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 liberated by various human activities and have potential contribution to produce heavy metal toxicity. The history of heavy metal poison-
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 fluoride that are commonly found in soil, minerals and rocks. (Łukiw 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 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, aluminium 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; Leheey 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; Namen 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 5.0 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
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, (Driscol 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 or Al-contaminated foods. Concentrations > 1000 mg/kg are most likely exposed through dietary ingestion of soil or waterproothing textiles, in antiperspirants and pesticides.

Aluminium causes toxic effect on biochemical parameters i.e. Plasma glucose, Urea, Creatinine, Cholesterol, Triglycerides, 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 peroxidation in certain animal and human beings, (Lagerwerft et al., 1974; Flora et al., 1986; Zaman et al., 1993; Kowalczyk et al., 2004; Vinothini 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, (Druke et al., 1966b). 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 Kissinieriene 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 phosphate poisoning were reported. Chief symptoms were vomiting and epigastric.
pall. Sensorium was normal in most of the patients. This might be due to 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 phosphooxidase 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 steroidal genesis by following ways. First Aluminium may block voltage sensitive calcium channels in hypothalamus and decreased the GnRH secretion which further voltage sensitive calcium channels in hypothalamus genesis by following ways. First Aluminium may block voltage sensitive calcium channels in hypothalamus and decreased the GnRH secretion which further voltage sensitive calcium channels in hypothalamus.

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

Now-a-days 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 flavonoids, 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 findings bind to DNA, gene expression and enzymes present in energy metabolism disrupts the proteins from cells, structural like skeletal 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; Kongkeaw et al., 2014; Rajan et al., 2015).

Jasonia candidans & 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 and neurotrophic effect, (Soliman et al., 2009).

Polyphenols are abundant in Jasonia montana and are used as antioxidants. Ethanolic extract of Jasonia candidans 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., 2005; Rasav et al., 2015).

Amelioration by Jasonia montana against lipid peroxidation in liver and kidney of iron-overloaded rats has been reported by Hussein et al., (2010). The decreased activity of brain marker Acetylcholinesterase (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 belerica, 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 poisoned mice. concurrent use of garlic and Triphala dry powder reduced aluminum concentration indicating the potential activity in combination against aluminium 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, (Chianani 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, (Sikka et al., 2015).

The metabolites of Turmeric such as glucoronesides 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 Wahlstrom 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-
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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 nervous 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 varieties 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 withanamides, (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, anti diabetic 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; Alafatayo 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., 2015; 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 NO 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).

CONCLUSION 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 vulgaris, Bacopa monniera, Jasonia candicans and Jasonia Montana, Terminalia chebula, Terminalia bellerrica,
Embelia officinalis, Curcuma longa, Withania somnifera Zingiber officinale, Roscoc, Allium cepa and Rosmarinus officinalis extracts against the toxic effects of the highly ubiquitous 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 thiol 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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