A Review Study of Antioxidants and The Cinnamon Oil Effects

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ABSTRACT

The aim of the study to estimate the antioxidant action and protecting effect of ethanolic cinnamon extract against CCl₄ induced toxicity in male rats. To determine the effect of different concentrations of ethanolic cinnamon extract on male rats that fed a high cholesterol diet that induced hyperlipidemia. The experiment has been conducted in the present study., aimed to evaluate the hepatoprotective, role of Cinnamomum zeylanicum ethanolic extract in carbon tetrachloride (CCl₄) induced hepatotoxic male rats, The cinnamon and its oil reported to have many beneficial uses in food preservation due to antioxidant of cinnamon. The Phenolic compounds extracted from cinnamon such as hydroxyl cinnamaldehyde and the hydroxycinnamic acid act as scavengers of peroxide radicals and avoid oxidative damage (Mathew and Abraham, 2006; Leela, 2008). Ranjbar et al, (2006) observed individuals consuming cinnamon tea showed increased total serum antioxidant status, increased thiols such as glutathione, NADPH, NADH, SOD, and decreased lipid peroxidation.

Keywords: Cinnamon oil, Antioxidants, CCl₄

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INTRODUCTION

Antioxidant means "against oxidation", antioxidants work to guard lipids, proteins and nucleic acids from peroxidation by radicals. They hinder or interval the oxidation of other particles by stopping the initiation or spread of oxidizing chain reactions. Antioxidants are effective because they are ready to give up their possess electrons to free radicals. After a free radical gains the electron from an antioxidant it no lengthier needs to attack the cell and the chain reaction of oxidation is destroyed (Dekkers *et al.*, 1996).

Medical plants are the oldest friends of humanity. They not only provided food and shelter but also served the mankind to cure different ailments, and according to the world health organization (WHO) traditional systems of medicines always played important role in the global health. In the traditional health medicinal plants providing a new areas of drug research (Verma *et al.*, 2014).

‘Cinnamon’, *Cinnamomum zeylanicum* (Lauracea), locally known as Qerfah or Darsin is an older and essential spice with wide-ranging requests in flavoring, perfumery, drinks and drugs

(Jayaprakasha *et al.*, 2002). In some previous studies, an essential oil of cinnamon is identified to have antibacterial (Jirovetz *et al.*, 2002), antifungal (Misra *et al.*, 2000), Previously, some studies also suggested that cinnamon owns strong free radical scavenging capability (Bafna and Balaraman, 2004), antioxidant and antimutagenic (Jayaprakasha *et al.*, 2007) activities cholesterol-lowering properties (Khan *et al.*, 2003; Subash *et al.*, 2007). Oxygen, necessary for maintaining life, sometimes becomes toxic, resultant in the generation of most aggressive agents such as reactive oxygen species (ROS), aerobic organisms service a battery of defense mechanisms such as antioxidant enzymes superoxide dismutase (SOD), catalase (CAT) and glutathione (GSH) to inhibit oxidative tissue damage (Halliwell and Gutteridge, 1989).

Free radicals are made in normal and/or pathological cell metabolism. Oxidation is necessary too many living organisms for the manufacture of energy to fuel biological processes. However, the uncontrolled creation of oxygen-derived free radicals is complex in the beginning of many diseases such as cancer, rheumatoid arthritis,

cirrhosis and arteriosclerosis as well as in degenerative processes related with ageing (Baghiani *et al.*, 2012).

Antioxidants

The antioxidants are group of organic molecules that prevent the progress of lipid oxidation. The main causes of food deterioration is oxidation, due to free radical production from its components, especially lipids. To prevent oxidation of foods, several synthetic antioxidants have been used widely by the food industry (Cubero *et al.*, 2002). However, scientific evidence that synthetic antioxidants produce toxic effects on consumers has led to the search of natural antioxidants sources. The origins of antioxidant are natural components such as flavonoids, phenolic acids, tannins, coumarins, lignans and their derivatives, and they show strong antioxidant activity (Potterat, 1997; Cao *et al.*, 1998).

The antioxidants comprise many materials that have important in guarding biological systems to avoid the toxic effects of oxidative stress on carbohydrates, lipids, proteins and DNA Figure (2-1), (Yuji *et al.*, 2010).

Figure 1: Antioxidative network in biological system (Yuji *et al.*, 2010).

Classification of antioxidant

There are several classifications of antioxidants, including endogenous antioxidants and exogenous antioxidant. (Jeppsson *et al.*, 2007).

1. **Endogenous antioxidants:-** include; bilirubin, thiols e.g. (lipoic acid, glutathione, N-acetyl cysteine), NADPH, NADH, Uric acid, Ubiquinone (coenzyme Q10), Enzymes :

- copper/zinc and manganese-dependent superoxide dismutase
- iron-dependent catalase
- selenium-dependent glutathione peroxidase

2. Exogenous antioxidants:-

- A- dietary antioxidants include: Vitamin C, Vitamin E, β -Carotene and other carotenoids, and Polyphenols, e.g., flavonoids, flavonols, flavones and proanthocyanidins.
- B- metal binding proteins include; Albumin (copper), Ferritin (iron), Ceruloplasmin (copper), Metallothionin (copper), Myoglobin (iron) and Transferrin (iron).

Oxidative stress

The oxidative stress is defined as an imbalance between oxidants and antioxidants in valid of the oxidants, potentially leading to damage (Sies, 1991). However, oxidative damage that cause weakens in physiological functions of cellular compounds. ROS is reactive oxygen species or RNS is reactive nitrogen species (Sies, 1991; Halliwell and Gutteridge, 2007). Reactive oxygen species consist from superoxide ($O_2^{\bullet-}$), hydroxyl ($\bullet OH$) and hydrogen peroxide (H_2O_2), though RNS are nitrogen dioxide ($NO_2^{\bullet-}$), nitric oxide (NO), and peroxy nitrite ($OONO-$) (Sies, 1991; Halliwell and Gutteridge, 2007).

Figure 2: Show diseases and damages caused by reactive oxygen species (Sies, 1991).

Oxidative stress damage

Oxidative damage of proteins

Proteins are targeted by oxidative damage inside the cells, because they have widely abundance and rapid interaction with radicals and excited-state species, including single oxygen (Sivalokanathan *et al.*, 2006). The vast modifications made protein oxidation. Backbone cleavage and protein cross

linking to more subtle modifications such as side chain oxidation, altered electrical changes and increase susceptibility to proteolysis. (Gracanin *et al.*, 2009).

Oxidative damage of lipid

Lipid peroxidation

Lipid peroxidation abbreviated as LPO defined as free radical intermediated chain reaction that can deactivated components of the cell. This process is associated with some complications like carcinogenesis (Beevi *et al.*, 2007).

Finger 3: Lipid peroxidation process (Marnett, 1999).

Malondialdehyde

Malondialdehyde (MDA) is a three- carbon atom, low-molecular weight aldehyde, produced by lipid peroxidation. It reacts with nucleophilic amine groups like lysine, arginine and the amino termini of amino acids. It also reacts with any ketones as aldehydes from other sources, for example; attached sugars or glycation products (Marnett, 1999). Because of their very short life time so that difficult in detection of ROS in vivo; In tissues and blood, MDA exists in two forms; bounded and unbounded to NH_2 and SH groups of nucleic acid, protein and lipoproteins (Draper *et al.*, 2000).

Figure 4: Structure of malondialdehyde (Marnett, 1999).

Glutathione

Glutathione is considered an intracellular peptide that have physiological functions such as detoxification of xenobiotics and/or their metabolites (Hayes and Strange, 2000). It have

antioxidant of endogenous structure created to stabilize free radical (Jackson and Loeb, 2001). The GSH has metabolic functions involved storage of cysteine, signal transduction and apoptosis (Main *et al.*, 2012). GSH presented in cytosol at percentage about 90%, and 10% is present in mitochondria and endoplasmic reticulum (Hwang *et al.*, 1992). Also, 85% of GSH is free and unbound and the remain is bound to certain proteins (Sies, 1999). As explained in figure (2-6) shows that H_2O_2 = Hydrogen peroxide, ROOH =Carboxy radical, GSH= Reduced glutathione, GSSG = Oxidized glutathione, PSH = Protein sulf hydryl, ROH = Hydroxyl radical, NADPH = Nicotine-amid dinucleotide phosphate reduced, NADP = Nicotine -amid dinucleotide phosphate oxidized.

Figure 5: Antioxidant functions of reduced glutathione (GSH) (Shelly, 1999).

Catalase

Catalase (CAT) is tetrameric enzyme established of four serious tetrahydrally organized subunits of 60KDa (Mates *et al.*, 1999). Catalase induced hydrogen peroxidase to water (H_2O) and molecular oxygen (O_2) and untaken at the peroxisome organelle. It have important role in protected of cells against oxidative damage (Cui *et al.*, 2003). Also, catalase control development of cells by stimulation of the extracellular indicators controlled the mechanism of kinase, important to increase the growth of cell that inhibited by oxidative stress (Hachiye and Akashi, 2005).

Oxidative damage to DNA

DNA nuclear and mitochondrial oxidative damage caused by ROS, leading to structural changes in DNA, such as base pair mutation, deletion and insertion. Oxidative DNA damage may be indirect through the rise of intracellular Ca^{++}

(Cabiscol *et al.*, 2000). The ROS types $\text{OH}^\cdot$ usually generate various products from the DNA bases which mainly include C-8 β -hydroxylation of guanine to form 8-oxo-7, 8 dehydro-2-deoxyguanine, 8-OH- adenine and 2-OH- adenine. It has been suggested that 8-hydroxy-2-deoxyguanosine can be used as biological marker for oxidative stress (Rowe *et al.*, 2008).

Free radicals

Free radicals (FR) are contain one or more unpaired electrons, an unpaired electron being one that is alone in an atomic, molecular oxygen is so important component for living organism. It helps in the process of oxidation, which is a basic component of aerobic life and of the metabolic process (Aiyegoro and Okoh, 2010). It makes this species very unstable and tends to react with other molecules to pair this electron and thereby generates more stable species. It is generated under physiological conditions during aerobic metabolism (Gueteens *et al.*, 2002).

The highly reactive molecules include Reactive Oxygen Species (ROS) and Reactive Nitrogen Species (RNS). ROS is a term collectively describing radicals and other non-radical reactive oxygen derivatives. These intermediates may participate in reactions giving rise to free radicals or damaging to organic substances. RNS are radical nitrogen-based molecules that can act to facilitate nitrosylation reactions (Caimi *et al.*, 2004).

Reactive oxygen species

Reactive oxygen species (ROS) are chemically-reactive particles including oxygen ions and peroxides. ROS are highly reactive due to the presence of unpaired valence shell electrons. ROS form as a natural byproduct of the normal metabolism of oxygen and have important roles in cell signaling and homeostasis (Devasagayam *et al.*, 2004).

Sources of free radicals and ROS

Free radicals and ROS are generated from normal metabolic process and from external sources.

A: Internal source

Mitochondrial respiratory chain is the main source of free radicals, during this process of ATP production and which a single electron is leaking out of the respiratory chain, reacts with molecular oxygen to form superoxide anion (Kumar, 2011). The stimulation of phagocytes reflects contributor of ROS generation in the human body during the killing of bacteria, virus and other xenobiotics. In addition, cytochrome (P450), xanthin oxidase, peroxisomes and conditions of ischemia/reperfusion

represent remarkable sources of free radicals (Babior, 2004).

B: External sources

ROS may generate by exposure to radiation, environmental pollutants, ultraviolet light, ozone, cigarette smoke, certain drugs, pesticides, industrial solution and anesthetics (Kumar, 2011).

Fenton chemistry

Haber-Weiss reaction

Figure 6: Haber-Weiss and Fenton reactions lead to the production of the hydroxyl radical, including the liberation of free iron from ferritin by superoxides. (Kell, 2009).

Cinnamon oil

Origin, uses and factors affecting

Essential oils are a rich source of biologically active compounds, cinnamon produces two different oils; cinnamon bark oil obtained from the dried inner bark, whereas cinnamon leaf oil is obtained from the leaves and twigs. It is important to distinguish between the two variations of cinnamon oil, cinnamon bark oil has a spicy smell whereas cinnamon leaf oil is said to smell like cloves; cinnamon leaf oil is considered to be considerably safer to use in aromatherapy (Jayaprakasha *et al.*, 2000). The cinnamon bark oil, bark oleoresin and cinnamon leaf oil are important value added products from cinnamon. Cinnamon bark oil is used in the food and pharmaceutical industries while, oleoresin is used mainly for flavoring food product such as cakes and confectionary (Gu *et al.*, 2004).

Temperature, humidity, duration of daylight (radiation), and wind patterns all have a direct influence on volatile oil content, especially in those herbs that have superficial histological storage structures (e.g. glandular trichomes). When the localization is deeper, the oil quality is more constant (Lawrence, 2002; Rohloff, 2004).

Chemical composition

From different parts of cinnamon (bark, roots and leaves) essential oils with variations in the composition by especially geographic and technical reasons can be obtained (Schmidt, 2006). Twenty-six compounds constitutes 97% of the volatile oil from cinnamon flowers were characterized with (*E*)-cinnamyl acetate (42%), *trans*- α -bergamotene (8%) and caryophyllene oxide (7%) as the major compounds (Jayaprakasha *et al.*, 2000). The combinations about thirty-four indicating 98% of volatile oil from the buds of *C. z.* were characterized using GC and GC-MS (Gu *et al.*, 2004). The important chemical constituents of *C. z.* oil are cinnamaldehyde and eugenol (Senanayake *et al.*, 1977).

Figure 9: Some of chemical essential structures of cinnamon (Meena *et al.*, 2012)

Biological activities

Antioxidant activity

The cinnamon and its oil reported to have many beneficial uses in food preservation due to

antioxidant of cinnamon. The Phenolic compounds extracted from cinnamon such as hydroxyl cinnamaldehyde and hydroxycinnamic acid act as scavengers of peroxide radicals and avoid oxidative damage (Mathew and Abraham, 2006; Leela, 2008). Ranjbar *et al.*, (2006) observed individuals consuming cinnamon tea showed increased total serum antioxidant status, increased thiols such as glutathione, NADPH, NADH, SOD and decreased lipid peroxidation

Antihyperlipidemic activity

Khan *et al.*, (2004) demonstrated that intake of cinnamon daily reduced serum glucose, triglyceride TG, LDL and total cholesterol in people with type II diabetes and thus showed clinically significant reduction in cardiovascular risk factor biomarkers. A study indicated that the cinnamon oils possess hypoglycemic, hypolipidemic and antioxidant effects rats (Al-Logmani *et al.*, 2009).

Antidiabetic activity

The cinnamon could reduce glucose level of the blood in non-insulin dependent diabetics. Further, the cinnamaldehyde proved as antidiabetic agent. Furthermore, the soluble polymeric compounds extracted from cinnamon have insulin enhancing biological activity in the in vitro assay measuring the insulin dependent effects on glucose metabolism and also function as antioxidants, these results suggest that compounds present in cinnamon may have useful for treatment of diabetes (Anderson *et al.*, 2004).

Nematicidal activity

Study by (Park *et al.*, 2005) showed cinnamon oil had high nematicidal activity to the male, female and juveniles of pinewood nematode *Bursaphelenchus xyl ophilus*. The active ingredient in the oil represented by cinnamyl acetate at a concentration of 32.81 $\mu\text{g/l}$ resulted in 50% mortality of nematodes, further the rate of 0.2 % (weight by volume of soil) of stem bark of cinnamon powder used for soil amendment significantly reduced by 91.1% gall number of *Meloidogyne incognita* infection (root gall formation) of tomato seedling compared with control (Kim *et al.*, 2003).

Anti-inflammatory activity

The cinnamon have anti-inflammatory activity whereas ethanolic extract (70%) from cinnamon was effective on cute inflammation in mice (Lee *et al.*, 2003). In other hand herbal ophthalmic with 0.5% cinnamon found very effective as anti-inflammatory agent on ocular inflammation in rabbits (Leela, 2008).

Antifungal activity

The antifungal properties of cinnamon have also drawn great attention from many researchers. The effect of cinnamon extract on mycelial growth inhibition of *phytophthora capsici*. Further studies on medicinal plant extracts were studied against development of mycelium of *Phytophthora capsici*, *Rhizoctonia solani*, *Fusarium solani*, *Colletotrichum gloeosporioides*, and *Botrytis cinerea* (Nguyen *et al.*, 2009). Similar effect was found by Tzortzakis (2008), against *Botrytis cinerea* affected by essential oil. In addition, Amiri *et al.*, (2008), found that mixture of eugenol and soy lecithin reduced the disease incidence caused by *Botrytis cinerea*. Cinnamaldehyde and eugenol also demonstrated to have inhibitory properties against *Aspergillus flavus*, *Aspergillus ochraceus*, *Aspergillus niger*, *Aspergillus terreus*, *Aspergillus citrinum* and *Penicillium viridicatum* (Singh *et al.*, 2007).

Insecticidal activity

cinnamon extracts such as cinnamaldehyde is a potent insecticide against adults of *Sitophilus oryzae* and *Callosobruchus chinensis*. The oil isolated from leaves of *Artemisia princeps* and seeds of cinnamon have repellent and insecticidal activities (Kim *et al.*, 2003).

Antibacterial activity

Valero and Salmeron (2003) reported that cinnamon extracts found to be effective against bacteria whereas oils of cinnamon have antibacterials activity to inhibit growth of *Bacillus cereus*. In other hand, alcoholic extracts of cinnamon found very effective against *Helicobacter pylori* (Tabak *et al.*, 1996). Furthermore it was present accompanying of cinnamon and nisin increasing death range of *Salmonella typhimurium* and *Escherichia coli* O157:H7 in apple juice (Yuste and Fung, 2004).

Toxicity and side effects

Cinnamon is used as a spice in food material in Asia so its safety is quite obvious, have reported acute toxicity of cinnamon in the animals is very low ratio i.e. Benzaldehyde (LD50 orally, 1300 mg/kg rat), cinnamaldehyde (LD50 orally, 2220 mg/kg rat), linalool (LD50 orally, 2790 mg/kg rat), and salicylaldehyde (LD50 orally, 520 mg/kg rat) (Budavari *et al.*, 1989). According to the United States Food and Drug Administration, cinnamon is generally recognized as safe (Generally recognized as safe- GRAS) when used in amounts commonly found in food (USFDA, 2006). The most common adverse effects reported with cinnamon were related to contact irritation or allergic reaction with the skin or mucus membranes, stomatitis (Nadiminti *et al.*, 2005; Endo and Rees, 2006).

CONCLUSION

From the current study, it can be concluded that

1. Oxidative stress have an essential role in CCl₄ that induced hepatotoxicity through the normal medical regimes of treatment.
2. Antioxidants have established to be active in enhancing CCl₄-induced toxicity in several preclinical and clinical intermediations.
3. *Cinnamomum zeylanicum* extracts have capability to dawn normalize free radicals raise, enhance liver, kidney and cholestatic biomarkers, perfect hepatic marker enzymes, decrease fibrosis severity and regularize the hepatic and kidney cells design.
4. *Cinnamomum zeylanicum* extracts prior and co-administration with CCl₄ providing immediate complete protections in biochemical, physiological and liver, kidney histological variations.
5. Ethanol cinnamon extract refer to the greatest effective because of its content of flavonoids, sterol, tannins, saponins and alkaloids.

REFERENCES

- Dekkers, J.;** Doornen, L. and Kemper, H. (1996). The role of antioxidant vitamins and enzymes in the prevention of exercise-induced muscle damage. *Sports Medicines*, 21(3): 213-238.
- Verma, N.;** Jha, K.; Chaudhary, S.; Singh, O. and Kumar, A. (2014). phytochemistry , pharmacology and traditional uses of *Leptadenia pyrotechnica* - An important medicinal plant. *Indian J. Pharm. Biol. Res.* 2(1): 128-134.
- Jayaprakasha, G. K.;** Rao, J. and Sakariah, K. K. (2002). Chemical composition of volatile oil from *Cinnamomum zeylanicum* buds. *Z. Naturforsch (C)* 57: 990-993.
- Jirovetz, L.;** Buchbauer, G.; Ngassoum, M. B.; Essia, N.; Jean, J.; Tatsadjieu, L. N. and Adjoudji, O. (2002). Chemical composition and antibacterial activities of the essential oils of *Plectranthus glandulosus* and *Cinnamomum*
- Misra, N.;** Khare, U. and Shukla, D. (2000). Antifungal activity of essential of *Cinnamomum zeylanicum* Nees against *Stachybotrys chartarum*. *J. Essentl. Oil-Bearing Plants*, 3: 97-110.
- Bafna, P. A.** and Balaraman, R. (2004). Anti-ulcer and antioxidant activity of DHC-1, a herbal formulation. *J. Ethnopharmacol.*, 90:123-127.
- Jayaprakasha, G. K.;** Negi, P. S.; Jena, B. S.; Rao, J. L. (2007). Antioxidant and antimutagenic activities of *Cinnamomum zeylanicum* fruit extracts. *J. Food Compos Anal*, 20: 6-330. **Khan, A.;** Safdar, M.; Ali, K. M.; Khattak, K. N. and Anderson, R. A. (2003). Cinnamon improves glucose and lipids of people with type 2 diabetes. *Diabetes Care* , 26: 8-3215.
- Halliwell, B.** and Gutteridge, J. M. C. (1989). *Free Radical in Biology and Medicine*, 2nd ed., Oxford University Press, Oxford, pp. 78- 93.
- Baghiani, A.;** Djarmouni, M.; Boumerfeg, S.; Trabsa, H.; Charef, N.; Khennouf, S. and Arrar, L. (2012). Xanthine Oxidase Inhibition and Antioxidant Effects of *Peganum harmala* Seed Extracts. *European Journal of Medicinal Plants*, 2(1): 42-56.
- Cubero, N.;** Monferrer, A. and Villalta, J. (2002). *Aditivos alimentarios*, Editorial Madrid: Mundi-Prensa, Ediciones A. Madrid Vicente., pp.1-239.
- Potterat, O.** (1997). Antioxidants and free radical scavengers of natural origin. *Curr. Org. Chem.*, 1: 415-440.
- Cao, G.;** Booth, S. L.; Sadowski, J. A. and Prior, R. L. (1998). Increases in human plasma antioxidant capacity after consumption of controlled diets high in fruit and vegetables. *Am. J. Clin. Nutr.*, 68: 1081-1087.
- Yuji, N.;** Lee, M.; Kato, Y.; Nagai, R. and Yonei, Y. (2010). Review Article Oxidative Stress Markers, Department of Molecular Gastroenterology and Hepatology, Kyoto Prefectural University of Medicine.
- Jeppsson, J. O.;** Arndt, T. and Schellenberg, F. (2007). Toward standardization of carbohydrate-deficient transferrin (CDT) measurements: I. Analyte definition and proposal of a candidate reference method. *Clin. Chem. Lab. Med.*, 45:558–562.
- Sies, H.** (1991). Oxidative stress: Introduction. In *Oxidative Stress: Oxidants and Antioxidants*; Academic Press: London, UK.
- Halliwell, B.** and Gutteridge, J. M. C. (2007). *Free Radicals in Biology and Medicine*. Clarendon Press: Oxford, UK.
- Sivalokanathan, S.;** Ilayaraja, M. and Balasubramanian, M. (2006). Antioxidant activity of Terminalia arjuna bark extracts on Nitrosodiethylamine-induced hepatocellular carcinoma in rats. *Mol. Cell Biochem.*, 281 (1-2): 87-93.
- Gracanin, M.;** Hawkins, C.; Pattison, D. and Michael, J. (2009). Singlet-oxygen-mediated amino acid and protein oxidation: Formation of tryptophan peroxides and decomposition products. *Davies Free Radical Biology and Medicine*, 47 (1): 92-102.
- Beevi, S.;** Rasheed, M. and Geetha, A. (2007). Evidence of oxidative and nitrosative stress in patients with cervical squamous cell carcinoma. *Clinica. Chimica. Acta.*, 375: 119- 123.
- Draper, H.;** Csallany, A. S. And Hadley, M. (2000). Urinary aldehydes as indicator of lipid peroxidation in vivo. *Free Red Biol. Med.*, 29: 1071- 1077.
- Marnett, L. J.** (1999). Lipid peroxidation-DNA damage by malondialdehyde. *Mutat. Res.*, 424(1-2): 83-95.
- Hayes, J. D.** and Strange, R.C. (2000). Glutathione S-transferase polymorphism and their biological consequences. *Pharmacology*, 16:154-166.
- Jackson, A. I.** and Loeb, L. A. (2001). The concentration of endogenous source of DNA damage to the multiple mutation in cancer. *Mutant. Res.*, 477: 7-21.
- Main, A. E. P.;** Anglely, M. T.; O'Doherty, C. E.; Thomas, P. and Micheal, F. (2012). The potential role of antioxidant and detoxification properties of glutathione in autism spectrum disorders: a systemic review and meta-analysis. *Metabolism*, 9: 35.
- Hwang, C.;** Slnsky, A. J. and Lodish, H. F. (1992). Oxidative redox state of glutathione in the endoplasmic reticulum. *Science*, 257: 1496-1502.

- Sies, H.** (1999). Glutathione and its cellular functions. *Free Radic. Biol. Med.*, 27: 916-921.
- Shelly, C. L. U.** (1999). Regulation of hepatic glutathione synthesis: current concepts and controversies. *FASEB. J.*, 13: 1169-1183.
- Mates, J. M.;** Perez-Gomez, C. and Castro, I. N. (1999). Antioxidant enzymes and human disease. *Clinical Chemistry*, 32: 595-603.
- Cui, X. Y.;** Fu, P. F.; Pan, D. N.; Zhao, Y.; Zhao, J.; and Zhao, B. C. (2003). The antioxidant effects of ribonuclease inhibitor. *Free Radic. Res.*, 37: 1079-1085.
- Hachiye, M.** and Akashi, M. (2005). Catalase regulates cell growth in HL60 human promyelocytic cells: Evidence for growth regulation by H₂O₂. *Radiat. Res.*, 163: 271-282.
- Cabiscol, E.;** Piulats, P.; Echave, E.; Herreor, A. and Ros, J. (2000). Oxidative stress promotes specific protein damage in *saccharomyces cerevisiae*. *J. Bio. Chem.*, 275: 27393-27398.
- Rowe, L.;** Degtyareva, R. and Doetsch, P. (2008). DNA damage-induced reactive oxygen species (ROS) stress response in *Saccharomyces cerevisiae*. *Free Radic. Biol. Med.*, 15: 1167- 1177.
- Aiyegoro, O.** and Okoh, A. (2010). Preliminary phytochemical screening and *In vitro* antioxidant activities of the aqueous extracts of *Helichrysum longifolium* DC. *BMC. Complementary and Alternative Medicine*, 10 (10): 1186-1472.
- Gueteens, G.;** Boeck, D.; Highlely, A.; Oosterom, and Bruijin, D. (2002). Oxidative DNA damage: Biological significance and methods of analysis. *Crit. Rev. clin. Lab. Sci.*, 39: 331-457.
- Caimi, G.;** Carollo, C. and LoPresti, R. (2004). Chronic renal failure: Oxidative stress, endothelial dysfunction and wine. *Clin. Nephro.*, 162: 331-335.
- Devasagayam, T. P. A.;** Tilak, J. C.; Boloor, K. K.; Sane, K. S.; Ghaskadbi, S. S. and Lele, R. D. (2004). Free Radicals and Antioxidants in Human Health: Current Status and Future Prospects. *Journal of Association of Physicians of India.*, 3(3): 465- 473.
- Kumar, S.** (2011). Free Radical and Antioxidants: Human Food System. *Pelagia Research Library*, 2 (1): 129-135.
- Kell, D.B.** (2009). Iron behaving badly inappropriate iron chelation as a major contributor to the aetiology of vascular and other progressive inflammatory and degenerative diseases. *BMC. Medical Genomics*, 2: 179.
- Jayaprakasha, G. K.;** Jaganmohan, R. L. and Sakariah, K. K. (2000). Chemical composition of the flower oil of *Cinnamomum zeylanicum* Blume. *Journal agricultural and food chemistry*, 48: 4294-4295.
- Gu, L.;** Kelm, M. A.; Hammerstone, J. F.; Beecher, G.; Holden, J.; Haytowitz, D.; Gebhardt, S. and Prior, R. L. (2004). Concentrations of proanthocyanidins in common foods and estimations of normal consumption. *J. Nutr.*, 134: 613-617.
- Lawrence, B.M.** (2002). Commercial Essential Oils: Truths and Consequences. In Swift K. A. D. (ed.). *Advances in flavours and fragrances: From the sensation to the synthesis*. RSC., Cambridge, p.57-83.
- Rohloff, J.** (2004). Production Practices and Quality Assessment of Food Crops. In Dris R. and Jain S. M. (eds.). *Quality handling and evaluation*. Kluwer academic publishers, 3: 73-128.
- Schmidt, E.** (2006). Composition and antioxidant activities of the essential oil of cinnamon (*Cinnamomum zeylanicum* Blume) leaves from Sri Lanka. *Journal of essential oil bearing plants*, 9 (2): 170 – 182.
- Senanayake, U. M.;** Wills, R. B. H. and Lee, T. H. (1977). Biosynthesis of eugenol and cinnamic aldehyde in *Cinnamomum zeylanicum*. *Phytochemistry*, 16: 2032–2033.
- Meena, V.;** Satya, S. N.; Prakash, S. D. and Avanigadda, S. (2012). A Review on Pharmacological Activities and Clinical effects of Cinnamon Species. Centre of Biotechnology, Department of Chemical Engineering, AUCE. (A), Andhra University, Visakhapatnam, India. *Res. J. P.B. C. S.*, 3(1): 653.
- Mathew, S.** and Abraham, T. E. (2006). Studies on the antioxidant activities of cinnamon (*Cinnamomum verum*) bark extracts, through various *in vitro* models. *Food chemistry*, 94: 520–528.
- Leela, N. K.** (2008). Cinnamon and cassia. In Parthasarathy V. A., Chempakam B. and Zachariah T. J. (eds.). *Chemistry of spices*, Cabi, Wallingford, 124-144.
- Ranjbar, A.;** Ghasmeinezhad, S.; Zamani, H.; Malekirad, A. A.; Baiaty, A.; Mohammadirad, A. and Abdollahi, M. (2006). Antioxidative stress potential of *Cinnamomum zeylanicum* in humans. A comparative cross-sectional clinical study. *Therapy* 3:113-117.
- Khan, A.;** Flanagan, V. P.; Schoene, N. W. and Graves, D. J. (2004). Isolation and characterization of polyphenol type-A polymers from cinnamon with insulin like biological activity. *Journal agricultural and food chemistry*, 52: 65-70.
- AL-Logmani, A. S.** and Zari, T. A. (2009). Effects of *Nigella sativa* L. and *Cinnamomum zeylanicum* Blume oils on some physiological parameters in streptozotocin- induced diabetic rats. *Boletin Latinoamericano y del Caribe de Plants Medicinales y Aromaticas*, 8(2): 86-96.
- Anderson, R. A.;** Broadhurst, C. L.; Polansky, M. M.; Schmidt, W. F.; Khan, A.; Flanagan, V. P.;

- Schoene, N. W. and Graves, D. J. (2004). Isolation and characterization of polyphenol type-A polymers from cinnamon with insulin like biological activity. *Journal agricultural and food chemistry*, 52: 65-70.
- Park, K. L.;** Park, J. Y.; Kim, K. H.; Choi, I. H.; Kim, C. S. and Shin, S. C. (2005). Nematicidal activity of plant essential oils and components from garlic (*Allium sativum*) and cinnamon (*Cinnamomum verum*) oils against the pine wood nematode (*Bursaphelenchus xylophilus*). *Nematology*, 7: 767-774.
- Kim, Y. H.;** Khan, H. U.; Kim, J. H.; Jeon, Y. H.; Lee, E. J. and Chang S. P. (2003). Efficacy of soil amendment with medicinal plant materials for the control of root-knot nematode (*Meloidogyne incognita*) in tomato. *Plant pathology journal*, 19(3): 138-142.
- Lee, J. S.;** Jeon, S. M.; Park, E. M.; Huh, T. L.; Kwon, O. S.; Lee, M. K. and Choi, M. S. (2003). Cinnamate supplementation enhances hepatic lipid metabolism and antioxidant defense systems in high cholesterol-fed rats. *J. Med. Food*, 6: 183-191.
- Nguyen, V. M.;** Nguyen, D. M. C.; Seo, D. J.; Park, R. D. and Jung, W. J. (2009). Antimycotic activities of cinnamon-derived compounds against *Rhizoctonia solani* *in vitro*. *Biological control*, (2): 9009-9220.
- Tzortzakis, N. G.** (2008). Impact of cinnamon oil-enrichment on microbial spoilage of fresh produce. *Innovative food science and emerging technologies*, 10 (1): 97-102.
- Amiri, A.;** Dugas, R.; Pichot, A. L. and Bompeix, G. (2008). *In vitro* and *in vitro* activity of eugenol oil (*Eugenia caryophyllata*) against four important postharvest apple pathogens. *International journal of food microbiology*, 126: 13–19.
- Singh, G.;** Maurya, S.; DeLampasona, M. P. and Catalan, C. A. N. (2007). A comparison of chemical, antioxidant and antimicrobial studies of cinnamon leaf and bark volatile oils, oleoresins and their constituents. *Food and chemical toxicology*, 45: 1650–1661.
- Valero, M.** and Salmeron, M. C. (2003). Antibacterial activity of 11 essential oils against *Bacillus cereus* in tyndallized carrot broth. *International journal of food microbiology*, 85:73-81.
- Tabak, M.;** Armon, R.; Potasman, I. and Neeman, I. (1996). *In vitro* inhibition of *Helicobacter pylori* by extracts of thyme. *Journal of applied bacteriology*, 80: 667-672.
- Yuste, J.** and Fung, D.Y. (2004). Inactivation of *Salmonella typhimurium* and *Escherichia coli* O157:H7 in apple juice by a combination of nisin and cinnamon. *Journal of food protection*, 67:371-317.
- Budavari, S. B.;** O'Neil, M. J.; Smith, A.; Heckelman, P. E. (1989). *The Merck Index*. Merck and Co, Rahway, N.J., 4(2): 37-39.
- USFDA** (2006). Everything added to food in the United States: a food additive.
- Nadiminti, H.;** Ehrlich, A. and Udey, M. C. (2005). Oral erosions as a manifestation of allergic contact sensitivity to cinnamon mints. *Contact Dermatitis* 52: 46.
- Endo, H.** and Rees, T. D. (2006) Clinical features of cinnamon-induced contact stomatitis. *Compend Contin Educ. Dent*, 27:403-407.