International Journal of Health Sciences and Research
www.ijhsr.org ISSN: 2249-9571

Original Research Article

Cardioprotective Effects of Lycopene against Cadmium Induced Toxicity in Albino Mice

Suman Sharma[1], P. Vijaya[2]

[1]Professor, [2]Research Scholar, Department of Zoology & Environmental Sciences, Punjabi University, Patiala.

Corresponding Author: P.Vijaya

Received: 22/06/2015 *Revised: 14/07/2015* *Accepted: 16/07/2015*

ABSTRACT

Objective and Study Design: The present study has been undertaken to evaluate the protective efficacy of lycopene on cadmium induced toxicity in heart of albino mice.
Materials and Methods: 24 Albino mice were divided into four groups. **Group I** mice were kept as control. **Group II** animals were administered a single dose of cadmium chloride (0.32mg/kg bw) intraperitoneally. **Group III** animals were injected with 20mg/kg bw of olive oil (positive control). Group IV animals were injected a single dose of $CdCl_2$ followed by a chronic dose of lycopene (20mg/kg bw). Autopsies were done at the intervals of 1, 5, 10 and 15 days post treatment.
Results: Cadmium administration led to decrease in weight of heart in mice as compared to control. Histopathological analysis in heart showed extensive haemorrhage between the cardiac myocytes and the blood vessels showed endothelial thickening with peri-vascular infiltration of inflammatory cells. Lycopene administration to mice showed increase in weight of heart and showed significant protection by alleviating cadmium induced cardiac injury.
Conclusion: It can be concluded from the present study that that lycopene treatment is able to prevent cadmium induced cardiac injury in mice.

Keywords: Cadmium (CD), lycopene, histopathology and heart.

INTRODUCTION

Heavy metals are natural component of earth's crust. They cannot be degraded or destroyed. [1] Some heavy metals are essential to maintain the metabolism of the human body and other organisms. However, at higher concentration they lead to poisoning. [2] Cadmium, a known heavy metal is ubiquitous environmental pollutant and is primarily used for electroplating and galvanizing other metals (as it is relatively resistant to corrosion), in electrical contacts, in soldering alloys, in nickel cadmium batteries, in television phosphors and as stabilizers for polyvinylchloride. It is also used as a pigment in plastics, paints and plasters. [3] It is specifically significant as it has a long half life (between 4 -19 years in human liver) and can threaten human health both through environmental and occupational exposures. [4,5]

CD possesses a significant threat to the human population and environment. Since the biological half life of cadmium in human is found to be long, cadmium has the ability to induce severe alternation in

various organs and tissues following either acute or chronic exposure. [6] Cadmium accumulates mainly in the liver followed by heart, gut and kidney. [7] There is greater susceptibility of the heart as compared to the kidney to cadmium in the presence of high dietary selenium. Cadmium treatment results in more extensive effects on glutathione peroxidase and superoxide dismutase in the heart as compared to kidney. [8] Epidemiologically, high Cd level was found to be associated with hypertension, stroke and cardiac arrest. [9] In literature, most of the studies depicted the effects of Cd on liver [10,11,12] and kidney. [13,14,15,16,17] But, studies on the heart are relatively scanty. Moreover, the studies on heart covered the oxidative stress parameters [18,19,20,21] and very few work was found on histopathology of heart.

Lycopene is a natural pigment synthesized by plants and microorganisms. It is highly lipophilic and is most commonly located within cell membranes and other lipid components. It is therefore expected that in the lipophilic environment, lycopene will have maximum ROS scavenging effects. In epidemiological and supplementation studies on human trials, lycopene was found to reduce cardiovascular risks due to its antioxidant properties. [22] Lycopene, because of its high number of conjugated double bonds, exhibits higher singlet oxygen quenching ability compared to β-carotene or α-tocopherol. [23] Continuous administration of lycopene can protect myocardium against ischemia reperfusion injury. [24]

The present work is aimed to evaluate the protective role of lycopene on cadmium induced histopathological changes in heart of albino mice.

MATERIALS AND METHODS

Animals: Swiss albino mice weighing 20±2g were procured from GADVASU, Ludhiana. They were kept and acclimatized to the laboratory conditions for 15 days under optimal conditions of light and temperature. They had *ad libitum* access to tap water. The animals were handled with humane care in accordance with the guidelines of the Institutional Animal Ethical Committee.

Chemicals: Cadmium chloride ($CdCl_2$) was bought from S.D FINE CHEM LIMITED, Mumbai. It was dissolved in double glass distilled water and administered intraperitoneally (i.p.) to mice. Lycopene was obtained from PASSIM Pharmaceuticals Limited, Baddi. It was dissolved in olive oil and administered intraperitoneally to mice.

Experimental Design: 24 albino mice were divided into four groups of six mice each. Group I – Control animals were given distilled water. Group II – Animals were administered a single dose of 0.32 mg/kg bw ($1/10^{th}$ of LD_{50}) of cadmium (i.p.). Group III – Animals were kept as positive control and were injected (i.p.) 20 mg/kg bw of olive oil daily. Group IV – Animals were injected an acute dose of 0.32 mg/kg bw of cadmium (i.p.) followed by a daily dose of 20 mg/kg bw of lycopene for 15 days. Autopsies were done on 1, 5, 10 and 15 days post treatment. Heart was removed, blotted dry and weighted.

Histopathological Studies: The heart tissue was fixed in Bouin's fixative, embedded in paraffin wax (58-60^oC) and 5-7µ thick sections were stained with haematoxylin and eosin stains.

Statistical analysis: The data was analyzed by using Student's *t*-test.

RESULTS AND DISCUSSION

CD administration does not produce any discernible signs and symptoms of sickness in mice. Also, no mortality was observed during the entire period of experiment. A reduction in weight of heart

was also observed in mice treated with cadmium in comparison to control group. This reduction may be attributed to the damaging effects of cadmium on heart tissue. Anderson H et al. [25] suggested that organ toxicity can be evaluated by considering the weight of the organs after exposure to toxicant in animal toxicity studies. In Cd + lycopene treated group, increase in weight of heart was observed. Thus improvement in organ weight indicates the protection afforded by lycopene (Figure1).

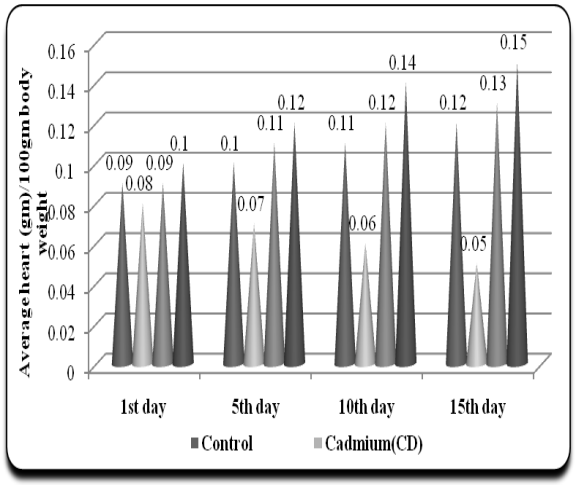

Figure.1 Weight of heart (gm/100gm body weight) in control, cadmium and antioxidant treated groups.

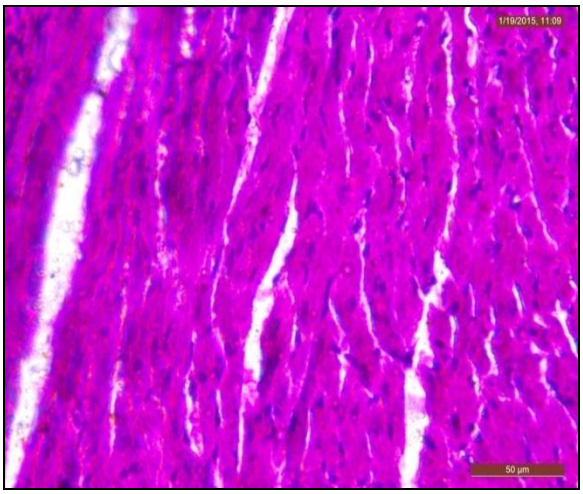

Figure 2: Showing normal heart structure. A semi-thin section in the cardiac myocytes showing a longitudinal section. The cells show branching with each other. Cross striations (arrows) and central nuclei (N) are seen. X400.

Histopathological examination of the heart of control group showed normal arrangement of cardiac muscles and nuclei. Endocardium, myocardium and epicardium were normal (Figure 2). Histology of heart of olive oil treated group showed normal structure at all the intervals of the experiment (Figure 3).

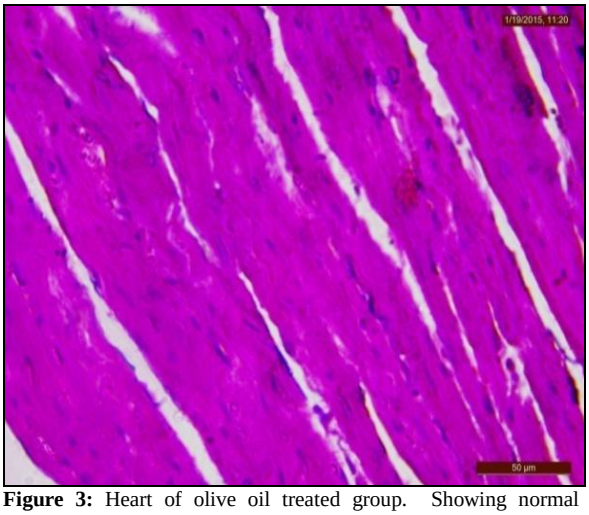

Figure 3: Heart of olive oil treated group. Showing normal cardiac myocytes. X400.

However, animals treated with Cd showed loss of normal heart architecture including extensive haemorrhage between the cardiac myocytes and the blood vessels showed endothelial thickening with peri-vascular infiltration of inflammatory cells (Figure 4, 5). Also, a focal area of degenerated cells was seen. This is in agreement with Lei W et al. [26] who observed myocardial oedema, vascular degeneration and infiltration of inflammatory cells in crab heart after cadmium exposure.

Ferramola ML et al. [27] observed foci of myocardial fibre necrosis in rats exposed to cadmium-induced oxidative stress. On the other hand, Zaslavina SV et al. [28] studied the structural changes of rat myocardium in the mother-foetus system exposed to cadmium and observed the reduction in volume of cardiomyocytes and blood vessels

in both mother and foetus with signs of diffuse oedema of myofibrils and dilatation of intercellular spaces.

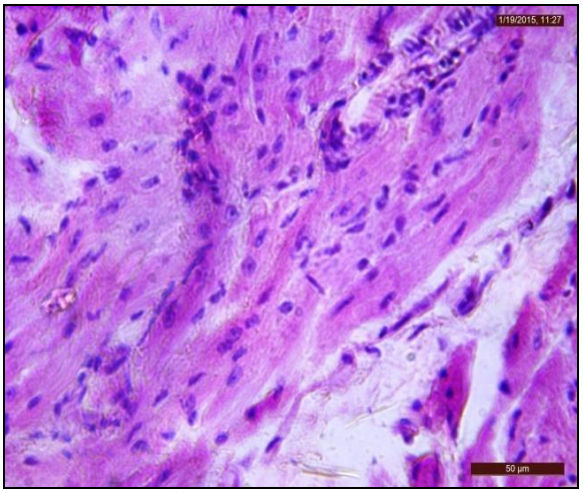

Figure 4: Heart of cadmium treated group showing an oblique section. Extensive haemorrhage (H) is seen between the cells. The blood vessels (BV) show endothelial thickening with peri-vascular infiltration of inflammatory cells. X400.

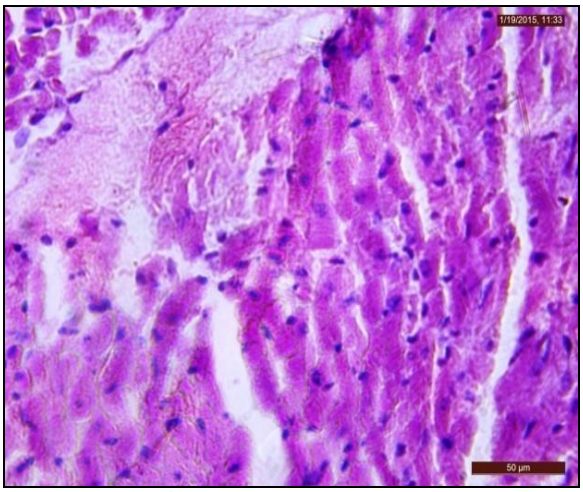

Figure 5: Heart of cadmium treated group showing hyperaemia, vacuolation between the cardiac myocytes. X400

Ferramola ML et al. [27] observed profound ultrastructural damages of the heart tissue in rats exposed to cadmium. Also, Patai K and Balogh I [29] found that $CdCl_2$ causes apparent changes in rat foetal myocardium with simultaneous mitochondrial impairments. Many authors studied the mechanism of cadmium toxicity, Ferramola ML et al. [21] suggested that, cadmium acts as a catalyst in the oxidative reactions of biological macromolecules and therefore, the toxicity associated with the metal might be due to the oxidative damage. Manca D et al., [30] Pathak N and Khandelwal S, [31] and Ercal N et al. [32] stated that, cadmium causes an increase in the production of reactive oxygen species (ROS) such as superoxide anion free radical, hydroxyl free radical as well as hydrogen peroxide. An enhanced production of ROS results in oxidative stress. Cells under oxidative stress display various dysfunctions due to lesions caused by ROS to lipid, proteins and DNA.

Messaoudi I et al. [33] added that, the degree of cell damage under the heavy metal stress depends on the rate of ROS formation and on the efficiency and capacity of detoxification and repair mechanisms. The cellular defence system against toxicity from ROS includes superoxide dismutase, catalase and glutathione peroxidases. Mitra E et al. [34] demonstrated that, the cadmium-induced cardiac damage is due to generation of oxidative stress as evident from elevated levels of tissue lipid peroxidation and protein carbonyl content and a decreased tissue level of reduced glutathione, the well known bio-markers of oxidative stress. Membrane lipids are highly susceptible to free radical damage. In the presence of free radicals, lipids can undergo highly damaging chain reaction of lipid peroxidation. Moreover, the heavy metal binds to other relevant biomolecules found in subcellular membrane, endoplasmic reticulum, mitochondria or within the nucleus causing their damage. [34] The cadmium also showed adverse effects on the structure of cardiac myocytes.

Lycopene treated group showed mild edema with significant reduction in infarction, showing normal myocardial architecture (Figure 6, 7).

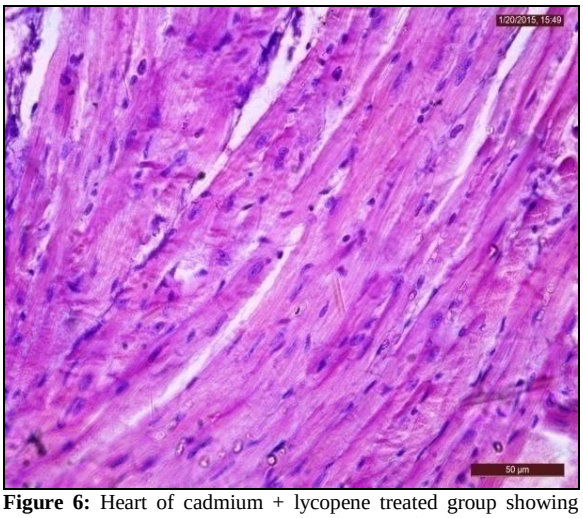

Figure 6: Heart of cadmium + lycopene treated group showing less hyperaemia with occasional loss of muscle fibre. X400.

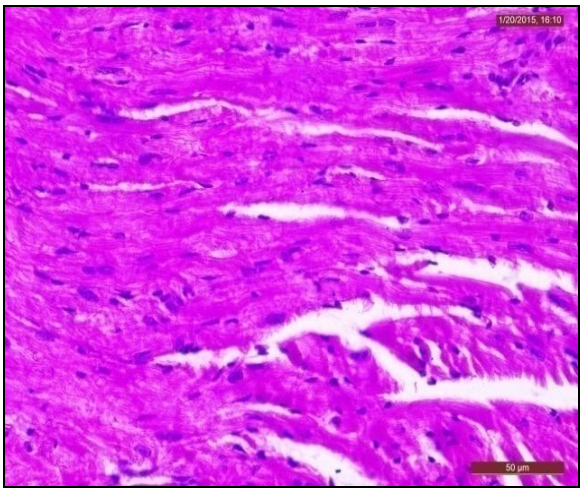

Figure 7: Heart of cadmium + lycopene treated group showing almost normal histoarchitecture of heart tissue. X400.

The present study showed that lycopene supplementation (20 mg/kg/bw) reduced the cardiac cellular changes induced by cadmium, indicating that lycopene contributes to the protection against, cardiac-morphological injury.

CONCLUSION

It is concluded that foods containing lycopene could protect cardiac tissue against heavy metal induced especially, cadmium-induced oxidative cardiac impairment. At this stage the precise mechanism of protection played by lycopene is not fully clear. Further researches are necessary to investigate the detailed molecular protective mechanism played by lycopene against cadmium-induced cardiac injury.

ACKNOWLEDGEMENT

The authors gratefully acknowledge the Department of Zoology & Environmental Sciences, Punjabi University, Patiala, for providing the necessary facilities to pursue the research work.

REFERENCES

1. Pinot F, Kreps SF, Bachelet M, Hainaut P, Bakonyi M, Polla BS. Cadmium in the environment: sources, mechanisms of biotoxicity and biomarkers. Res Environ Health. 2000; 15: 299-323.
2. Ferner DJ. Toxicity heavy metals. eMed. *J.* 2001; 2: 1.
3. Waisberg G M, Joseph P, Hale H, Beyersonann D. Molecular and cellular mechanism of cadmium carcinogenesis. Toxicol. 2003; 192: 95-117.
4. Jeong SH, Habeebu SSM, Klaassen CD. Cadmium decrease gap junctional intercellular communication in mouse liver. Toxicol Sci. 2000; 57, 156-166.
5. Duruibe JO, Ogwuegbu MOC, Egwurugwu J N. Heavy metal pollution and human biotoxic effects. Int J Phys Sci. 2007; 2 (5): 112-118.
6. Urani C, Melchioretto P, Canevalic C, Morazzoni F, Gribaldo L. Metallothionein and hsp 70 expression in HEPG2 cells after prolonged cadmium exposure. Toxicol In Vitro. 2007; 21: 314-319.
7. Hawkins WE, Tate LG, Sarphie TG. Acute effects of cadmium on the spot leiostomus-xanthurus (teleostei : Tissue distribution and renal ultrastructure. J Toxicol Environ Health. 1980; 6 (2).
8. Jamall IS, Naik M, Sprowls JJ, Trombetta LD. A comparison of the effects of dietary cadmium on heart and kidney antioxidant enzymes: Evidence for the greater vulnerability of the heart to cadmium toxicity. J App Toxicol. 1989; 9: 339-345.

9. Tellez-plaza M, Navas-Acien A, Crainiceanu CM, Guallar E. Cadmium exposure and hypertension in 1999-2004. National Health and Nutrition Examination Survey (NHANES). Environ Health Perspect. 2008; 116: 51-56.
10. Renugadevi J, Prabu SM. Cadmium-induced hepatotoxicity in rats and protective effects of naringenin. ExpToxicol Pathol. 2010; 62(2): 171 - 181.
11. Belyaeva EA, Korotkov SM, Saris NE. In vitro modulation of heavy metal-induced rat liver mitochondria dysfunction: a comparison of copper and mercury with cadmium. J Trace Elem Med Biol. 2011; 25: 63-73.
12. Sharma S, Kaur S, Kaur K. 2013. Histopathological and Histometric effects of cadmium on liver of albino mice. Biochem Cell Arch. 2013; 13(1): 47-51.
13. Jadhav SH, Sarkar SN, Patil RD, Tripathi HC. Effect of Subchronic Exposure via drinking water to a mixture of Eight Water-contaminating metals: A biochemical and histopathological study in male rats. *Arch Environ Contam Toxicol*. 2007; 53: 667 - 677.
14. Kalender S, Kalender Y, Durak D, Ogutcu A, Uzunhisarcikli M, Cevrimli BS, Yildirim M. Methyl parathion-induced nephrotoxicity in male rats and protective role of vitamins C and E. Pest Biochem Physiol. 2007;88:213-218.
15. Prozialeck WC, Edwards JR, Lamar PC, Liu J, Vaidya VS, Bonventre JV. Expression of kidney injury molecule-1 (kim-1) in relation to necrosis and apoptosis during the early stages of Cd-induced proximal tubule injury. Toxicol Applied Pharmacol. 2009; 238: 306-314.
16. Bawazir AE. Effect of chocolate brown HT with olive oil on some neurotransmitter in different brain regions, physiological and histological structure of liver and kidney of male albino mice. J Evol Biol Res. 2012; 4(1): 13 - 23.
17. Babaknejad N, Moshtaghie AA, Shahanipour K, Bahrami S. The protective roles of zinc and magnesium in cadmium-induced renal toxicity in male Wister rats. Iranian J Toxicol. 2015; 8(27): 1160-1167.
18. Yiin SJ, Chern CL, Sheu JY, Lin TH. Cadmium-induced liver, heart and spleen lipid peroxidation by selenium. Biol Trace Elem Res. 2000; 78: 219-230.
19. Chattopadhyay A, Biswas S, Bandyopadhyay D, Sarker C, Datta AG. Effect of isoproterenol on lipid peroxidation and antioxidant enzymes of myocardial tissue of mice and protection by quinidine. Mol Cell Biochem. 2003; 245: 43-49.
20. Manna P, Sinha M, Sil PC. Amelioration of cadmium-induced cardiac impairment by taurine. Chem Biol Interact. 2008; 174: 88-97.
21. Ferramola ML, Anton RI, Anzulovich AC, Gimenez MS. Myocardial oxidative stress following sub-chronic and chronic oral cadmium exposure in rats. Environ Toxicol Pharmacol. 2011; 32: 17-26.
22. Gerster H. The potential role of lycopene for human health. J Am Coll Nutr 1997; 16:109–26.
23. Di Mascio P, Kaiser S, Sies H. Lycopene as the most efficient biological carotenoid singlet oxygen quencher. Arch Biochem Biophys 1989; 274:532–8.
24. Bansal P, Gupta SK, Ojha SK, Nandave M, Mittal R, Kumari S, *et al*. Cardioprotective effect of lycopene in the experimental model of myocardial ischemia-reperfusion injury. Mol Cell Biochem. 2006; 289:1-9.
25. Anderson H, Larsen S, Splid H, Christenson ND. Multivariate statistical analysis of organ weights in toxicity studies. Toxicol. 1999; 136: 67.

26. Lei W, Wang L, Liu D, Xu T, Luo J : Histopathological and biochemical alteration of the heart induced by acute cadmium exposure in the freshwater crab sinopotamon yangtsekiense. Chemosphere. 2011; 84 (5): 689-94.
27. Ferramola ML, Perez-Diaz MF, Honore SM, Sanchez SS, Anton RI, Anzulovich AC and Gimenez MS: Cadmium-induced oxidative stress and histological damage in the myocardium. Effects of a soy-based diet. Toxicol Appl Pharmacol. 2012; 263 (3): 380-9.
28. Zaslavina SV, Sklianov IUI, Bgatova NP. Structural changes of rat myocardium in the mother-foetus system exposed to cadmium. Morfologiia. 2007; 132(6): 42-5.
29. Patai K, Balogh I. Nickel and cadmium-induced foetal myocardial changes in the mouse: The hazards of cigarette smoke in pregnancy. Acta Chir Hung. 1988; 29(4): 315-21.
30. Manca D, Richard AC, Trottier B, Chevallier G. Studies on lipid peroxidation in rat tissues following administration of low and moderate doses of cadmium chloride. Toxicol. 1991; 67: 303-323.
31. Pathak N, Khandelwal S. Oxidative stress and apoptotic changes in murine splenocytes exposed to cadmium. Toxicol. 2006; 220: 26-36.
32. Ercal N, Gurer-Orhan H, Aykin-Burns N. Toxic metals and oxidative stress part 1: mechanisms involved in metal-induced oxidative damage. Curr Top Med Chem 2001; 1: 529-539.
33. Messaoudi I , Hammouda F, EL-Heni J, Baati T, Said K. Reversal of cadmium-induced oxidative stress in rat erythrocytes by selenium, zinc or their combination. Exp Toxicol Pathol. 2010; 62: 281-288.
34. Mitra E, Ghosh AK, Ghosh D, Mukherjee D , Chattopadhyay A, Dutta S, Pattari SK, Bandyopadhyay D. Protective effect of aqueous curry leaf (Murraya Koenigii) extract against cadmium-induced oxidative stress in rat heart. Food Chem Toxicol. 2012; 50: 1340-1353.

How to cite this article: Sharma S, Vijaya P. Cardioprotective effects of lycopene against cadmium induced toxicity in albino mice. Int J Health Sci Res. 2015; 5(8)507-513.

****