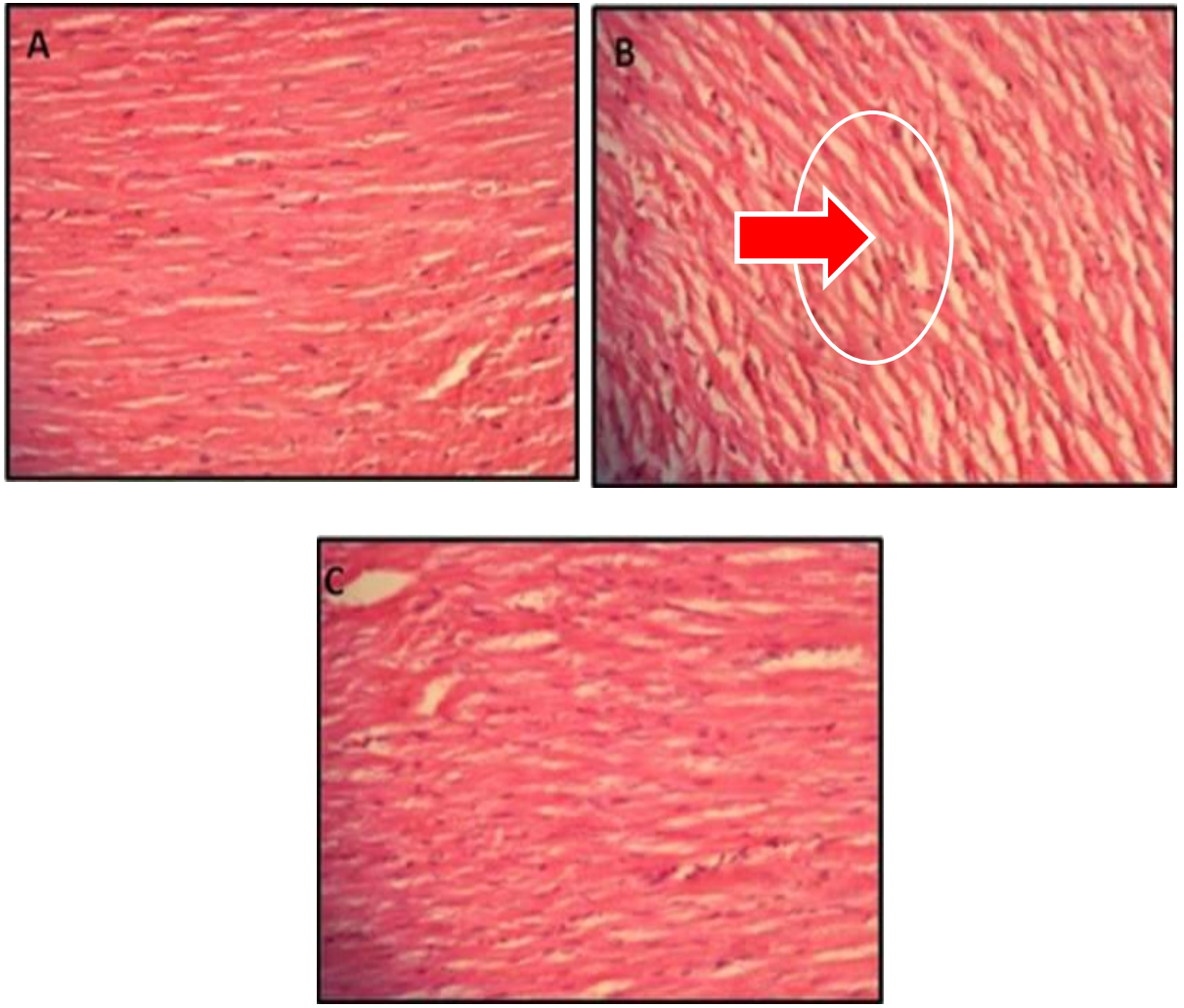
Thoracic aorta of control, ATH, ATH+ARCE stained with von kossa



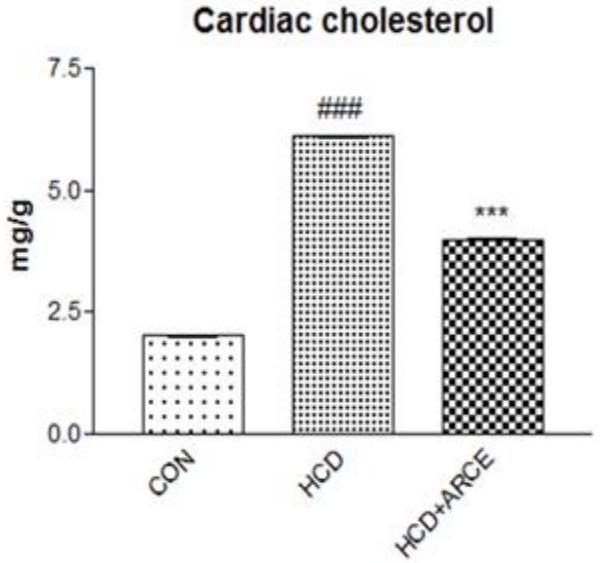
Thoracic aorta of control, ATH, ATH+ARCE stained with Weigert's stain.

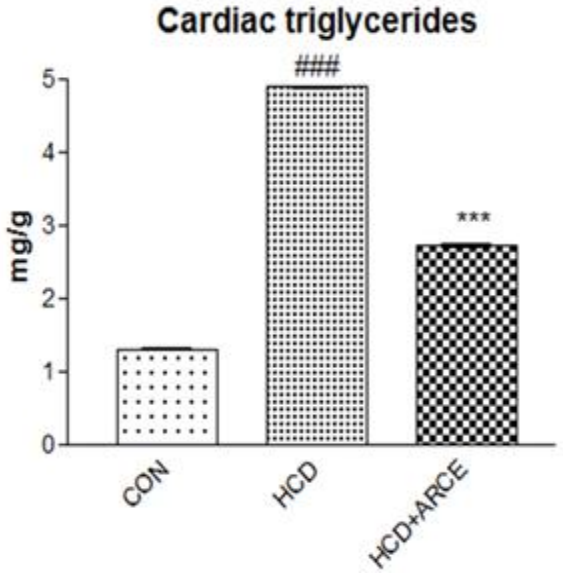


Photomicrographs of heart of control (A), HCD (B) and HCD+ARCE (C) rats stained with hematoxyline and eosin

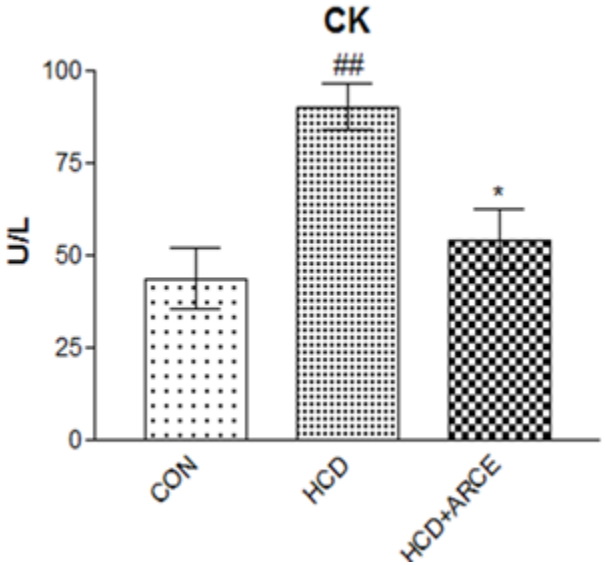


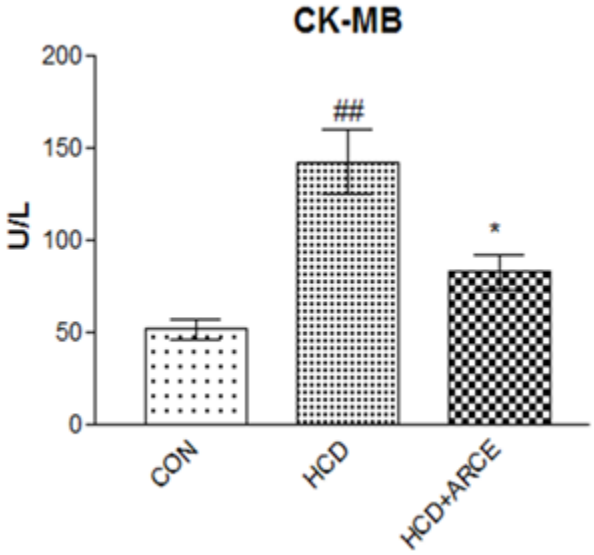
Cardiac lipid profile

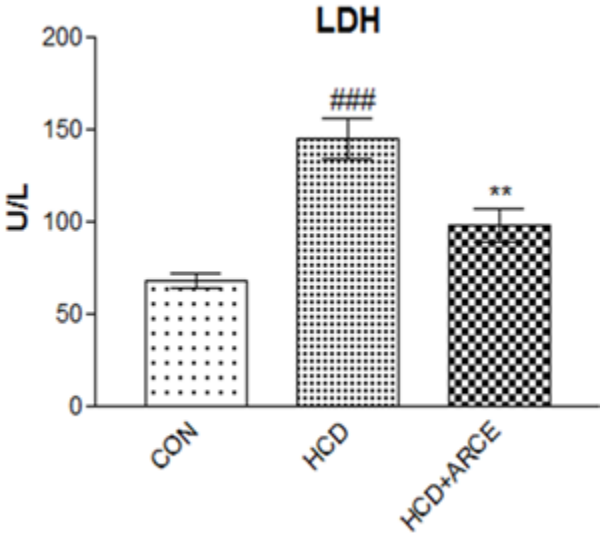




Markers of cardiac damage.







ARCE supplementation resulted in significant prevention of atheromatous plaque formation, calcium deposition and elastin derangements.

ARCE was able to prevent HCD induced depletion in the cardiac antioxidants and related damages.

Possibly high content of cyanidin class of anthocyanins eg. cyanidin-3-glucoside.

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Research Article

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Anthocyanin-rich red cabbage (*Brassica oleracea* L.) extract attenuates cardiac and hepatic oxidative stress in rats fed an atherogenic diet

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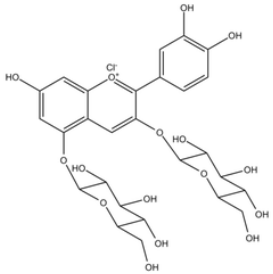
Abstract

BACKGROUND: Oxidative stress induced by reactive oxygen species plays an important role in the aetiology of several diseases including atherosclerosis and coronary heart disease. Anthocyanin-rich extracts have been shown to possess a variety of therapeutic roles, including antioxidant, cardioprotective and hepatoprotective properties. The present inventory was undertaken to evaluate the protective role of anthocyanin-rich red cabbage extract (ARCE) on an atherogenic (ATH) diet-induced hypercholesterolaemia and related cardiac and, hepatic oxidative stress in rats.

RESULTS: ARCE (100 mg kg^{-1} body weight) treatment of rats fed the ATH diet significantly prevented elevation in serum and tissue lipids, circulating levels of cardiac and hepatic damage markers, and resulted in excretion of lipids through faeces. Also, the ARCE extract significantly attenuated alterations in the cardiac and hepatic antioxidants and lipid peroxidation, and histopathological changes in cardiac and hepatic tissue.

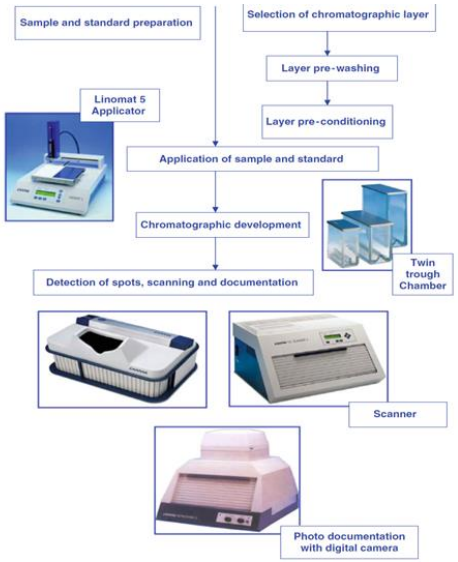
CONCLUSION: Thus, the present study provides the first scientific evidence for a protective role of ARCE against ATH diet-induced hypercholesterolaemia and cardiac and hepatic oxidative stress.

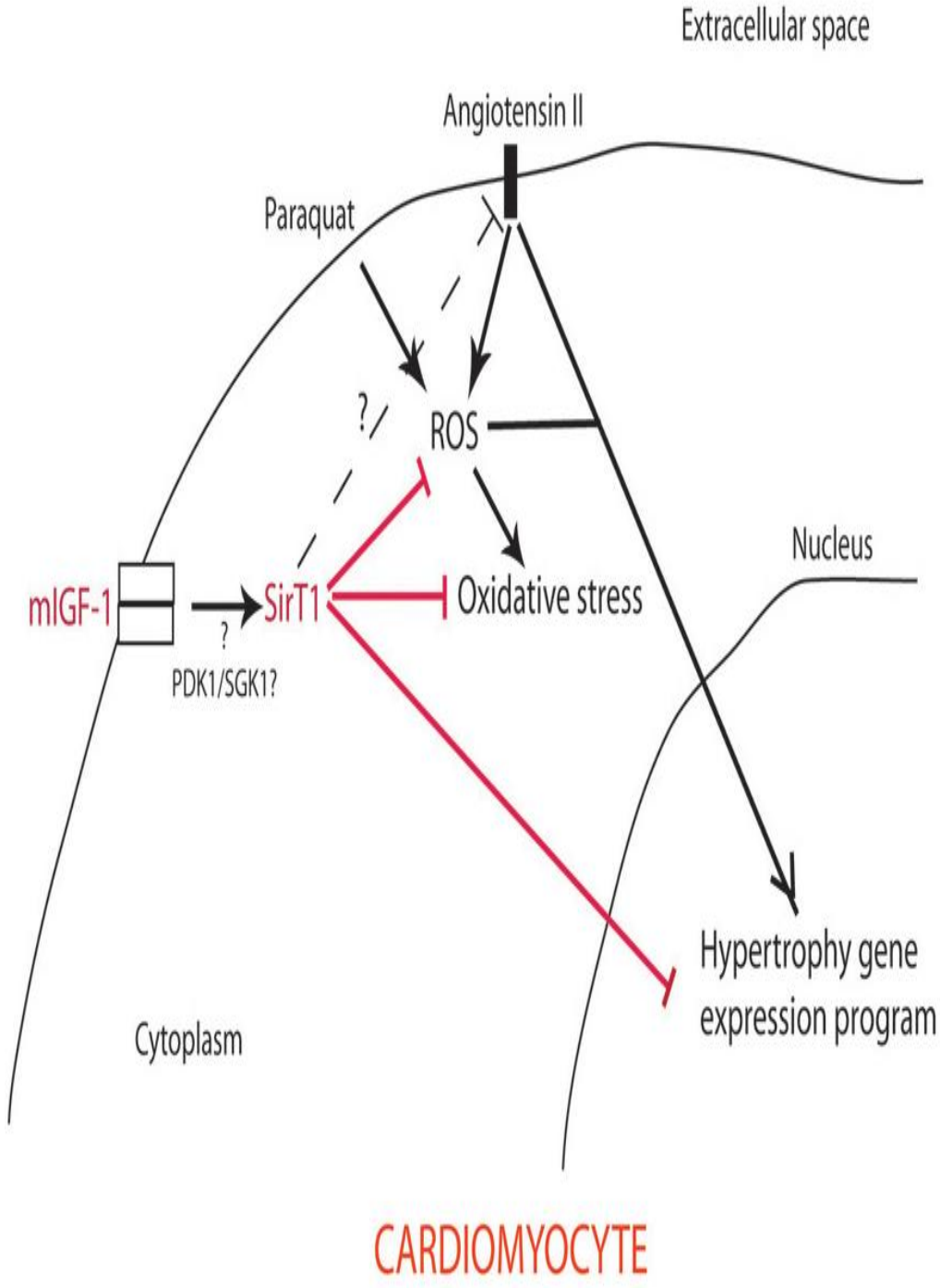
Keywords: *Brassica oleracea* L.; hypercholesteolaemia; oxidative stress; histopathology



Anthocyanin rich Red Cabbage extract

Pretreatment with red cabbage extract





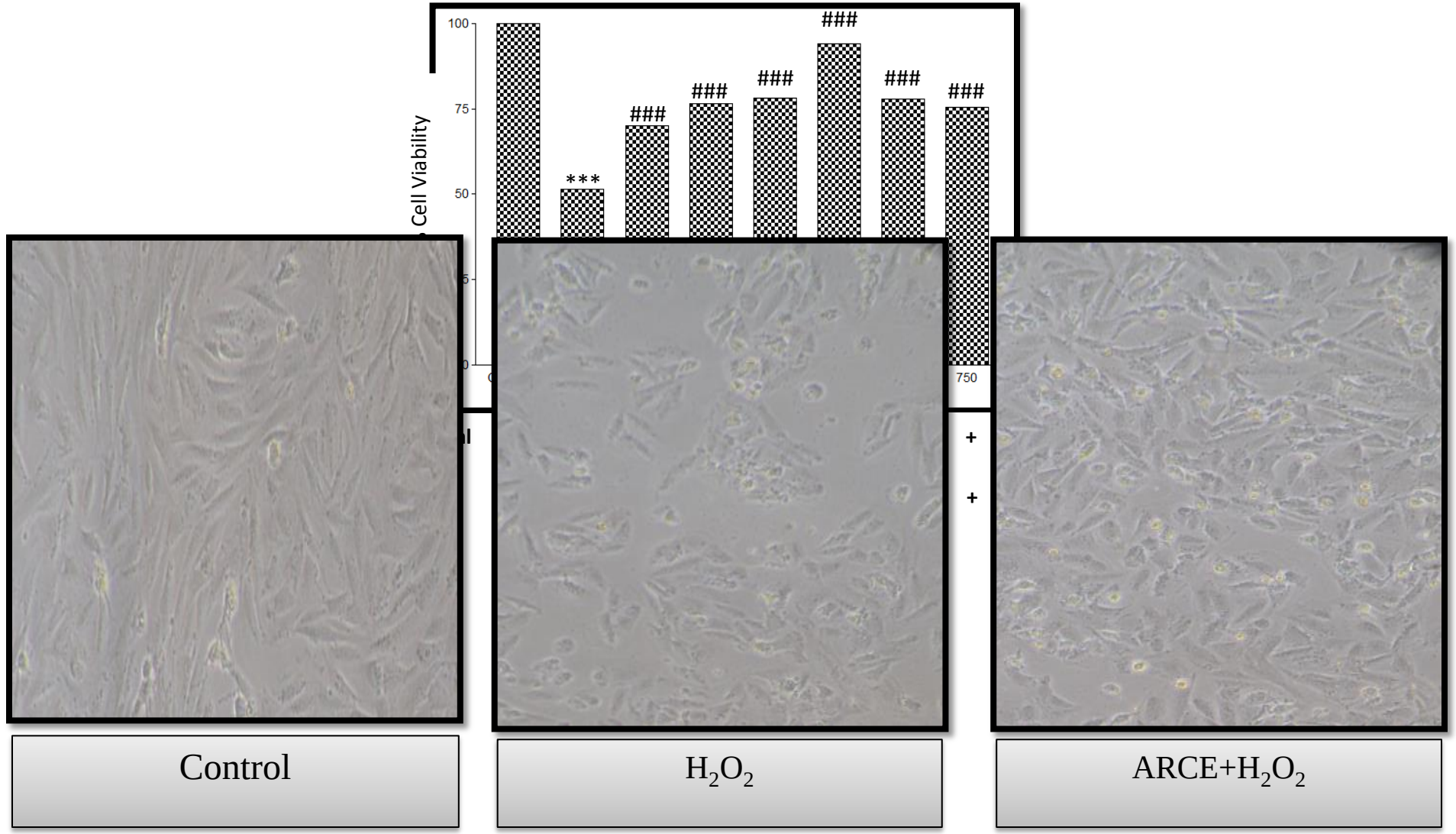
Intracellular ROS

Lipid Peroxidation

DNA damage

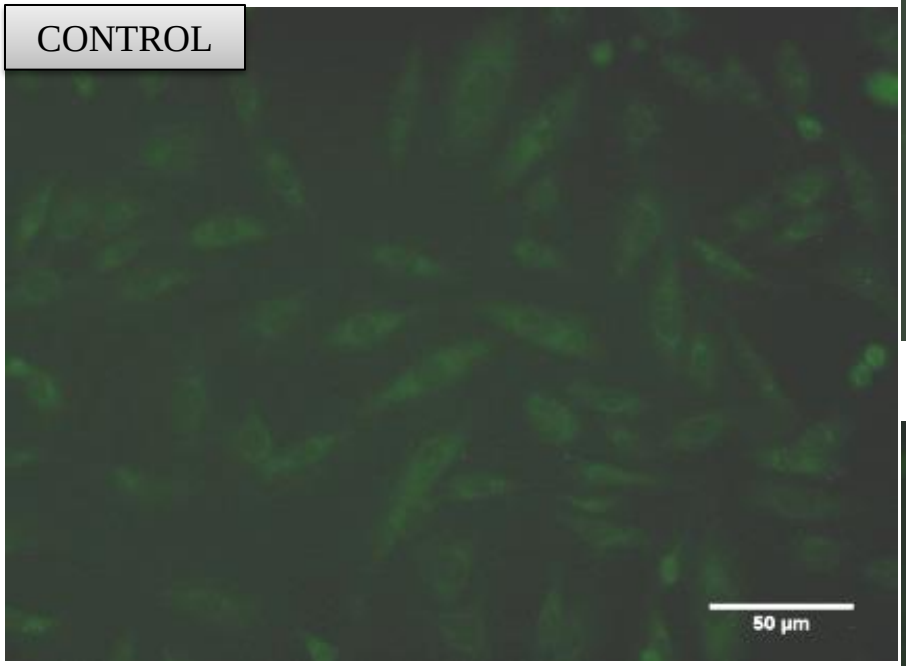
Cell viability

Mitochondrial functionality

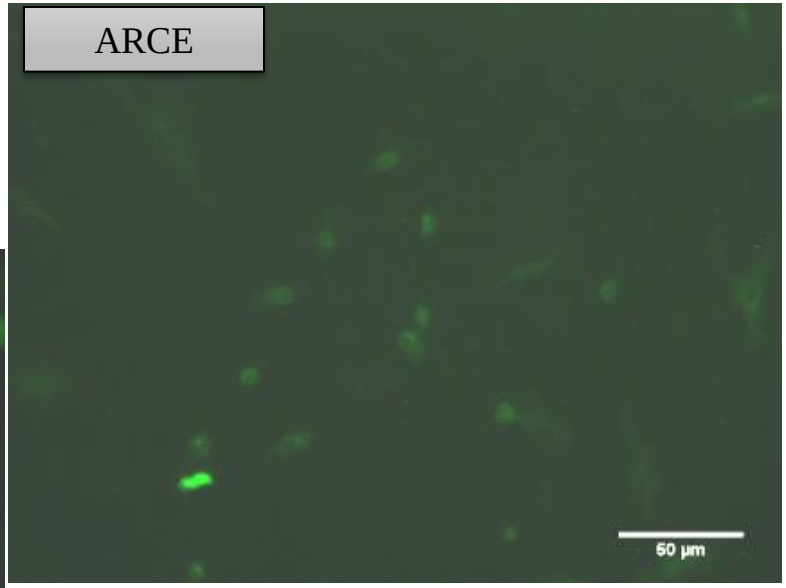

Cell Viability
100
75
50
###
***
###
###
###
###
###
###
750
+
+
Control
H_2O_2
ARCE+H_2O_2

RHODAMINE

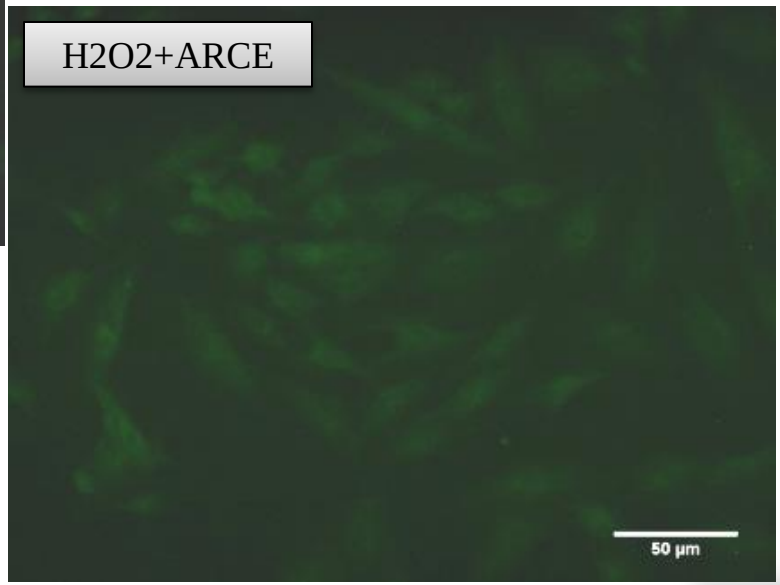
CONTROL



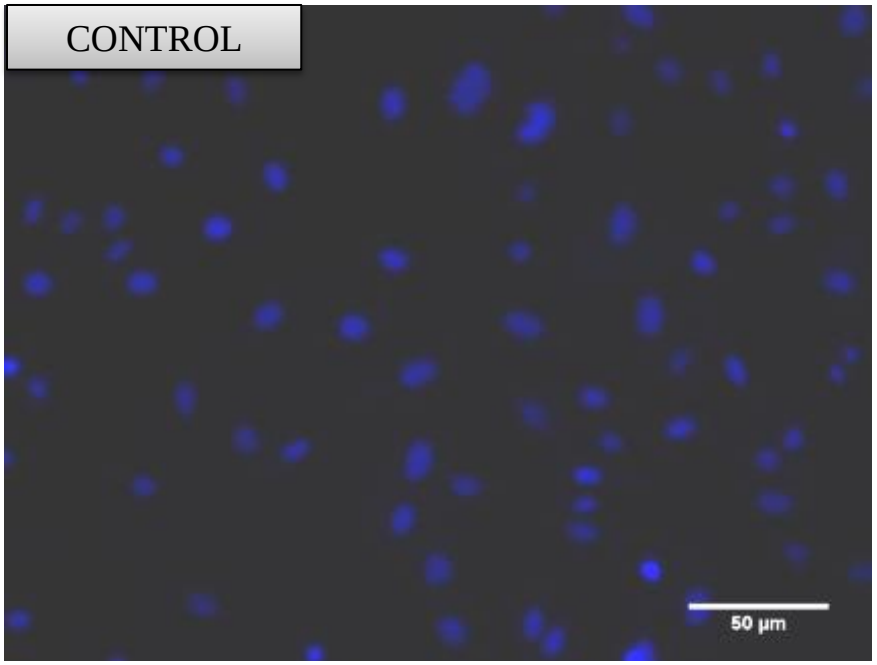
ARCE



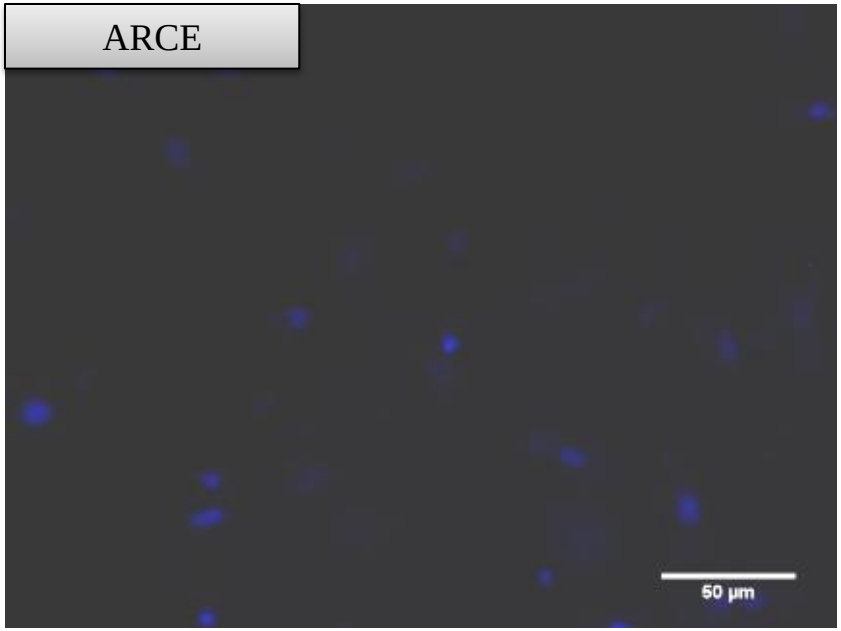
H2O2+ARCE



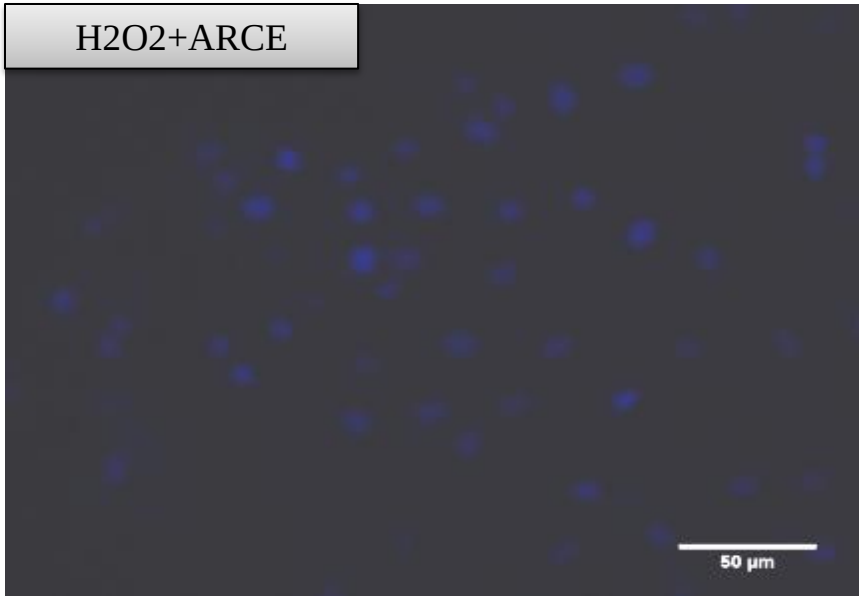
CONTROL



ARCE

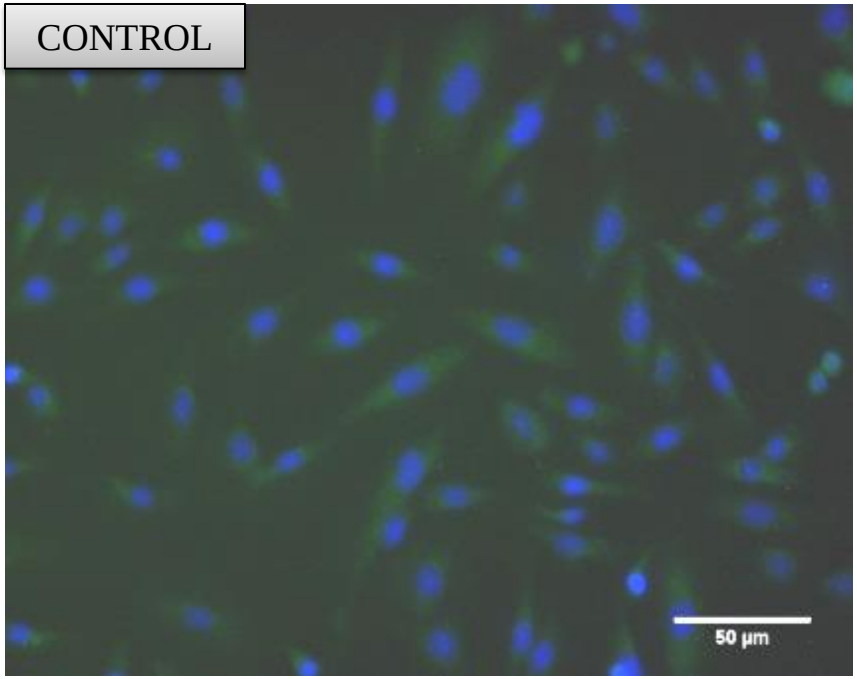


H2O2+ARCE

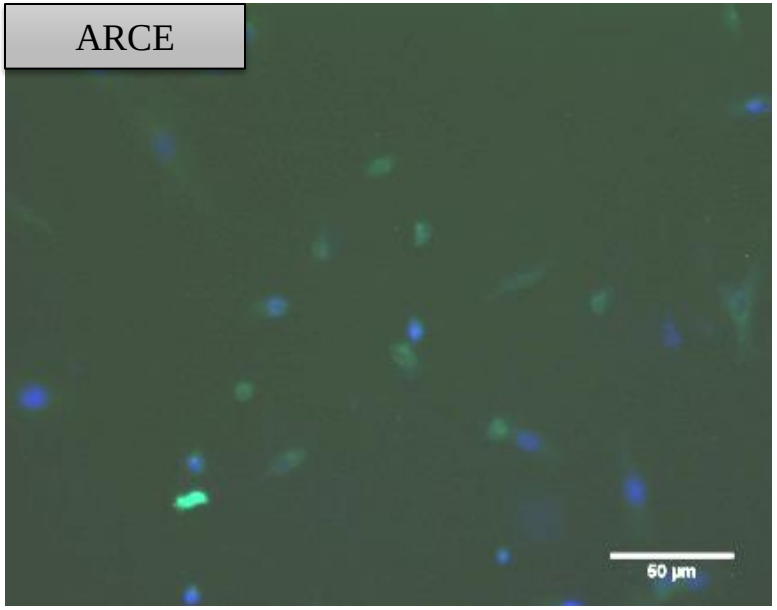


CTCF: Corrected total cell fluorescence

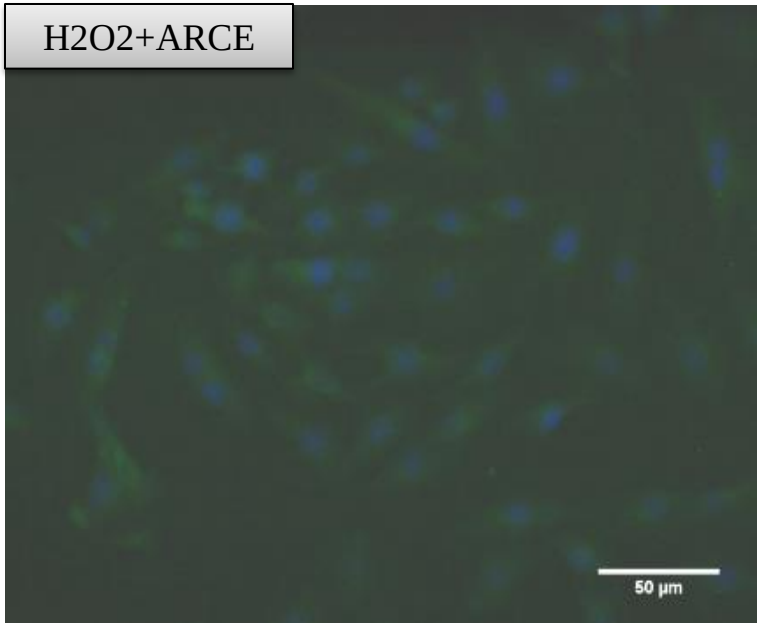
CONTROL

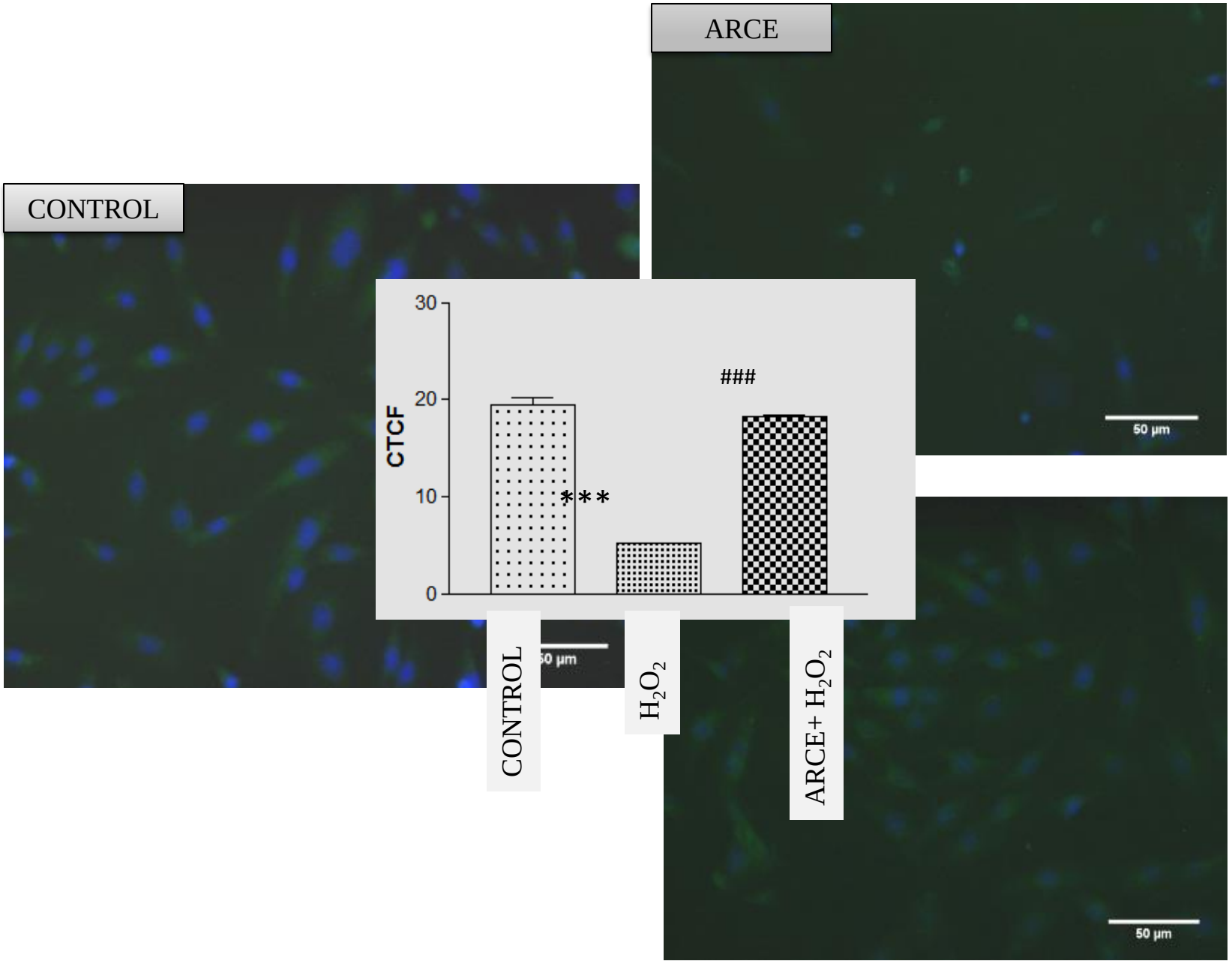


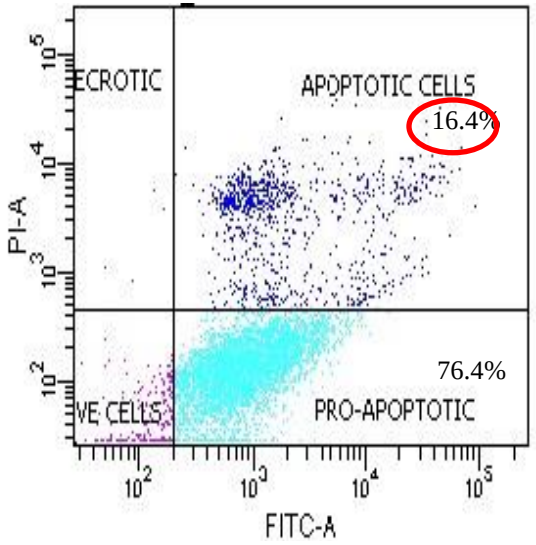
ARCE



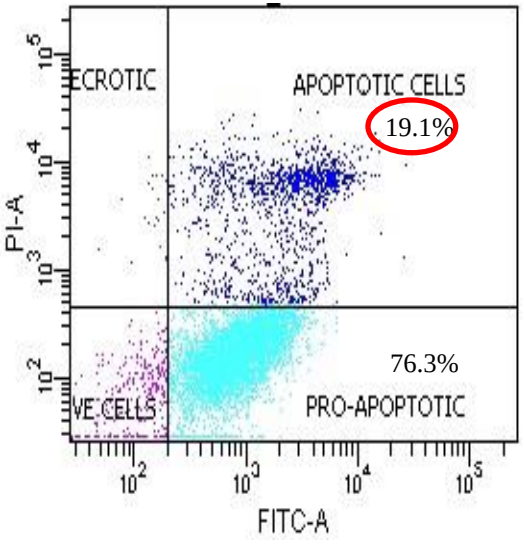
H2O2+ARCE



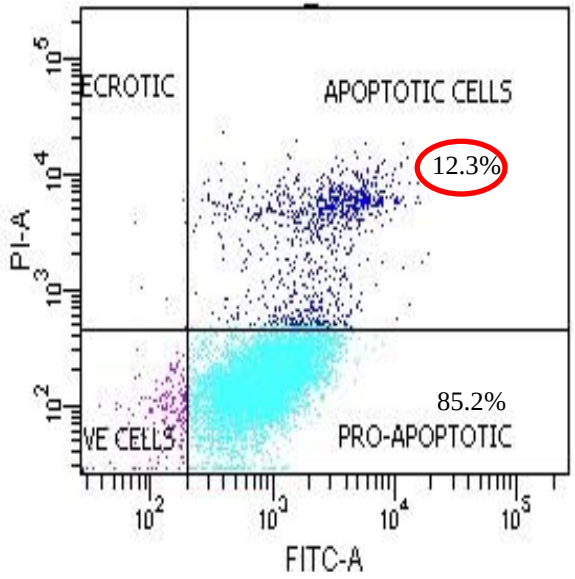

ARCE
CONTROL
CTCF
30
20
10
0
***
###
50 µm
50 µm
50 µm
CONTROL
H2O2
ARCE+ H2O2



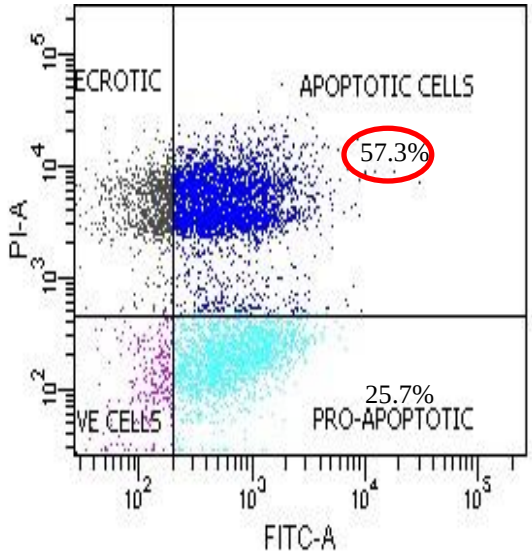
CONTROL



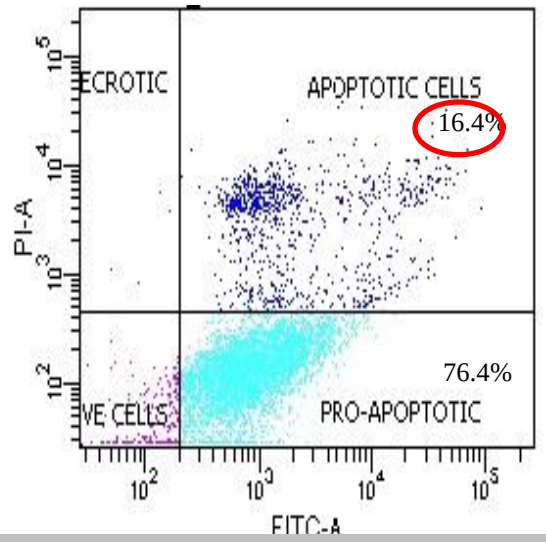
ARCE+H2O2

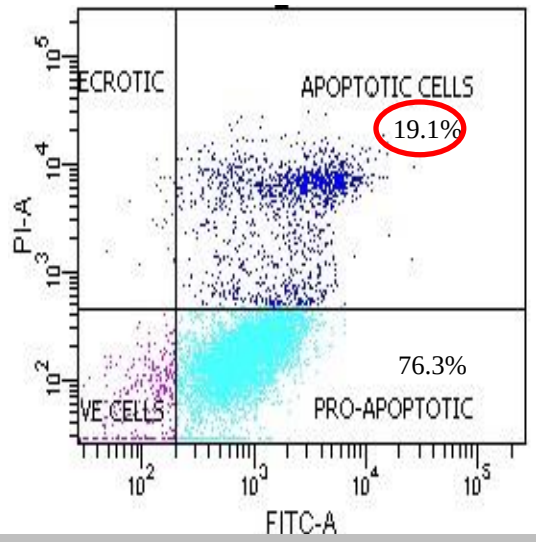


ARCE

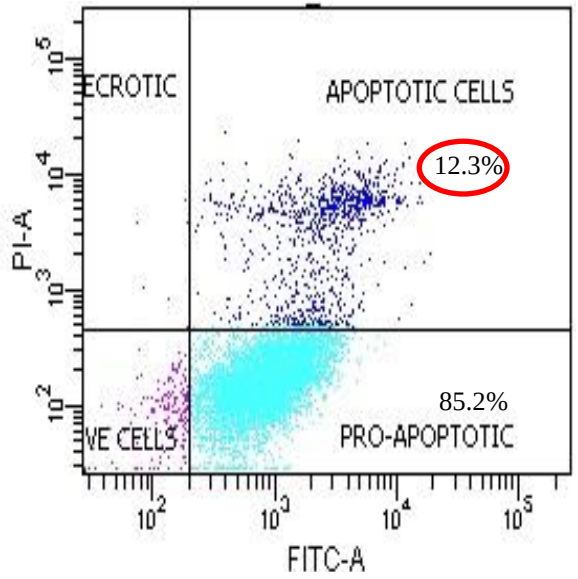


H2O2

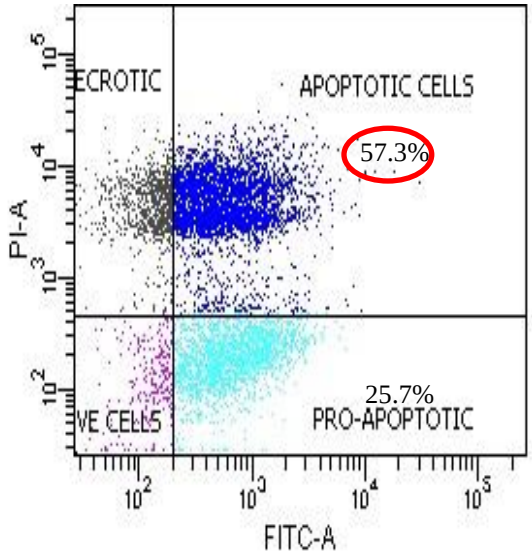




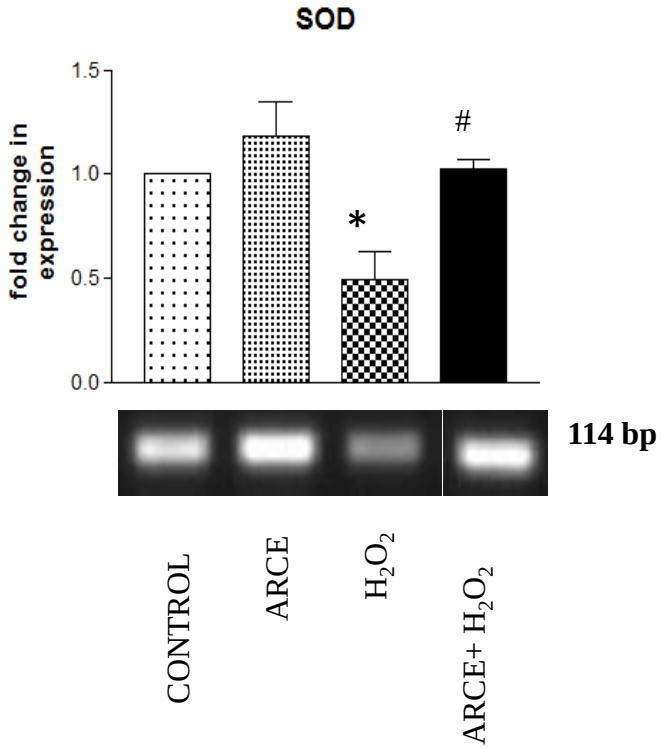
ARCE down-regulates apoptosis

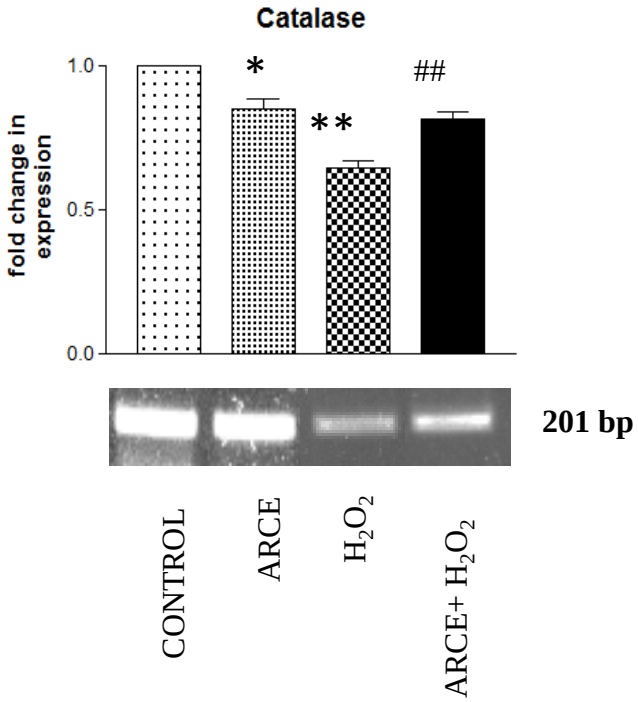


ARCE

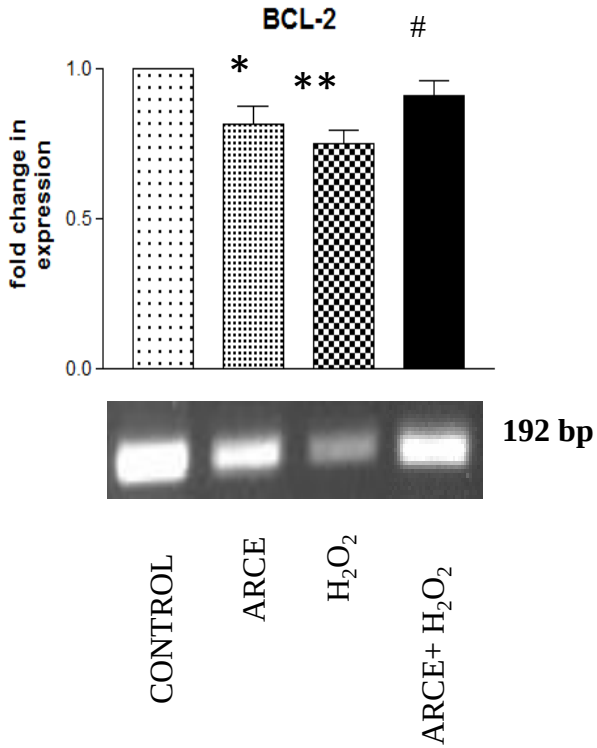


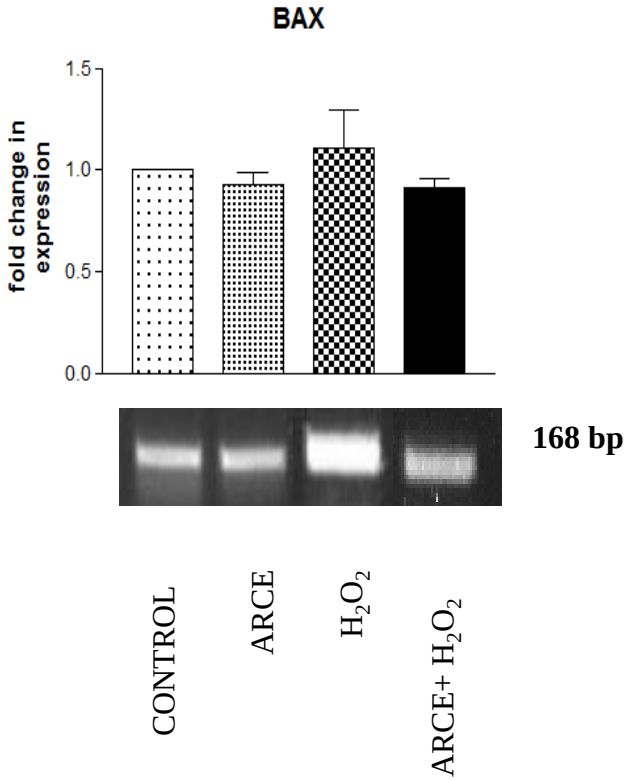
H2O2





ARCE prevents depletion of intracellular antioxidants

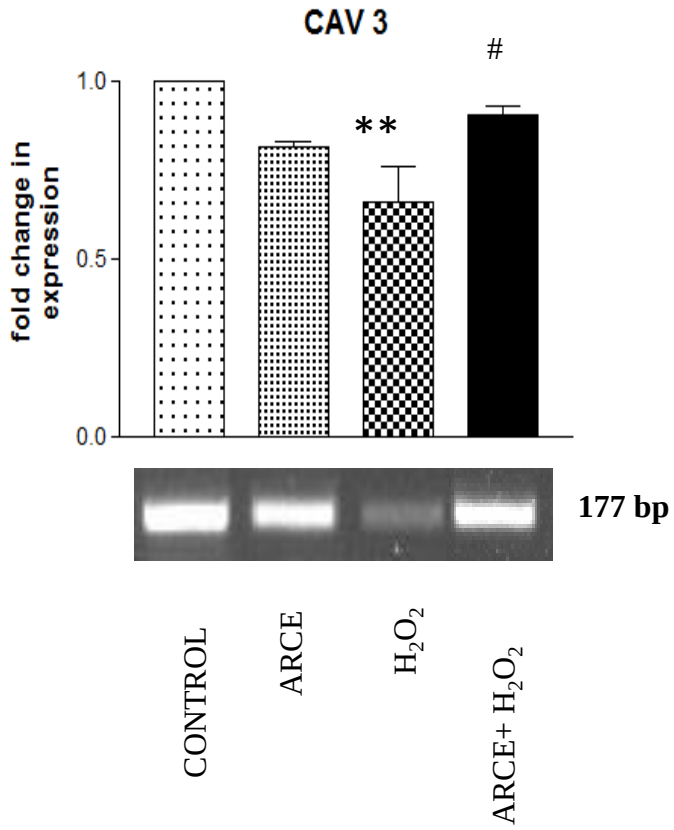




ARCE down-regulates apoptosis

Cav-3, the muscle-specific isoform, mediates interactions with cytoskeletal elements and is responsible for caveolae formation in cardiac cells.

Cardiac Cav-3 expression has been reported to decrease in cases of myocardial infarction , cardiac hypertrophy , heart failure, and chronic hypoxia .



ARCE prevents down-regulation of CAV3

In a Nutshell

- Functional foods draw considerable interest due to their effectiveness against a myriad of human diseases and hence, anthocyanins and their therapeutic potentials continue to fascinate the research fraternity.
- Hence, novel sources of anthocyanins are subjected to scientific scrutiny through innovative research models and protocols to seek answers pertaining to their therapeutic targets in metabolic pathways.





MY TEAM







thank
you!