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An update on the role of medicinal plants in amelioration of aluminium toxicity

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ABSTRACT

Aluminium (Al) is the third most common element as well as the natural component (8%) of earth-crust and is known as the oldest toxic metal to various organisms including humans. It is commonly found in our environment and reached to animals via drinking water, food, breathing, contact with soil and also by extensive use of deodorants, antacids, cookware, baking powder, processed cheeses. The level of aluminium was increasing continuously in animals including humans and is being deposited in various tissues day by day, which causes toxic effects on kidney, liver, pancreases, testis, bone marrow, digestive system, circulatory system, nervous system etc. Long-term exposure of this toxic metal resulted in the slow progression of physical and neurological degenerative processes, which mimics Alzheimer's disease, Parkinson's disease, muscular dystrophy, multiple sclerosis and cancer. With the increasing prevalence and toxicity of this kind of hazardous metals, medical science is also in progress and various researchers are working in the area to eliminate the adverse effects of metals, but unfortunately we are still far away from the effective treatment of aluminium poisoning. A great deal of this research indicates that plants have the potential to remove toxic/lethal effects of heavy metals. The present review provides updated information about toxicological effects/profile of aluminium in animals including human being and its detoxification by medicinal plants, herbs, phytoextracts, minerals that are abundantly found in nature.

KEY WORDS: ALUMINIUM, ALZHEIMER'S, PARKINSON'S DISEASE, HEAVY METALS, MEDICINAL PLANTS, PHYSIOLOGICAL PARAMETERS.

INTRODUCTION

Heavy Metals like copper, silver, zinc, cadmium, gold, mercury, lead, chromium, iron, nickel, tin, arsenic, selenium, molybdenum, cobalt, manganese, and aluminium are natural components of Earth's crust, which cannot be degraded, therefore plants and animals have been exposed by them since the beginning of life on earth. Heavy metals are among the contaminants in the environment which are mainly librated by various human activities and have potential contribution to produce heavy metal toxicity. The history of heavy metal poison-

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ing has been reviewed many times in the books, research papers and reviews, whom all are stated that residual metals in the environment is a serious threat to animal, human health and aquatic ecosystem, (Ganrot *et al*., 1986; Cha *et al*., 1987; Baker *et al*., 1991; Jarup *et al*., 2003; Krewski *et al*., 2007; Yokel *et al*., 2008; Ezejiofor, *et al*., 2013; Miraj *et al*., 2014; Benouadah *et al*., 2015).

In all the heavy metals aluminium is most commonly used metal, abundantly distributed in our environment and is most toxic to the various animals including humans. It was first produced experimentally in 1825 by the Danish chemist Hans Christian Oersted and later the German, French, and Austrian chemists Friedrich Wohler, Henri Sainte Claire Deville, and Carl Joseph Bayer upgraded isolation efficiencies and purification technologies. Due to its reactivity, aluminium is found only in combination with other elements like oxygen, silicon or fluorine that are commonly found in soil, minerals and rocks. (Lukiw *et al*., 2001; Verstraeten *et al*., 2008; Proudfoot *et al*., 2009; Kawahara *et al*., 2010, Negishi 2011; Hussein *et al*., 2013; Jefferson *et al*., 2014; Exley *et al*., 2015).

Human beings and animals they are naturally exposed to relatively large amounts of aluminium from food, water and air. Other Source of expose to aluminium in salt, deodorants, antacids, cookware, baking powder, processed cheeses, (Guilbert *et al*., 1986; Kosier *et al*., 1990; Yokel *et al*., 2001; Solfrizzi *et al*., 2003; Frank *et al*., 2009; Tchounwou *et al*., 2011; Darbre *et al*., 2013; Najar *et al*., 2014; Laghlimi *et al*., 2015).

Recently, however, aluminum toxicity has increased precipitously. Today, nearly 80% of those tested for metal toxicity reveal excessively high hair aluminium levels. It is linked with a number of disorders in man including Alzheimer's disease, Parkinson's, dementia and osteomalacia, neurological degenerative, muscular dystrophy, multiple sclerosis and cancer, (Pignatti and Mariani, 2002; Kawahara *et al*., 2005; Verstraeten *et al*., 2008; Kumar and Gill, 2009; Turner *et al*., 2014; McGreevy *et al*., 2015).

Aluminium level in drinking water varies due to presence of aluminium coagulants 100 µg/L or greater, (Wettstein *et al*., 1991). Higher doses of aluminium consumed exceeds the body's capacity to excrete it, the excess is then deposited in various tissues, including nerves, brain, muscle, bone, heart, liver, kidneys, spleen, testis, (Harrington *et al*., 1994; Stacchiotti *et al*., 2006).

It is completely useless or toxic for the human and other living organism or essential micronutrients but toxic when overdosed aluminium toxicity has been reported to impair the formation and release of parathyroid hormone. The parathyroid glands concentrate aluminium above levels in surrounding tissues. Treatment of aluminium toxicity in renal failure patients often reactivates hyperparathyroidism, which to a certain extent is helpful for bone remodelling and healing, (Arieff *et al*., 1979, 1980; Leehey *et al*., 1985; Hendrick *et al*., 1992; Arieff, 1993; Kanwar *et al*., 1996; Pande 2006; Flora *et al*., 2008 Rebecca *et al*., 2014; Hegazy *et al*., 2015).

These metals have been found to be lethally hazardous to both animals and human above certain levels. it's have been inevitably exposed to metals due to their ubiquity in nature, contaminated air, water, soil and food, wide use in industry and long-term persistence in the environment. These metals are also potent carcinogenic and mutagenic, (Patterson *et al*., 1965; Bugiani *et al*.,1982; Malluche 2002; Goncharuk 2012; Mohan *et al*., 2014; Clemente *et al*., 2015).

The pollution of the aquatic environment with metals has become a serious health concern because of their toxicity and accumulation by organisms, (Mendil *et al*., 2010; Shah *et al*., 2010). The greatest concern for aluminium toxicity in North America occurs in areas that are affected by wet and dry acid deposition, such as eastern Canada and the north-eastern U.S. Acid mine drainage, logging, and metal levels in water treatment and soil, plant effluents can cause serious problems containing aluminium can be other major sources of Al, (DW *et al*., 1996).

In solution, the metal can combine with several different agents to affect toxicity. aluminium is extremely common throughout the world and is innocuous under circumneutral or alkaline conditions. However, in acidic environments, it can be a major limiting factor to direct (toxic) and indirect (e.g. food chain) effects on wildlife vertebrates like fish, amphibians, reptiles, birds and mammals, (Lewin *et al*., 1920; Sparling & Lowe., 1996; Anane and Creppy, 2001; Damien *et al*., 2004; Newairy *et al*., 2009; Akhigbe *et al*., 2011; Gibbons 2015).

The toxicity of aluminium has been studied extensively in fish, less so in invertebrates, amphibians, and birds, and not at all in reptiles and free-ranging mammals. For aquatic organisms, Al bioavailability and toxicity are intimately related to ambient pH; changes in ambient acidity may affect Al solubility, dissolved Al speciation, and organism sensitivity to Al. At moderate acidity (pH 5.5 to 7.0), fish and vertebrates may be stressed due to Al adsorption onto gill surfaces and subsequent asphyxiation. At pH 4.5 to 5.5, Al can impair ion regulation and augment the toxicity of H^+. aluminium toxic mode of action binding to functional groups both apically located at the gill surface and intracellularly located within lamellar epithelial cells disrupts the barrier properties of the gill epithelium. The gill is the principal target organ and results in accelerated cell necrosis, sloughing and death of the fish, (Clark *et al*., 1985; Freda, 1989; Gensemer *et al*., 1999; Aurthman

et al., 2011; Maharajan & Parurukmani 2012; Slaninova *et al.,* 2014; Abadi *et al.,* 2015).

Aluminium sulphate is used as a mordant in dyeing, in the leather industry, paper industry, fire-proofing, waterproofing textiles, in antiperspirants and pesticides. After the use of aluminium sulphate in these industries it can be reached to underground water through soil partials and also seen in histopathological changes aquatic water bodies, where it exert toxic effect on fishes and amphibians, reptiles, birds and mammals liver, kidney, digestive system, respiratory system, nervous system, (Driscoll *et al*., 1980; Nyholm *et al*., 1981;Clark *et al*.., 1987; Exley *et al*., 1991; Peuranen *et al*., 1993; Howells *et al*., 1994; Gensemer *et al.,* 1999; Freda 2001; Hadi *et al*., 2012; Govind *et al.* 2014; Gilani *et al*., 2015).

In amphibians, embryos and young larvae are typically more sensitive than older larvae. Early-breeding amphibians, which lay eggs in ephemeral ponds and streams subject to spring runoff, are most at risk from Al and acidification; those that breed later in the year in lakes or rivers are least vulnerable. Birds and mammals are most likely exposed through dietary ingestion of soil or Al-contaminated foods. Concentrations > 1000 mg. Kg^{-1} in food may be toxic to young birds and mammals. Clinical sing in these animals are consistent with rickets because Al precipitates with P in the gut. Due to excessive use of agrochemicals and changing environmental conditions; aluminium are being accumulated in soils and are posing a serious threat to animals and human life. The main tissues targeted by them include: the liver, kidneys, bowel, brain and nervous system, spleen and testis. Dietary intake of heavy metals, Aluminium via bioaccumulation and biomagnifications has long term expose detrimental harmful effects not only on human health, but also the entire food chain including the vertebrates and the invertebrates, (Sharma and Agrawal, 2005, Ali *et al*., 2007; Ali *et al*., 2009; Ali *et al*., 2012; Ali & Naaz 2013 and Ali, 2014).

Elevation in the liver enzymes (AST, ALT and ALP) was noticed in aluminium toxicity due to liver dysfunction and disturbance in the biosynthesis of these enzymes which all are indicative of liver damage and thus impaired liver function, (Ajith *et al*., 2007). Transaminases are intracellular enzymes and the most sensitive biomarkers, released into the circulation after damage and necrosis of hepatocytes like AST and ALT can be used in the assessment of liver function. Aluminium caused a significant elevation in the activity of ALP.

Increase in the activity of ALP can attributed to severe damage to cell membranes or increased permeability of plasma membrane. However, they reported that the increase in the activity of ALP in blood might be due to the necrosis of liver, kidney and lung. The aluminium treated group, (Klein *et al.,* 1989; Chinoy *et al.,* 2001; Demerdash *et al.,* 2004; Saied *et al.,* 2014; Kalaiselvi *et al*., 2015).

Aluminium causes toxic effect on biochemical parameters i.e. Plasma glucose, Urea, Creatinine, Cholesterol, Trigycerides, Total Protein showed an increasing trend because prolonged metallic stress in the experimental animals makes adaptation difficult and creates weakness, anemia. These parameters have been effectively used as potential biomarkers of aluminium toxicity to animals and human in the field of environmental biomonitoring. The other toxic effects of these contaminants are also known decrease to the antioxidant enzymatic activity due to presence of ROS and vitamin C that are the indication of lipid peoxidation in certain animal and human beings, (Lagerwerft *et al*., 1974; Flora *et al*., 1986; Zaman *et al*., 1993; Kowalczyk *et al*., 2004; Vinodhini and Narayanan, 2008; Newairy *et al*., 2009; Ashor *et al*., 2015).

Different doses of aluminium to rats significantly decreased level of red blood cell count and white blood cell count, total haemoglobin due to cause of found anemia and results showing that erythrocyte life span and inhibition of haemoglobin synthesis. Microcytic anemia was due to iron deficiency. High Al levels also leads to microcytic anemia as Fe is unable to reverse the Al associated anemia, it was deduced that Al interferes with the metabolism of Fe, (Kaiser *et al*., 1984).

High concentration of Al decreases the average osmotic fragility of red cells in animals with renal failure, (Drueke *et al*., 1986b). In High Al levels in plasma and red cells also leads to severe anemia but it can be reversed by terminating the Al concentration, (Cannata *et al*., 1983; Basha *et al*., 2012; Ibrahim *et al*., 2012, Mahdy *et al*., 2012, Hore *et al*., 2014; Pfadenhauer *et al*., 2014 Kisnieriene *et al*., 2015).

Increased lipid peroxidation was reported in the rats consuming diets with AlCl3. Hematological parameters blood used for the determination of erythrocyte count, hemoglobin content and Hct, mean corpuscular volume (MCV), Mean corpuscular hemoglobin (MCH) and mean corpuscular hemoglobin concentration (MCHC) values were studied according to Feldman *et al*., (2000). Total and differential leukocytic count Total leukocyte count was performed by using improved neubauer hemocytometer. Chronic exposure and inhalation of aluminium flake powder leads to dilation and hypertrophy of the right side of the heart in male factory workers who eventually died (McLaughlin *et al*., 1962; Mitchell *et al*., 1961; Ghorbel *et al*., 2015).

The cardiac effects may have been secondary to pulmonary fibrosis and poor pulmonary function, (Singh RB, *et al*., (1989). Patients of peripheral circulatory failure induced due to aluminium phosphide poisoning were reported. Chief symptoms were vomiting and epigastric

pain. Sensorium was normal in most of the patients. This might be because of direct toxic action of phosphine on myocardium and later when phosphine gets excreted either through lungs or kidney leads to improvement in LV systolic function, (Gupta *et al*., 1995; Pandey *et al*., 2013; Elabbassi *et al*., 2014; Solgi *et al*., 2015).

Aluminium and Enzyme activities due to its high reactivity, Al3+ is able to interfere with several biological functions, including enzymatic activities in key metabolic pathways, (Akeson *et al*., 1989). Salts of Al may bind to DNA and RNA, inhibit such enzymes as hexokinase, acid and alkaline phosphatases, phosphodiesterase and phosphooxydase Al intoxication through the inhibition of kinase enzyme has been reported. Hexokinase is a Mg-ATP dependent enzyme that catalyzes the first step involved in glucose utilization, (Ward *et al*., 2012).

Al-ATP is a competitive inhibitor of hexokinase against the natural sustrate Mg-ATP. The inhibition of hexokinase activity in testis caused by aluminium might be related to minimization of glucose uptake and utilization by germ cells, (Pandey *et al*., 2013; Chen *et al*., 2014; Mohammad *et al*., 2015).

Aluminium toxicity may result in a drastic reduction or a complete failure of spermatogenesis and steroidogenesis by following ways. First Aluminium may block voltage sensitive calcium channels in hypothalamus cells and decreased the GnRH secretion which further responsible for the decrease in FSH and LH in pituitary as GnRH synthesis and secretion also depends on Ca^{2+}, (Platt *et al*., 1994; Shahraki *et al*., 2004). Decreased level of FSH and LH disrupts the process of spermatogenesis and secretion of testosterone by Leydig cells.

Secondly, FSH and LH exert their actions on steroidogenesis by mainly regulating intracellular Ca^{2+} concentration through Voltage-Dependent Ca^{2+} Channels (VDCCs) in Sertoli cells and Leydig cells, (Lee *et al*., 2011; Mehranjani *et al*., 2012; Zanatta *et al*., 2013 Zhao *et al*., 2014; Prabsattroo *et al*., 2015).

Now-a-day's aluminium toxicity is a widespread problem facing all over the world in all forms of living organism, vertebrates like fish, amphibians, reptiles, birds, mammals, animals and including humans, degradation of the environment and health. Over millions of reference articles on aluminium toxicity exist various data bases as of 1900 to 2015, all recognizing the aluminium toxicity.

IMPORTANT ROLE OF PLANT EXTRACTS IN DETOXIFICATION OR AMELIORATING THE EFFECTS OF ALUMINIUM TOXICITY

Nevertheless the fact that the phytochemicals contain plenty of flavonoids and polyphenols like antioxidants, they may also help ameliorate the heavy metals mediated toxicity in human and other animals.

Coriandrum sativum belongs to the family *Umbelliferae*, known for its carminative and cooling properties. Its coriander extracts have phenolic compounds and flavonoides, these compounds contribute to the antioxidative activity, (Wangensteen *et al*., 2004). Phenolic substances such as flavonoids, cumarins, cinnamic acid and caffeicacids are believed to have antioxidant properties, which plays an important role against degeneration, (Wiseman *et al*., 2000).

Coriander seed's aqueous extract showed protection and an improvement in therapeutic action on pyramidal cell of cerebral cortex against neurodegenerative disorders and Alzheimer' disease induced by aluminium chloride treatment, (Enas *et al*., 2011). Antioxidant activity of coriander seed aqueous extract, was due to antioxidant enzymes which promoted oxygen to the brain, which could prevent oxidative damage caused by interaction between aluminium cation and unstable oxygen from abnormal mitochondria and protect pyramidal cells in cerebral cortex against damage induced by aluminium chloride overload, (Walton *et al*., 2007; Lu *et al*., 2013; Aslani *et al*., 2014; Benso *et al*., 2015).

Wattakaka volubilis which belongs to *Asclepiadaceae* family it is a tall wood climber which is densely densely lenticulate branches, quite beneficial for amelioration of metal toxicity, (Yogita *et al*., 2013). occurring throughout the warmer regions of India and Nicobar Islands. *W.volubilis (Linn)* is used as a phytomedicine compound for liver diseases, (Rani *et al*., 2014). It has been also demonstrated that *W. volubilis* methanolic extract of powder form was very effective against the aluminium toxicity in rats, (Bais *et al*., 2015).

Clinical observation this study showed that enzymatic analysis and histological, biochemical, organ weight, body weight examination were carried out. The extract of Wattakaka volubilis (Linn) was found to possess hepatoprotective activity in a dose dependent manner and the effect was comparable with silymarin, a standard drug.

The extract significantly reduce the toxicity of Aluminium sulphate caused in liver due to the presence of phytoconstituents such as alkaloids, sterols, tannins, triterpenoids and flavonoids which are also known hepatoprotectant. *Wattakaka volubilis* leaf extract showed the highest hepatoprotective activity in against Aluminium Sulphate induced hepatotoxicity. The possible action may be due to its hepatoprotective constituents and antioxidant compounds present in the extract, (Rani *et al*., (2014).

Bacopa monniera (B. monniera), A small creeping herb locally known as 'Brahmi' in India, belongs to the family of *Scrophulariaceae*, and is mostly found throughout India, *B. monniera* have been recommended by ancient Ayurvedic for the treatment of neurological

disorders associated with free radical induced damages, (Stough *et al*., 2001). it has been demonstrated that in the Journal of Alzheimer's Disease examines the evidence for the so-called aluminum hypothesis and find binds to DNA, gene expression and enzymes present in energy metabolism disrupts the proteins from cells, structural like Skeleton fatal effect on nerve fibers in the human brain result that nerve cells damaged and increased risk of Alzheimer's disease, (Russo & Borrelli *et al*., 2005; Murthy *et al*., 2013; Kongkeawa *et al*., 2014; Rajan *et al*., 2015).

Jasonia candicans & *Jasonia montana* which belong to *Asteraceae* are well known detoxification agents. Their extracts have displayed the potent effects against Al toxicity due to their anti-cholinesterase activity, anti-inflammatory action, antioxidant capacity in addition to anti-amyloidogenic potential and neurotrophic effect, (Soliman *et al*., 2009).

Polyphenols are abundant in *Jasonia montana* and are used as antioxidants. Ethanolic extract of *Jasonia candicans* and *Jasonia montana* were used in regression of the neurodegeneration characteristics of Alzheimer's disease, (Hussein *et al*., 2011). High content of terpenes, sesquiterpenes and flavonoids in the ethanolic extract of the selected plants was responsible for the anticholinesterase activity, anti-inflammatory action, antioxidant capacity and neurotrophic effect of these extracts, (Kim *et al*., 2012). Elevation in brain (Cox-2) gene expression Acetylcholinesterase (AchE) activity, Tumour Necrosis Factor (TNF-α), Transforming Growth Factor β (TGF-β) and 8 hydroxydeoxyguanosine (8-OHdG). Growth Factor (IGF-1) was reported in experimental animal having Al toxicity, (Ahmed *et al*., 2013, 2014; Razavi *et al*., 2015).

Amelioration by *Jasonia montana* against lipid peroxidation in liver and kidney of iron-overloaded rats has been reported byHussein *et al*., (2010). The decreased activity of brain marker Acetylcholinestrase (AchE) is direct indication of oxidative damage resulting in free radical generation. Treatment with therapeutic agents (*Triphala* and *garlic*) caused reversal of the biochemical parameters thereby recouping the variables towards normal levels, (Sinha *et al*., 2011). Triphala is a traditional ayurvedic herbal formulation consisting equal parts of three medicinal plant fruits namely *Terminalia chebula, Terminalia bellerica, Emblica officinalis. Triphala* has been used *E.officinalis has* been reported as a rich source of vitamin C, which plays an important role in scavenging free radicals properties of *Triphala*, (Jagetia *et al*., 2002; Selvakumar *et al*., 2006; Mukherjee *et al*., 2006 Baliga *et al*., 2012; Bafna *et al*., 2013; Reddy *et al*., 2014; Gupta *et al*., 2015).

Garlic (*Allium sativum L.)* is one of the oldest Indian medicinal plant *Garlic* its has been valued for centuries for its medicinal properties. *Garlic* (*Allium sativum L.*) is one of the earliest known medicinal plant (Metwally *et al*., 2009) possesses many healthful properties that are related to its bioactive compounds, vitamins and minerals and trace elements (Selenium and Germanium). a wide range of medicinal properties,immunomodulatory hepatoprotective, antimutagenic and anticarcinogenic effects.

Reviews have shown that garlic can protect us from various pollutants and heavy metals like arsenic and lead Depending on personal requirements or preferences, *garlic* supplements are available in a wide range of potencies, (Gupta *et al*., 2015).

The plant extract of *Triphala* and *Garlic per se* and in combination were used to treat aluminium poised mice. concurrent use of *garlic* and *Triphala* dry powder reduced aluminum concentration indicating the potential activity in combination against alunimium toxicity in albino mice, (Cha *et al*., 1987; Sinha *et al*., 2011; Eteng *et al*., 2012; Ranjbar *et al*., 2013; Ting *et al*., 2014; Niino *et al*., 2015).

Turmeric (*Curcuma longa*) which belongs to Zingiberaceae family is a rhizomatous herbaceous perennial plant. The active constituents are turmerone oil and water soluble curcuminoids, including *curcumin*, (Kim *et al*., 2001; Sandur *et al.,* 2007). *Curcumin* is the principal curcuminoid and is responsible for the yellow color of the *turmeric* root, (Shishodia *et al.,* 2005; Yang *et al.,* 2005). *Turmeric* is anti-inflammatory, antiseptic, and antibacterial and has long been used in the Indian system of medicine to treat a variety of conditions and also helps in detoxification of liver, balance cholesterol levels, fight allergies, stimulate digestion, and boost immunity, (Chainani *et al.,* 2003). Epidemiologic studies show a 4.4-fold lower incidence of AD in Southeast Asian countries where turmeric is commonly used as a dietary spice. *Turmeric* undergoes metabolism in the liver particularly via glucuronidation, (Sikha *et al.,* 2015).

The metabolites of *Turmeric* such as glucoronides appear to lack any pharmacological activity. The systemic elimination of Turmeric is another contributing factor for low bioavailability. Protective effects demonstrated (Ghoneim *et al*., 2002) by *curcumin* against ischaemia/reperfusion insult in rat forebrain. The initial review reports demonstrated by Wahlstorm and Blennow result showed that after giving the oral administration of 1g/kg *curcumin* to rats, more than 75% of *curcumin* was excreted in feces and negligible amount was detected in urine of animal model, (Wahlstrom and Blennow, 1978). *Turmeric* Showed that Neuroprotective properties of the natural phenolic antioxidants *curcumin* and *naringenin* but not quercetin and fisetin in a 6-OHDA model of PD may be related to their antioxidant capabilities and their capability to penetrate into the brain (Parkinson's dis-

ease), (Olanow *et al*., 1999; Zbarsky *et al*., 2005; Lang *et al*., 2006; Kumar *et al*., 2014; Lin *et al*., 2015).

Ashwagandha (*Withania somnifera*) which belongs to *Solanaceae* has been used extensively in Ayurveda as a nervine tonic, aphrodisiac, and 'adaptogen' and helps the body adapt to stress, (Mishra LC, *et al*., 2000). It has rejuvenative (rasayana), antioxidant activity, free radical scavenging activity. Alkaloid extract of *Ashwagandha* root exhibited a calming effect on the central nervous system (CNS). *Ashwagandha* contains varities of steroidal compounds, amino acids (including tryptophan), and high amounts of iron, (Russo *et al*., 2001; Kelley *et al*., 2008; Wollen *et al*., 2010). One of the components, *Withanamides* has been shown to scavenge free radicals generated during the initiation and progression of AD. Neuronal cell death triggered by amyloid plaques was also blocked by with anamides, (Dhuley *et al*., 1998; Parihar *et al*., 2003).

Ashwagandha has been reported to increase memory and learning, (Tohda *et al*., 2005). Aqueous extracts of this herb have been found to increase cholinergic activity, including increases in the acetylcholine content and cholineacetyl transferase activity in rats, (Schliebs *et al*., 1997; Tohda *et al*., 2000; Kuboyama *et al*., 2002). Treatment with the methanol extract of *Ashwagandha* caused neurite outgrowth in a dose- and time-dependent manner in human neuroblastoma cells and induced significant regeneration of both axons and dendrites, (Singh *et al*., 1982; Kuboyama *et al*., 2005 Singh *et al*., 2011; *Haque et al*., 2013; Prabu *et al*., 2014; Chitra *et al*., 2015).

Ginger which belongs to Zingiberaceae family (*Zingiber officinale Roscoe)* is one of the most commonly used herbal tea *ginger* is rich in a large number of bioactive substances, including gingerols and shogaols, phenolic ketone derivatives. *Ginger* is used medicinally for its hepatoprotective and antioxidant, antidiabetic and hypolipidemic and anti-obesity effects. the protective effect of ginger due to lowering of the enhanced activity of AST and ALT in treated mice, (Moselhy *et al*.,2012; Mahmoud *et al*.,2013; Alafiatayo *et al*.,2014; Kalaiselvi *et al*.,2015).

Allium cepa has been associated with reduced lipid peroxidation index (malondialdehyde (MDA) and increased superoxide dismutase (SOD). Al-induced changes on reproduction profile such as hormones, sperm quality and lipid peroxidation was reversed by *A.cepa*, (Ige and Akhigbe, 2012). Phytochemical screening of *A. cepa* showed that it contains abundant flavonoids, and weak saponins, tannins, glycosides, sterols, and triterpenoids, (Achary *et al*., 2008). *Allium cepa* flavonoids reduced testosterone level; they improved the sperm quality by preventing lipid peroxidation. *Allium cepa* inhibited testosterone synthesis at the testicular level probably by inhibiting cholesterol conversion. Effects on the female reproductive systems can include such things as menstrual problems, altered sexual behavior, infertility, altered puberty onset, altered length of pregnancy, lactation problems, altered menopause onset and pregnancy outcome, (Qin *et al*., 2013: Vahdani and Khaki 2014; Rajeshwari *et al*., 2015).

Oral Al exposure during pregnancy can cause a syndrome including growth retardation, delayed ossification, and malformation at Al doses that also reduced maternal weight gain. At the perinatal age, aluminum is highly neurotoxic and inhibits prenatal and postnatal brain development. In addition, maternal dietary exposure to excess aluminum during gestation and lactation which did not produce maternal toxicity would be capable of causing permanent neurobehavioral deficits in weanling mice and rats, (Golub *et al*., 1986; Hussein *et al*., 2013; Muhammed *et al*., 2014; Berihu *et al*., 2015).

Rosmarinus officinalis commonly known as *Rosemary* which belongs to *lamiaceae*. Their extract contains a high amount of total phenolics, is able to donate electrons, and therefore should be able to donate electrons to reactive radicals, converting them into more stable and unreactive species, (Dorman *et al*., 2003). The protective action by rosemary extract in brain tissue through decreases in NOS activity, and subsequently, NO production. Therefore, they suggest that rosemary extract has an antioxidant effect as a free radical scavenger in this organ rosemary contains essential oils, terpenoids, flavonoids and alkaloids. Some of its constituents such as rosmarinic acid (RA) have been reported as powerful antioxidant protecting against free radicals damage and to reduce hepatotoxicity other researchers revealed the potential of RA for prevention of neurodegenerative diseases such as stroke, AD and PD, usually caused by an excess of free radicals. Unlike many drugs and natural antioxidants, RA was found to be able to cross blood brain so called pathologically activated-therapy, (Lipton, 2007; Weiss *et al*., 2009; Mahdy *et al*., 2012; Fathia *et al*., 2013; Jennifer *et al*., 2014; Loto *et al*., 2015).

CONCULSION AND FUTURE PERSPECTIVES

Previous reviews and this recent update on aluminium toxicity demonstrate that use of aluminium is on a significant rise and it is not safe but the accumulation of aluminium in the body has yet to become the subject of serious investigation and consideration in medicine. Considering this state of affairs, the present review has tried to provide compiled reports and summarised statements to evaluate the protective effects of medicinal plant extracts like *Coriandrum sativum , Wattakaka volubilis*, *Bacopa monniera, Jasonia candicans* and *Jasonia Montana, Terminalia chebula, Terminalia bellerica,*

Emblica officinalis, Curcuma longa, Withania somnifera Zingiber officinale, Roscoe, Allium cepa and Rosmarinus officinalis extracts against the toxic effects of the highly hubiquitous metal aluminium which is increasing in animals and human beings leading to serious health problems. To combat with this malady, medicinal plants can be potent drugs which, have the potential of antitoxic, antioxidant, detoxification with amelioration effects against heavy metals.

Medicinal plant extracts have a considerable role to play in the amelioration of Al toxicity in animals and human caused by higher Aluminium accumulation in body organ Use of Al was increasing day by day and it become a recent hazard, by it excessive use. Even though, till quite recently, at the molecular level, our understanding of how aluminium exert these toxic effects is still rudimentary. There is a general consensus that proteins are key targets of aluminium. Metals interfere with the biological activity of native, folded proteins through diverse modes of interaction; they may bind to free thiols or other functional groups in proteins displace essential metal ions in metalloproteins; or catalyze oxidation of amino acid side chains. In this situation, the need of the hour is to develop safe and non toxic natural detoxification agents which can be used for amelioration of ever increasing metal exposure and toxicity These earlier and recent studies reviewed here, make us strongly believe that natural supplementation perspective, though observed in animal model, will have sustainable curative value among the already afflicted populations, neutralizing impact on freshly emerging metal toxicity scenario and possible proactive protection to those potentially susceptible to aluminium exposure. Indian herbs have high potential in overcoming Al toxicity in animal models. It hold extreme promise for future treatment of Al toxicity in animals and human.

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REFERENCES

Achary V.M., Jena S, Panda K.K., Panda B.B. (2008). Aluminium induced oxidative stress and DNA damage in root cells of *Allium cepa* L. Ecotoxicol Environ Saf. 70(2):300-10.

Ahmed H. H., Booles H.F., Khalil W.K.B., Ashmaoui H.M.El., Othman S.M. (2013).Possible Therapeutic Role of *Jasonia candicans* and *Jasonia montana* Extracts in The Regression of Alzheimer's Disease in Experimental Model. Ame. J. of Bioche. & Biotech. Vol.9, Issue 2.pp. 144-161.

Ahmed H.H., Salem A.M., Sabry G.M., Husein A.A., Kotob S.E. (2014). Medicinal plants offer multimechanistic approaches in management of Alzheimer's disease. J. of Che. and Pharm. Res. 6(11):879-892.

Ajith T.A., Hema U, Aswathy M.S. (2007). *Zingiber officinale* Roscoe prevents acetaminophen-induced acute hepatotoxicity by enhancing hepatic antioxidant Status. Food and Chemical Toxicology. 45:2267-2272.

Akeson M.A., Munns D.N., Burau R.G. (1989). Adsorption of Al^{+3} to phosphatidylcholine vesicles. Biochimica et Biophysica Acta 986. 33-40.

Akhigbe R.E., Olatunji L.A., Soladoye A.O., Oyeyipo IP. (2011). Effect of angiotensin1-converting enzyme inhibitor, captopril, on body weight, and food and water consumption in oral contraceptive-treated rats. Am J Biochem Mol Biol 1: 95-100.

Alafıatayo A.A., Syahid A., Mahmood M. (2014). Total Anti-Oxidant Capacity, Flavonoid, Acid and Polyphenol Content in Ten Selected Species of Zingiberaceae Rhizomes. Afr Tradit Complement Altern Med. 11(3): 7-13.

Alfrey A.C, Hegg A., Craswell P. (1980). Metabolism and toxicity of aluminum in renal failure. Am J Clin Nutr 33(7):1509-1516.

Alfrey A.C. (1993). Aluminum toxicity in patients with chronic renal failure. Ther Drug Monit. 15(6):593597.

Alfrey A.C., LeGendre G.R., Kaehny WD. (1976).The dialysis encephalopathy syndrome. Possible aluminum intoxication. N Engl J Med. 294(4):184-8.

Ali A.S, Khan I., Ali S.A. (2007). Toxicological monitoring using earthworms. Toxicology and Science of Poisons, Avishkar Publication jaipur 167-186.

Ali A.S. (2014). Responses of the earthworm *Eisinia foetida* coelomocytes to aluminium chloride using the neutral red retention assay Biosc.Biotech.Res.Comm. Vol. 7 (1) 42-45.

Ali A.S., Khan I., Ali S.A. (2009). Bioremediations of contaminated soil using earthworms. In Handbook of Agriculture Biotechnology Ed DK Maheshwari. Ali A..S, Naaz I (2013). Earthworm Biomarkers: The new tools of environment impact assessment. Biosc Biotech Res Comm 6: 163-169.

Ali S.A., Mitra J., Ali A.S. (2012). Biochemical markers for toxicological assessment. A review In: The ugly face of Environment, Delhi Publication New Delhi, 135-145.

Arieff A.I., Cooper J.D., Armstrong D. (1979). Dementia, renal failure, and brain aluminum. Ann Intern Med 90(5):741-747.

Ashor A.W., Siervo M., Lara J., Oqqioni C., Afshar S., Mathers J.C. (2015).Effect of vitamin C and vitamin E supplementation on endothelial function: a systematic review and meta-analysis of randomised controlled trials. Br J Nutr.113(8): 1182-94.

Aslani A., Ghannadi A., Khalafı Z. (2014). Design, formulation and evaluation of *green tea* chewing gum. Adv Biomed Res.3: 142.

Bafna P.A and Balaraman R. (2013). Protective effect of DHC-1, a Polyherbal formulation, against CCL4 induced Liver damage. Hygeia. Journal for drugs and medicines 5:10-18.

Bais S., Gill N. S., Kumar N., (2015). Neuroprotective Effect of Juniperus communis on Chlorpromazine Induced Parkin-

son Disease in Animal Model. Chinese Journal of Biology Vol. 2015, Article ID 542542, 7 p.

Baker A.J.M., Brooks R.R. (1989).Terrestrial higher plants which hyperaccumulate metal elements- A review of their distribution, ecology and phytochemistry. Biorecovery 1: 81-126.

Baker A.J.M., Reeves R.D., McGrath S.P. (1991). In situ decontamination of heavy metal polluted soils using crops of metal accumulating plants—a feasibility study. p. 539–544. In R.E. Hinchee and R.F. Olfenbuttel (ed.) In Situ Bioreclamation. Butterworth Heinemann Publishers, Stoneham, MA.

Baliga M.S., Meera S., Mathai B., Rai M.P., Pawar V., Palatty P.L. (2012). Scientific validation of the ethnomedicinal properties of the Ayurvedic drug Triphala: a review. Chin J Integr Med.18(12):946-54.

Benso B., Rosalen P.L., Alencar S.M., Murata R.M. (2015). Malva sylvestris Inhibits Inflammatory Response in Oral Human Cells. An In Vitro Infection Model. PLoS One.10 (10): e0140331.

Berihu B.A., Afwerk M., Debeb Y. G., Gebreslassie A. (2015). Review on Histological and Functional Effect of Aluminium Chloride on Cerebral Cortex of the Brain. Int.J. of Pharm Sci. and Research (IJPSR) Vol. 6 No.8.pp 1-12.

Bugiani O., Ghetti B. (1982). Progressing encephalomyelopathy with muscular atrophy, induced by aluminum powder. Neurobiol Aging. 3(3):209-22.

Cannata J.B., Fernandez-Soto, I., Fernandez-Menezes, M.J., Fernandez-Martin, J.L., McGregor, S.J., Brock, J.H., Halls, D., (1991). Role of iron metabolism in absorption and cellular uptake of aluminium. Kidney Int. 39, 799–803.

Cha C.W. (1987). A study on the effect of garlic to the heavy metal poisoning of rat. J. Korean Med Sci. 2(4): 213-24.

Chainani N. (2003). Safety and anti-inflammatory activity of *Curcumin* component of *turmeric (Curcuma longa)*. J Alter Compl Med.9:161-8.

Chen T., Ning D., Sun H., Li R., Shang M., Li X., Wang X., Chen W., Liang C., Li W., Mao Q., Li Y., Deng C., Wang L., Wu Z., Huang Y., Xu J., Yu X. (2014). Sequence Analysis and Molecular Characterization of *Clonorchis sinensis* Hexokinase, an Unusual Trimeric 50-kDa Glucose-6-Phosphate-Sensitive Allosteric Enzyme. PLoS One. 9(9):107940.

Chitra B., Ramaswa R. (2015). An overview on the role of siddha practices in the prevention and management of age related neurodegenerative disorders with special reference to senile dementia. Indo. Amer. Jour. of Pharm. Res.5 (4):1510-1521.

Clemente R., Pardo T., Madejon P., Madejon M., Bernal M.P. (2015). Food byproducts as amendments in trace elements contaminated soils. Food Research Interntional.Vol.73, p; 176-189.

Cunnigham S.D., Anderson T.A., Schwab P., Hsu F.C. (1996). Phytoremediation of soils contaminated with organic pollutants. Adv Agronomy 56: 55-114.

Das A., Dikshit M., Nath C. (2001). Profile of acetylcholine esterase in brain areas of male and female rats of adult and old age. Life Sci. 68:1545–1555.

Das A., Shanker G., Nath C., Pal R., Singh S., Singh H.K. (2002). A comparative study in rodents of standardized extracts of *Bacopa monniera* and *Ginkgo biloba* anti-cholinesterase and cognitive enhancing activities. Pharmacol Biochem Behav.73:893e900.

Dhuley J.N. (1998). Effect of *Ashwagandha* on lipid peroxidation in stress-induced animals. J Ethnopharmacol.60:173–178.

Dorman H.J.D., Peltoketo A., Hiltunen R., and Tikkanen M.J. (2003).Characterization of the antioxidant properties of deodourised aqueous extracts from selected *Lamiaceae herbs*. Food Chem.83: 255-262.

Drueke T.B., Lacour M., Touam B., Jucquel J.P., Plachot J.J., Witmer G., Galle P., (1986). Effect of aluminum on hematopoesis. Kidney 29, 45–48.

Duruibe J.O., Ogwuegbu M. O., Egwurugwu J.N. (2007). J. N. Heavy metal pollution and human biotoxic effects. International Journal of Physical Sciences Vol. 2 (5), pp.112-118.

Eidelberg D., Sotrel A., Joachim C., Selkoe D., Forman A., Pendlebury W.W., Perl DP. (1987). Adult onset Hallervorden-Spatz disease with neurofibrillary pathology. Brain.110:993–1013.

Elabbassi W., Chowdhury M.A., Fachtartz A.N. (2014). Severe reversible myocardial injury associated with aluminium phosphide toxicity: A case report and review of literature. Journal of the Saudi Heart Association Volume 26, Issue 4, pp216–221.

Enas A., Khalil. (2011). Evaluation of the Possible Protective and Therapeutic Influence of *Coriander* (*Coriandum sativum L.*) Seed Aqueous Extract on Hippocampal Pyramidal Cells Against Alzheimer's Disease Induced by Aluminum Chloride in Adult Male Albino Rats. Researcher.3 (1):22-29. (ISSN: 1553-9865).

Eteng M.U., Onwuka F.C., Akpanyung E.O., Osuchukwu N.C., Bassey S.C. (2012). Reversal of cadmium induced toxicity following dietary supplementation with garlic, ginger and cabbage in male Wistar rats. J Nat Prod Plant Resour 2: 169-174

EZejiofor, Udebuani, Ezeji, Ayalogbu, Azuwuike, Adjero, Ihejirika, Ujowundu, Nwaogu, Ngwogu. (2013). Environmental metals pollutants load of a densely populated and heavily industrialized commercial city of Aba, Nikeria. J. Toxicol. Environ. Health Sci. Vol.5 (1) pp.1-11.

Farina E., Fioravanti R., Chiavari L., Imbornone E., Alberoni M., Pomati S., Pinardi G., Pignatti R., Mariani C. (2002). Comparing two programs of cognitive training in Alzheimer's disease: a pilot study. Acta Neurologica Scandinavica. 105:365–371.

Fathia A. M., Mohga S.A., Khaled G., Wahhab A., Mahitab I. (2013). Effect of some nutraceutical agents on aluminium-induced functional neurotoxicity in senile rats: I. Effect of rosemary aqueous extract and docosahexaenoic acid. Journal of Applied Sciences Research, 9 (3): 2322-2334.

Flora SJS., Tandon S.K .(2008). Preventive and therapeutic effects of thiamine. ascorbic acid and their combination in aluminium intoxication. Acta Pharmacol Toxicol 58: 374-8.

Frank, W. B. (2009). Aluminum Ullmann's Encyclopedia of Industrial Chemistry. Wiley-VCH. doi:10.1002/14356007.a01_459.pub2.

Ganrot P.o. (1986). Metabolism and possible health effect of aluminium. Environ. Health, Perspect, 65: 363-441.

Garruto R.M., Shankar S.K., Yanagihara R., Salazar A.M., Amyx H.L., Gajdusek D.C. (1989). Low-calcium, high-aluminum diet-induced motor neuron pathology in cynomolgus monkeys. Acta Neuropathol. (Berl).78:210–9.

Ghoneim AI., Naim A.B., Khalifa A.E., Denshary E.S. (2002). Protective effects of *Curcumin* against ischaemia/reperfusion insult in rat forebrain. Pharmacol Res.46:273–279.

Ghorbel I., Maktouf S., Kallel C., Chaabouni S.E., Boudawara T., Zeghal N. (2015). Disruption of erythrocyte antioxidant defense system, haematological parameters, induction of pro-inflammatory cytokines and DNA damage in liver of co-exposed rats to aluminium and acrylamide. Chemico-Biological Interactions Vol.236pp.31-40.

Gibbons D., Morrissey C., Mineau P. (2015). A review of the direct and indirect effects of neonicotinoids and fipronil on vertebrate wildlife. Envi.l Sci. and Poll. Res. Vol.22, Issue 1, pp.; 103-118.

Golub M.S., Domingo J.L. (1996). What we know and what we need to know about developmental aluminum toxicity. J Toxicol Environ Health.48: 585-597.

Gorinstein S., Leontowicz H., Leontowicz M., Drzewiecki J., Najman K., Katrich E. Barasch D., Yamamoto k., Trakhtenberg S. (2006). Raw and boiled garlic enhances plasma antioxidant activity and improves plasma lipid metabolism in cholesterol-fed rats. Life Sciences.78:655 – 663.

Govind P., Madhuri S., Shrivastav A.B. (2014). Fish Cancer by Environmental Pollutants, 1st Edn., Narendra Publishing House, Delhi, India.

Guilbert, J. F., Park, C. F. (1986). The Geology of Ore Deposits. W. H. Freeman. pp. 774–795. ISBN 0-7167-1456-6.

Guo C.H., Lin C.Y., Yeh M.S., Hsu G.S.W. (2005). Aluminum-induced suppression of testosterone through nitric oxide production in male mice, Environment Toxicology Pharmacology.19:33- 40.

Gupta M.S., Malik A., Sharma V.K. (1995). Cardiovascular manifestations in aluminium phosphide poisoning with special reference to echocardiographic changes. J Assoc Physicians India 43 (11): 773-4, 779-80.

Gupta R., Gupta A., Singh R.L. (2015). Hepatoprotective Activities of Triphala and Its Constituents. Int. J of Pharma Research & Review, 4(1):34-55.

Gupta V.K., Singh S., Agrawal A., Siddiqi N.J., Sharma B. (2015). Phytochemicals Mediated Remediation of Neurotoxicity Induced by Heavy Metals. Biochemistry Research International Volume 2015, Article ID 534769, 9 pages.

Hadi A.A. and Alwan S.F. (2012). Histopathological changes in gills, liver and kidney of fresh water fish, *Tilpia zillii*, expsed to aluminium. Int. J. of Pharm. & Life Sci. (IJPLS), Vol.3,Issue 11;2071-20812074

Hala A.H., Khattab, Inas, Z.A. Abdallah and Gehan, Kamel M. (2010).Grape seed extract alleviate reproductive toxicity caused by aluminium chloride in male rats. Journal of American Science.6(12):1200-1209.

Hanna W.J., Grant C.L. (1962). Spectrochemical analysis of the foliage of certain trees and ornamentals for 23 elements. Bull Torrey Bot Club 89: 293-302.

Haque M.R., Ansari S.H., Rashikh A. (2013). *Coffea arabica* Seed Extract Stimulate the Cellular Immune Function and Cyclophosphamide-induced Immunosuppression in Mice.Iran J Pharm Res. 2013 Winter.12 (1): 101–108.

Harrington C., Wischilk C., McArthur F., Taylor G., Edwardson J. and Candy J.M. (1994): Alzheimer's-disease-like changes in tau protein processing: association with aluminium accumulation in brains of renal dialysis patients. Lancet 343: 993-997.

Hashem FA. (2009). Camel's Milk Protects against Aluminum Chloride-Induced Toxicity in the Liver and Kidney of White Albino Rats. American Journal of Biochemistry and Biotechnology 5 (3): 98-108, ISSN 1553-3468.

Hendrick M.J., Goldschmidt M.H., Shofer F.S., Wang Y.Y., Somlyo A.P. (1992). Postvaccinal [after vaccination] sarcomas [cancer tumors] in the cat: epidemiology and electron probe microanalytical identification of aluminum. 52(19):5391-4.

Hore P., Ahmed M., Nagin D., Clark N. (2014). Intervention model for contaminated consumer products: a multifaceted tool for protecting public health. Am J Public Health 104: 1377–83.

Hussein H., Mahmoud O.M. (2013). Effects of maternal administration of aluminium chloride on the development of the skeletal system of albino rat foetuses protective role of *Saffron*. Eur. J. Anat. 17 (2): 63-71.

Hussein H.H., Mahmoud M. O. (2013). Effects of maternal administration of aluminium chloride on the development of the skeletal system of albino rat foetuses protective role of saffron. Eur. J. Anat. 17 (2): 63-71.

Hussein M.A. (2011). Potential mechanism for the antioxidant effects of *Jasonia montana*. J. of Pharm.Res. & Reviews 1, (1):19-28.

Hussein M.A., Farghaly H.S. (2010). Protective effects of *Jasonia montana* against lipid peroxidation in liver and kidney of iron-overloaded rats. Australian J. Basic Appl. Sci., ISSN, 4: 2004-2012.

Ige S.F, Akhigbe R.E. (2012).The role of *Allium cepa* on aluminum-induced reproductive dysfunction in experimental male rat models. J Hum Reprod Sci. 5: 200-5.

Jagetia G.C., Baliga M.S., Malagi K.J., Sethukumar K.M. (2002). "The evaluation of the radio protective effect of *Triphala* (an ayurvedic rejuvenating drug) in the mice exposed to gamma-radiation." Phytomed. 9 (2):99-108.

Jarup L. (2003). Hazards of heavy metal contamination. British Medical Bulletin 68: 167-182.

Jefferson Lab – Science Education (2014). Its Elemental: The element aluminium. Retrieved from: http://education.jlab.org/itselemental/ele013.html

Jennifer E., Slemmer and Weber J.T. (2014). Assessing Antioxidant Capacity in Brain Tissue: Methodologies and Limi-

tations in Neuroprotective Strategies. Antioxidants 3:636-648.

Kaiser L., Schwartz, K., Hledin B., Mayor G. (1984). Microcytic anemia secondary to intraperitoneal aluminum in normal and uremic rats. Kidney Int. 26, 269–274.

Kalaiselvi A., Reddy G.A., Ramalingam V. (2015). Ameliorating Effect of Ginger Extract *(Zingiber officinale Roscoe)* on Liver Marker Enzymes, Lipid Profile in Aluminium chloride Induced Male Rats.IJPSPP.7 (1): 52-58.

Kalaiselvi A., Reddy G.A., Ramalingam V. (2015). Ameliorating Effect of *Ginger* Extract (*Zingiber officinale Roscoe*) on Liver Marker Enzymes, Lipid Profile in Aluminium chloride Induced Male Rats. Ind. J. of Pharm. Sci. And Drug Res. 7(1):52-58.

Kanwar VS., Jenkins J.J. Mandrell BN., Furman W.L. (1996). Aluminum toxicity following intravesical alum irrigation for hemorrhagic cystitis. 27(1):64-7.

Kawahara M. (2005). Effects of aluminum on the nervous system and its possible link with neurodegenerative diseases. Journal of Alzheimer's Disease.8 (2):171–182.

Kawahara M., Negishi K. (2011). Link between Aluminium and the Pathogenesis of Alzheimer's Disease: The Integration of the Aluminum and amyloid cascade Hypotheses. Int. J. Alzheimers Dis.276393. PMCID: PMC3056430.

Kelley B.J., Knopman D.S. (2008).Alternative medicine and Alzheimer disease. Neurologist.14:299–306.

Kim D.S., Park S.Y., Kim J.K. (2001). Curcuminoids from *Curcuma longa* L. (*Zingiberaceae*) that protect PC12 rat pheochromocytoma and normal human umbilical vein endothelial cells from betaA(1–42) insult.Neurosci Lett.303:57–61.

Kim G., Hyo, Oh S., Myung, (2012). Herbal Medicines for the Prevention and Treatment of Alzheimer's Disease. Cur. Pharma. Desi.Vol. 18, (19):57-75.

Kisnieriene V., Lapeikaite I. (2015). When chemistry meets biology: the case of aluminium - a review. CHEMIJA. Vol. 26. No. 3. P. 148-158.

Kongkeawa C., Dilokthornsakula P.,Thanarangsarita P., impeanchoba N., Scholfielda, C.N. (2014). Meta-analysis of randomized controlled trials on cognitive effects of *Bacopa monnieri* extract. Journal of Ethnopharmacology Vol. 151, Issue 1, pp. 528–535.

Kosier J.H. (1990). Aluminum toxicity in the 1990. *ANNA J.* 26(4):423-4.

Krewski D., Yokel R.A., Nieboer E., Borchelt D., Cohen J., Harry J., Kacew S., Lindsay J., Mahfouz A.M., Rondeau V. (2007). Human health risk assessment for aluminium, aluminium oxide and aluminium hydroxide.J. Toxicol. Environ. Health B Crit. Rev. 10 (Suppl 1)1-269.

Kuboyama T., Tohda C., Komatsu K. (2005). Neuritic regeneration and synaptic reconstruction induced by withanolide A. Br J Pharmacol.144:961–971.

Kuboyama T., Tohda C., Zhao J., Nakamura N., Hattori M., Komatsu K. (2002). Axon- or dendrite-predominant outgrowth induced by constituents from *Ashwagandha*. Neuroreport.13:1715–1720.

Kumar V. and Gill K.D. (2009). Aluminium neurotoxicity: neurobehavioral and oxidative aspects, Archives of Toxicology 83; 965-978.

Kumar V., Gill K.D. (2014). Oxidative stress and mitochondrial dysfunction in aluminium neurotoxicity and its amelioration: A review. Neurotoxicology Vol.41, pp. 154-166.

Kutlubay R., Oguz E.O., Can B., Guven M.C., Sinik Z. and Tuncay O.L. (2007). Vitamin E protection from testicular damage caused by intraperitoneal aluminium, International Journal of Toxicology.26:297-306.

Laden K., Felger C.B. (1988) Antiperspirants and deodorants: cosmetic science and technology series vol 7, Marcel Dekker, New York.

Laghlimi M., Baghdad B., Hadi H., Bouabdli A. (2015). Phytoremediation Mechanisms of Heavy Metal Contaminated Soils: A Review Open Journal of Ecology, 5, 375-388.

Lang A. E. (2006). Randomized controlled trial of intraputamenal glial cell line-derived neurotrophic factor infusion in Parkinson disease. Ann Neurol 59: 459–66.

Lee J.H., Ahn H.J., Lee S., Chan J., Min C.K. (2011). Effects of L- and T-type Ca^{2+} channel blockers on spermatogenesis and steroidogenesis in the prepubertal mouse testis, Journal of Assisted Reproduction and Genetics 28:23–30.

Leehey D.J, Daugirdas J.T., Ing T.S., Reid R.W. (1985). Spurious hyperphosphatemia due to hyperlipidemia. Arch Intern Med. 145(4):743-4.

Lewis W., Lewis M. P. F. (2003). Medical Botany; Plants Affecting Human Health, edition 2. John Wiley & Sons, Inc., Hoboken, New Jersey.45.

Lin W.T., Chen R.C., Lu W.W., Liu S.H., Yang F.Y. (2015). Protective effects of low-intensity pulsed ultrasound on aluminum-induced cerebral damage in Alzheimer's disease rat model. Scientific Reports **5**, Article number: 9671.

Lipton, S.A. (2007). Pathologically activated therapeutics for neuroprotection. Nat. Rev. Neurosci.8: 803-808.

Lu H., Hu J., Li J., Pang W., Hu Y., Yang H., Li W., Huang C., Zhang M., Jiang Y.(2013). Optimal dose of zinc supplementation for preventing aluminum-induced neurotoxicity in rats. Neural Regen Res.8 (29): 2754–2762.

Lu M. H., Kennedy G. L. (1986). Teratogenic evaluation of mancozeb in the rat following inhalation exposure. Toxicol. Appl. Pharmacol. 84: 355–68.

Lukiw W.J. (2001). Aluminum and gene transcription in the mammalian central nervous system. In: Exley C, editor. Aluminum and Alzheimer's disease, The Science That Describes the Link. New York, NY: Elsevier Press; p. 47–68.

Lunk H.J. (2015). Discovery, properties and application of chromium and its compounds. Chem. Texts.

Mahmoud R.H., Elnour W.A. (2013).Comparative evaluation of the efficacy of ginger and orlistat on obesity management, pancreatic lipase and liver peroxisomal catalase enzyme in male albino rats. European Review of Medicinal and Pharmacological Sciences.17:75-83.

Malluche H.H. (2002). Aluminium and bone disease in chronic renal failure. Nephrol Dial Transplant.17;21-24.

Manna P.R., Chandrala S.P., Stocco D.M., (2006). Pindependent signaling regulates steroidogenesis in mouse Leydig cells in the absence of StAR phosphorylation, Journal of Molecular Endocrinology 37:81-95.

McGreevy JW., Hakim CH., Mclntosh MA., Duan D. (2015). Animal models of Duchenne muscular dystrophy : from basic mechanisms to gene therapy. Model Mech. 8 (3): 195-213.

McLachlan D.R.C, Bergeron C., Smith J.E., Boomer D., Rifat S.L. (1996). Risk for neuropathologically confirmed Alzheimer's disease and residual aluminum in municipal drinking water employing weighted residential histories. Neurology.46:401–5.

McLaughlin A.I.G., Kazantzis G., King E., Teare D., Porter R.J. (1962). Pulmonary fibrosis and encephalopathy associated with the inhalation of aluminum dust. Br J Ind Med 19:253-263.

Mehranjani M.S.,Taefi R. (2012). the protective role of vitamin E on the testicular tissue in rats exposed to sodium arsenite during the prenatal stage till sex maturity: A stereological analysis. Iran J Reprod Med.10 (6): 571–580.

Meinkoth J.H., Clinkenbeard K.D. (2000). Normal hematology of the dog. In: Feldman BF, Zinkl JG, Jain NC, eds. Schalm's Veterinary Hematology. 5th ed. Baltimore, MD: Lippincott Williams & Wilkins.1057-1063.

Metwally M.A.A. (2009). Effects of *Garlic (Allium sativum)* on Some Antioxidant Activities.in Tilapia Nilotica (Oreochromis niloticus). World Journal of Fish and Marine Sciences.1 (1): 56-64.

Miraj M., Jakkala L., Khan N., Ali A.S. (2014). On the toxicity of certain metals and its amelioration through herbal extracts. Biosci. Biotech. Res. Comm. 7 (2):99-107.

Mishra L.C., Singh B.B., Dagenais S. (2000). Scientific basis for the therapeutic use of *Withania somnifera.(Ashwagandha)*: A review. Alternative Medicine Reviews.5:334–346.

Mitchell J., Manning G.B., Molyneux M. (1961). Pulmonary fibrosis in workers exposed to finely powdered aluminum. Br J Ind Med 18:10-20.

Mohammad N.S., Arafa M.H., & Atteia H.H. (2015). Coenzyme Q10 and fish oil synergistically alleviate aluminum chloride-induced suppression of testicular steroidogenesis and antioxidant defense. Volume 49, Issue 11, pp 1319-1334.

Mohammed A., Kahtani A.l. (2010). Renal Damage Mediated by Oxidative Stress in Mice Treated with Aluminium Chloride.Protective Effects of *Taurine*. Journal of Biological Sciences.10: 584-595.

Mohan, Sarswat, Yong, Pittman (2014). Organic and inorganic contaminants removal form water with biochar, a renewable, low cost and sustainable adsorbent-A critical review. Bioresour. Technol. Bioretech. 01;120.

Moselhy W.A., Helmy N.A., Halim B.R., Nabil T.M., Hamid M.I. (2012). Role of ginger against the reproductive toxicity of aluminium chloride in albino male rats. Reprod Domest Anim. 47(2): 335-345.

Mukherjee P.K., Rai S., Bhattacharyya S., Debnath P.K., Biswas T.K., Jana U., Pandit S., Saha B.P. and Paul P.K. (2006).Clinical Study of *Triphala* – A Well Known Phytomedicine from India 2006 Iranian journal of pharmacology and therapeutics. 5:51-54.

Murthy S., Gautam M. K., Goel S., Purohit V., Sharma H., Goel R. K. (2013). Evaluation of In Vivo Wound Healing Activity of *Bacopa monniera* on Different Wound Model in Rats. Biomed Res Int. 972028.pp. 1-9.

Nathan P.J, Tanner S., Lloyd J., Harrison B., Curran L., Oliver C., Stough C. (2004). Effects of a combined extract of *Ginkgo biloba* and *Bacopa monniera* on cognitive function in healthy humans. Hum Psychopharmacol.19 (2):91-6.

Niino T., Arizaga M.V. (2015). Cryopreservation for preservation of potato genetic resources. Breed Sci. 65(1): 41-52.

Olanow C.W., Tatton W.G. (1999). Etiology and Pathogenesis of Parkinson's Disease. Annual Review of Neuroscience. Vol. 22:123-144.

Pande S., Ritter C.S., Rothstein M. (2006). FGF-23 and sFRP-4 in chronic kidney disease and post-renal transplantation. Nephron Physiol. 104(1):p23-32.

Pandey G., Jain G.C. (2013). A Review on Toxic Effects of Aluminium Exposure on Male Reproductive System and Probable Mechanism of Toxicity. Int. J. of Toxi. and Appl. Pharma.3(3): 48-57.

Parihar M.S., Hemnani T. (2003). Phenolic antioxidants attenuate hippocampal neuronal cell damage against kainic acid induced excitotoxicity. J Biosci.28:121–128.

Paul B., Tchounwou P.B., Yedjou C.G., Patlolla AK., and Sutton J. D (2011). Heavy Metals Toxicity and the Environment. Indian J Pharmacol 43(3): 246–253.

Peruquetti R.L., Taboga S.R., Oliveira M.T.V. (2010). Expression of acid phosphatase in the seminiferous epithelium of vertebrates, Genetics and molecular research. 9; 620-628.

Pizent A., Tariba B., Zivkovic T., Reproductive toxicity of metals in men, Archives of Industrial Hygiene and Toxicology 63: 35-46.

Platt B., Busselberg D. (1994). Actions of aluminum on voltage-activated calcium channel currents, Cellular and Molecular Neurobiology 14:819-829.

Prabsattroo T., Wattanathorn J., Iamsaard S., Somsapt P., Sritragool O., Thukhummee W., Muchimapura S. (2015). *Moringa oleifera* extract enhances sexual performance in stressed rats. J Zhejiang Univ Sci B.16 (3): 179–190.

Prabu P.C., Panchapakesan S. (2014). Prenatal developmental toxicity evaluation of *Withania somnifera* root extract in Wistar rats. Drug and Chemical Toxicology. Vol.38, Issue1,pp.50-56.

Proudfoot A.T. (2009). Aluminium and zinc phosphide poisoning. Clin Toxicol (Phila). 47(2):89-100.

Qin R., Jiang W., Liu D. (2013).Aluminum can induced alteration in the cellular localization and expression of three major nucleolar proteins in root tip cells of *Allium cepa var.* Agrogarum L. Vol. 90. Issue 2, PP.827-834.

Rajan K.E., Preethi J.,Singh H.K. (2015). Molecular and Functional Characterization of *Bacopa monniera*: A Retrospective Review. Evid Based Complement Alternat Med.945217.12 p.

Rajeshwari A., Kavitha S., Alex S.A., Kumar D., Mukherjee A., Chandrasekaran N., Mukherjee A. (2015). Cytotoxicity of Aluminium oxide nanoparticles on *Allium cepa* root tip-effects of oxidative stress generation and biouptate. Envioron. Sci. Pollut. Res. 22:11057-11066.

Rani S. U., Chitra M., Jainu M. (2014). Hepatoprotective Effect of *Wattakaka volubilis* Extract on Aluminium Sulphate Induced Liver Toxicity. International Journal of Pharmaceutical Sciences and Drug Research.6 (2): 169-173.

Ranjbar S.H., Zahedi H.S., Abdollahi M., Larijani B. (2013). Trends in publication of evidence-based Traditional Iranian medicine in endocrinology and metabolic disorders. J Diabetes Metab Disord.12:49.

Raymond A., Wuana and Felix E., Okieimen (2011). Heavy Metals in Contaminated Soils: A Review of Sources, Chemistry, Risks and Best Available Strategies for Remediation. ISRN Ecology Article ID 402647, 20p.

Razavi B.M., and Hosseinzadeh H. (2015). Saffron as an antidote or a protective agent against natural or chemical toxicities. Daru J. of Pharma. Sci. 23:31. pp. 1-9.

Rebecca M., Hoerth, Britta M., Seidt, ShahM., Schwarz C., Bettina M., Willie, Georg N. Duda, Fratzl P., Wagermaier W. (2014). Mechanical and structural properties of bone in non-critical and critical healing in rat. Acta Biomaterialia Volume 10, Issue 9; Pages 4009–4019.

Reddy P.N., Tammineni P., Radhika G.J., Reddy P.K., Pallu R. (2014). Hepatoprotective Effects of Terminalia chebula Fruit Extract against 2-AAF–Induced Hepatic Damage in Albino Mice: Role of MDR1 and COX-2. Journal of Herbs, Spices & Medicinal Plants 20:402-420.

Russo A., Izzo A.A., Cardile V., Borrelli F., Vanella A. (2001). Indian medicinal plants as antiradicals and DNA cleavage protectors. Phytomedicine. 8:125–132.

Sahin E., Colla S., Liesa M., Moslehi J., Müller F.L., Guo M., Cooper M., Kotton D., Fabian A.J., Walkey C. (2011). Telomere dysfunction induces metabolic and mitochondrial compromise. Nature. 470:359–365.

Salt D.E., Smith R.D., Raskin I. (1998). Phytoremediation. Annu. Rev Plant Physiol Plant Mol Biol 49: 643-668.

Sandur S.K., Ichikawa H., Pandey M.K., Kunnumakkara A.B., Sung B., Sethi G, Aggarwal B.B. (2007). Role of pro-oxidants and antioxidants in the anti-inflammatory and apoptotic effects of curcumin (diferuloylmethane) Free Radic Biol Med.43:568–580.

Schliebs R., Liebmann A., Bhattacharya S.K., Kumar A., Ghosal S., Bigl V. (1997) .Systemic administration of defined extracts from *Withania somnifera* (Indian Ginseng) and Shilajit differentially affects cholinergic but not glutamatergic and GABAergic markers in rat brain. Neurochem Int.30:181–190.

Selvakumar D., Srikumar R., Manikandan S., Parthasarathy N.J., and Rathinasamy S. (2006). Antioxidant property of *Triphala* on cold stress induced oxidative stress in experimental rats. Journal of Health science.52 (6)843-847.

Shahraki M.R., Zahedi A.S., Sarkaki A.R. (2004). The Effect of Aluminum Injection in Lateral Ventricle on Sex Hormones in Male Rat, Shiraz E-Medical Journal 5: 1-10.

Sharma, R.K. and Agrawal M. (2005). Biological effects of heavy metals: An overview. *J.* Environ Biol. 26(2): 301-313.

Shati A., Elsaid G., Hafez E. (2011). Biochemical and molecular aspects of aluminium chloride-induced neurotoxicity in mice and the protective role of *Crocus sativus* L. extraction and honey syrup. Neuroscience.175:66e74.

Shin R.W., Kruck T.P., Murayama H., Kitamoto T. (2003). A novel trivalent cation chelator Feralex dissociates binding of aluminum and iron associated with hyperphosphorylated tau of Alzheimer's disease. Brain Res.961:139–46.

Shin S.H., Kim M.K. (2004). Effect of dried powders or ethanol extracts of *Garlic* flesh and peel on lipid metabolism and antithrombogenic capacity in 16- month-old rats. Hanguk Yongyang Hakhoechi. 37 (7), 515– 524.

Shiraki H., Yase Y. (1991). Amyotrophic lateral sclerosis and Parkinsonism-dementia in the Kii peninsula: comparison with the same disorders in Guam and with Alzheimer's disease, Handbook of Clinical Neurology, vol. 15, pp. 273–300.

Shishodia S., Amin H.M., Lai R., Aggarwal B.B. (2005). Curcumin (diferuloylmethane) inhibits constitutive NF-kappaB activation, induces G1/S arrest, suppresses proliferation, and induces apoptosis in mantle cell lymphoma. Biochem. Pharmacol.70:700–713.

Sikha A., Harini A., Hegde P.L. (2015). Pharmacological activities of wild turmeric (*Curcuma* aromatic Salisb): a review. Journal of Phrmacognosy and Phytochemistry 3(5):01-04.

Singh N., Bhalla M., Jger P.D., Gilca M. (2011). An Overview on *Ashwagandha*:A Rasayana (Rejuvenator) of Ayurveda. Afr J Tradit Complement Altern Med. 8(5 Suppl): 208–213.

Singh N., Singh S.P., Sinha J.N., Shanker K., Kohli R.P. (1982). *Withania somnifera* (Ashwagandha) A rejuvenator herbal drug which enhances survival during stress (An adaptogen) Int J Crude Drug Res.3:29–35.

Singh R.B., Rastogi S.S., Singh D.S. (1989). Cardiovascular manifestations of aluminium phosphide intoxication. J Assoc Physicians India.37:590–2.

Singh T., Goel R.K. (2015).Neuroprotective effect of *Allium cepa L.* in aluminium chloride induced neurotoxicity. Neurotoxicology, 49:1-7.

Sinha N., Sharma N., Johri S. (2011). Phytotherapeutic approach against aluminium induced biochemical changes in albino mice. Journal of Pharmaceutical Research and Opinion. 1: 4 121 – 125.

Skidmore-Roth L. (2003). Handbook of Herbs and Natural Supplements 2nd edition. Int. J. Of Food Microbio.83:331-335.

Solfrizzi V., Panza F., Capurso A. (2003): The role of diet in cognitive decline. J. Neural Transm. 110, 95-110.

Solgi R., Baghaei A., Golaghaei A., Hasani S., Baeeri M., Navaei M., Ostad S.N., Hosseini R., Abdollahi M. (2015). Electro-

physiological and molecular mechanisms of protection by iron sucrose against phosphine-induced cardiotoxicity: a time course study.Toxicology Mechanisms and Methods. Vol. 25 pp.249-257.

Soliman F.M., Moussa M.Y., Abdallah H.M., Othman S.M. (2009). Cytotoxic activity of flavonoids of *Jasonia montana Vahl. (Botsch) (Astraceae)* growing in Egypt. Australian J. Basic Appl. Sci.3: 148-152.

Sparling D.W. and Lowe TP., (1996). Environmental hazards of aluminum to plants, invertebrates, fish, and wildlife. Rev Environ Contam Toxicol.; 145:1-127.

Stacchiotti A., Rodella L.F., Ricci F., Rezzani R., Lavazza A., Bianchi R. (2006): Stress proteins expression in rat kidney and liver chronically exposed to aluminium sulphate. Histol Histopathol, 21: 131-140.

Stough C., Lloyd J., Clarke J., Downey L.A., Hutchison C.W., Rodgers T., Nathan P.J. (2001).The chronic effects of an extract of *Bacopa monniera* (Brahmi) on cognitive function in healthy human subjects. Psychopharmacology (Berl).156(4):481-4.

Strong M.J., Garruto R.M.(1991). Chronic aluminium-induced motor neuron degeneration: clinical, neuropathalogical and molecular biological aspects. Can J Neurol Sci. 18(3): 428-31.

Styren S.D., Kamboh M.I., Dekosky S.T. (1998). Expression of differential immune factors in temporal cortex and cerebellum: the role of α-1-antichymotrypsin, Apolipoprotein E, and reactive glia in the progression of Alzheimer's Disease. J Comp Neurol. 396:511–20.

Sun H., Hu C., Jia L., Zhu Y., Zhao H., Shao B., Wang N., Zhang Z., Li Y. (2011). Effects of Aluminum Exposure on Serum Sex Hormones and Androgen Receptor Expression in Male Rats, Biological Trace Element Research. 144; 1050-1058.

Taylor G.A., Moore P.B., Ferrier I.N., Tyrer S.P. and Edwardson J.A. (1998).Gastrointestinal absorption of aluminium and citrate in man. J. Inorg. Biochem. 69, 165-169.

Ting H., Deep G., Agrawal C., Agrawal R. (2014). The strategies to control prostate cancer by chemoprevention approaches. Mutat Res.1-15.

Tohda C., Kuboyama T., Komatsu K. (2000). Dendrite extension by methanol extract of *Ashwagandha* (roots of *Withania somnifera*) in SK-N-SH cells. Neuroreport.11:1981–1985.

Tohda C., Kuboyama T., Komatsu K. (2005). Search for natural products related to regeneration of the neuronal network. Neurosignals.14:34–45.

Tomljenovic L., Shaw C.A. (2012). Mechanism of aluminium adjuvant and auto immunity in pediateic population Journal of toxicology 21: 223-230.

Tripathi S., Mahdia A.A., Nawaba A., Chandera R., Hasanb M., Siddiquib M.S., Mahdic F., Mitrad K., Bajpaid V.K. (2009). Influence of age on aluminum induced lipid peroxidation and neurolipofuscin in frontal cortex of rat brain: A behavioral, biochemical and ultrastructural study. Brain Res. 1253:107– 116.

Ugwoke CEC., Ezugwe CO. (2010). Phytochemical screening and promiximate composition and onion bulb (*Allium cepa L*). J Pharm Allied Sci.7, ISSN: 1596-8499.

Uversky V. N., Li J., Fink A. L. (2001). Metal-triggered structural transformations, aggregation, and fibrillation of human α-synuclein: a possible molecular link between parkinson's disease and heavy metal exposure, Journal of Biological Chemistry, vol. 276, no. 47, pp. 44284–44296.

Vahdani V., Khaki A. (2014). Effect of *Allium cepa* Seed Extract on Serum Testosterone in Rats.Crescent Journal of Medical and Biological Sciences Vol. 1, No. 3, Summer 110-112.

Verbeeck RM., Driessens FC., Rotgans J. (1990). Aluminium in tooth pastes and Alzheimer's disease. 87(2):141-4

Verstraeten S.V., Aimo L., and Oteiza P.I. (2008). Aluminium and lead: molecular mechanisms of brain toxicity, Archives of Toxicology 82; 789–802.

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Wahlström B., Blennow G.A. (1978). Study on the fate of *Curcumin* in the rat. Acta Pharmacol Toxicol (Copenh).43(2):86-92.

Walton J.R. (2007). An aluminum–based rat model for Alzheimer's disease exhibits oxidative damage inhibition of PP2A activity, hyperphosphorylated and granulavacular degeneration. J Inorg Biochem. 101(9):1275-84.

Wangensteen H., Samuelsen A.B., Malterud K. E. (2004). Antioxidant activity in extracts from *Coriander*. Food Chem; 88: 293-297.

Ward P.S., Thompson C.B. (2012). Metabolic reprogramming: a cancer hallmark even warburg did not anticipate.Cancer Cell. 21:297–308.

Wettstein A. (1991) Failure to find a relationship between mnestic skills of octogenarians and aluminium in drinking water. International archives of occupational and environmental health, 63:97-103.

Wiseman H., Okeilly, J.D., Aldlercreutz, H., Mallet, A.J., Bowery, E.A., Sanders, A.B. (2000). Isoflavones phytoestrogen consumed in soya decrease F2-isoprostane concentrations and increase resistance of low density lipoprotein to oxidation in humans. Am. J. Clin. Nutr; 72: 397-400.

Wollen K.A. (2010). Alzheimer's disease: the pros and cons of pharmaceutical, nutritional, botanical, and stimulatory therapies, with a discussion of treatment strategies from the perspective of patients and practitioners. Altern Med Rev.15:223–244.

Yang F., Lim G.P., Begum A.N., Ubeda O.J., Simmons M.R., Ambegaokar S.S., Chen P.P., Kayed R., Glabe C.G., Frautschy S.A., Cole G.M. (2005). Curcumin inhibits formation of amyloid beta oligomers and fibrils, binds plaques, and reduces amyloid in vivo. J Biol Chem. 280:5892–5901.

Yogita S., Prachi A., Arun J., Maya B. (2013). Antibacterial and Antifungal Activity of Roots of *Wattakaka volubilis*. Global J of Pharm.7 (3): 283-287.

Yokel R.A., Hicks C.L., Florence R.L. (2008). Aluminium bioavailability from basic sodium aluminium phosphate, an approved food additive emulsifying agent, incorporated in cheese. Food chem. Toxicol. 46:2261-2266.

Yousef M.I., Kamel I.K., Guendi I.E.E., Demerdash F.M. (2007). An in-vitro study on reproductive toxicity of aluminum chloride on rabbit sperm: the protective role of some antioxidants, Toxicology 239.213- 223.

Yumoto S., Ngai H., Matsuzaki H., Kobayashi T., Tada W., Ohki Y. (2000). Transplacental passage of Aluminum from pregnant rats to fetus and aluminium transfer through maternal milk to milk suckling rats. Nucl Instrum Methods Phy Res B.172:925-929.

Zanatta A.P., Zanatta L., Gonçalves R., Zamoner A., Silva F.R.M.B. (2013). Rapid Responses to Reverse T3 Hormone in Immature Rat Sertoli Cells: Calcium Uptake and Exocytosis Mediated by Integrin. PLoS One 8(10): e77176.

Zbarsky V., Datla K.P., Parkar S., Rai D.K., Aruoma O.I., Dexter D.T. (2005). Neuroprotective properties of the natural phenolic antioxidants curcumin and naringenin but not quercetin and fisetin in a 6-OHDA model of Parkinson's disease. Free Radic Res.39:1119–1125.

Zhao X., Sheng L., Wang L., Hong J., Yu X., Sang X., Sun Q., Ze Y., Hong F. (2014). Mechanisms of nanosized titanium dioxide-induced testicular oxidative stress and apoptosis in male mice. Part Fibre Toxicol.11: 47.