WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 6.805
Volume 5, Issue 6, 2160-2146. Review Article ISSN 2277– 7105

ROLE OF AYURVEDA HERBS IN DRUG INDUCED TOXICITY

Dr. Malvika Saini,[1]* Dr. Sarvade Dattatraya,[1] Dr. Sumit Nathani,[2] Dr. Mita Kotecha[3]

[1]P.G. Scholar, Department of Dravyaguna Vigyan, National Institute of Ayurveda, Jaipur, Rajasthan, India.

[2]Assistant professor, Department of Dravyaguna Vigyan, National Institute of Ayurveda, Jaipur, Rajasthan, India.

[3]Professor, Head of Department, Department of Dravyaguna Vigyan, National Institute of Ayurveda, Jaipur, Rajasthan, India.

Article Received on
20 April 2016,

Revised on 11 May 2016,
Accepted on 02 June 2016

DOI: 10.20959/wjpr2016-6447

***Corresponding Author**
Dr. Malvika Saini
P.G. Scholar, Department of Dravyaguna vigyan, National Institute of Ayurveda, Jaipur, Rajasthan, India.

ABSTRACT

Drug toxicity is a common health problem now a day's in population. 6% of hospital admissions and 2.5% of emergency department visits for injuries or poisonings may be due to adverse drug reactions or drug toxicity. An estimated 183,000 (range: 95,000-226,000) drug-related deaths were reported in 2012. That figure corresponds to a mortality rate of 40 deaths per million among the population aged 15-64. Toxic effects produced as a result of continuously using some drugs, is a major cause of mortality & morbidity among population. NSAIDs, antibiotics, proton pump inhibitors, H2 blockers, paracetamol etc. are some of the drugs which are widely used in population for getting quick results. Pantaprazole, ranitidine etc. are generally prescribed to every patient whether they really need it or not. Similarly there are many drugs which are prescribed to patients regularly e.g. NSAIDs for musculoskeletal problems, aspirin as anti-inflammatory & in cardiovascular disease, ciprofloxacin as antibiotic. But they produce severe organ toxicity. PPI & H2 blockers are nephrotoxic, paracetamol causes hepatotoxicity, ciprofloxacin causes neurotoxicity. But our Ayurveda is so vast that it provides treatment not only to fight with the disease but also it detoxifies the body from toxins produced by modern drugs. Herbs like *Bhumi amalaki, Brahmi, Gokshur, Punarnava* etc. provides protection & detoxify the organs like liver, kidney & brain. The present paper deals with organ toxicity caused by modern drugs & role of Ayurveda to curb this problem.

KEYWORDS: drug toxicity, organ toxicity, Ayurveda herbs & formulations.

INTRODUCTION

Drug-related side effects and adverse reactions, also called **adverse drug reaction** (ADR), **adverse drug event** (ADE) or **drug toxicity**, is defined as the "manifestations of the adverse effects of drugs administered therapeutically or in the course of diagnostic techniques. It does not include accidental or intentional poisoning."[1]

The World Health Organization defines it as

An adverse drug reaction (ADR) is 'a response to a medicine which is noxious and unintended, and which occurs at doses normally used in man'. In this description it is of importance that it concerns the response of a patient, in which individual factors may play an important role, and that the phenomenon is noxious (an unexpected therapeutic response, for example, may be a side effect but not an adverse reaction).[2]

6% of hospital admissions[3] and 2.5% of emergency department visits for injuries or poisonings[4] may be due to adverse drug reactions.

These ADRs may include organ toxicity or may involve the whole system like nephrotoxicity, hepatotoxicity or neurotoxicity.

Hepatotoxic drugs: Drugs are an important cause of liver injury. More than 900 drugs & toxins have been reported to cause liver injury, and drugs account for 20-40% of all instances of fulminant hepatic failure. Approximately 75% of the idiosyncratic drug reactions result in liver transplantation or death.[5]

Amoxycilline-clavulanic acid (common antibiotic), acetaminophen (analgesic & anti-pyretic), valproic acid, phenytoin (anti-epileptic drug), methotrexate (chemotherapeutic agent), paracetamol (anti-pyretic), isoniazid (anti-tubercular), niacin (vitamin- B5), iboprufen (NSAID) are some of the drugs which causes hepatotoxicity.[5]

Possible mechanisms of drug induced liver injury: Disruption of the hepatocyte: Covalent binding of the drug to intracellular proteins can cause a decrease in ATP levels, leading to actin disruption. Disassembly of actin fibrils at the surface of the hepatocyte causes blebs and rupture of the membrane.

• Cytolytic T-cell activation: Covalent binding of a drug to the P-450 enzyme acts as an immunogen, activating T cells and cytokines and stimulating a multifaceted immune response.

• Apoptosis of hepatocytes: Activation of the apoptotic pathways by the tumor necrosis factor-alpha receptor of Fas may trigger the cascade of intercellular caspases, which results in programmed cell death.

• Bile duct injury: Toxic metabolites excreted in bile may cause injury to the bile duct epithelium.[6]

• The pathogenesis of drug-induced liver injury usually involves the participation of a toxic drug or metabolite that either elicits an immune response or directly affects the biochemistry of the cell. In either case, the resultant cell death is the event that leads to the clinical manifestation of hepatitis.[7]

The manifestations of drug-induced hepatotoxicity are highly variable, ranging from asymptomatic elevation of liver enzymes to fulminant hepatic failure. Common symptoms may include nausea, vomiting, abdominal pain, loss of appetite & jaundice.

Ayurveda herbs to detoxify liver

***Phyllanthus amarus* Schum.& Thonb (*Bhumi amalki*):** It belongs to family euphorbiaceae. It is a well-known plant from ancient times. Traditionally it is being used in respiratory disorders, jaundice, fever, oedema, hyperacidity, liver & in spleen disorders. In jaundice, its root paste is used with milk. Decoction of whole plant is used in liver & spleen disorders, so also can be used in hepatotoxicity.[8] This activity has also been proven experimentally.

Ethanolic extract of P. amarus showed hepatoprotection against aflatoxin poisoining. *Phyllanthus amarus* extract was found to show hepatoprotective effect by lowering down the content of thiobarbituric acid reactive substances (TBARS) and enhancing the reduced glutathione level and the activities of antioxidant enzymes, glutathione peroxidase (GPx), glutathione-S transferase (GST), superoxide dismutase (SOD) and catalase (CAT)[9]. Extracts of *Phyllanthus amarus* have been shown to exert hepatoprotective effect against CCl4 induced HepG2 cell damage in rabbits. Pre-treatment with extract of *Phyllanthus amarus*, reduced paracetamol-induced acute liver damage in rats as monitored by estimating the

SGOT. In the *in vitro*-study, PA (1-4 mg/ml) increased %MTT reduction assay and decreased the release of AST and ALT in rat primary cultured hepatocytes being treated with ethanol.[10] It is a component of famous marketed hepatoprotective product, liv-52.

***Eclipta alba* Hassk. (*Bhringraj*)**

It is used as alterative, anthelmintic, expectorant, antipyretic, antiasthmatic, tonic, deobstruent in hepatic and spleen enlargement and significant anti-inflammatory activity from ancient times. Its juice is used in jaundice, liver & spleen disorders.[8]

It has been reported to be useful in liver ailments & has been shown to possess hepatoprotective activity against carbon- tetrachloride induced liver cell damage & paracetamol induced hepatic damage in Mice. Treatment with ethanol extract of *E. alba* was found to protect the mice from hepatotoxic action of paracetamol as evidenced by significant reduction in the elevated serum transaminase levels.[11]

***Andrographis panniculata* (Burm.f.) Wall ex.Nees (*Kaalmegha*)**

It belongs to family acanthaceae. It is a very good medicine for liver disorders. Its decoction is used. Its activity on hepatotoxicity is also proven by various researches.

Methanolic extract of A. panniculata shows antihepatotoxic activity in CCl_4 intoxicated rats. This action is attributed to Andrographolide, the major antihepatotoxic component of the plant. It also exerted a pronounced protective effect in rats against hepatotoxicity induced by Dgalactosamine, paracetamol and ethanol. Andrographolide inhibited the CCl4-induced increase in the activity of serum glutamate oxaloacetate transaminase, serum glutamate pyruvate transaminase, alkaline phosphatase, bilirubin and hepatic triglycerides. Oxidative damage through free radical generation involved in the hepatotoxic effect of carbon tetrachloride (CCl4) and paracetamol (PC). An anti-oxidant property of Andrographolide is claimed to be one of the mechanisms of hepatoprotective effect.[12]

***Solanum nigrum* Linn. (*Kakmachi*):** It is an anti-ageing, anti-oedema & diuretic herb. Its leaves are used in oedema. Its juice is being used in chronic hepatomegaly & toxicity from ancient times.[8] Now it is also proven by modern researches.

S. nigrum extract showed hepatoprotection against thioacetamide induced liver fibrosis in mice. SNE reduced the hepatic hydroxy proline and α -smooth muscle acting protein levels in TAA treated mice. SNE inhibited TAA-induced collagen (α1) (I), transforming growth

factor-β1 (TGF-β1) and mRNA levels in the liver. Histological examination also confirmed that SNE reduced the degree of fibrosis caused by TAA treatment. Its aqueous extract also showed protection against liver damage caused by carbon tetra chloride.[13]

***Picrorhiza kurroa* Royle ex Benth. (*Kutki*)**

It is a well-known plant from ancient times & is being used in chronic fever, jaundice, hepatic & spleen disorders, anaemia, in digestive disorders, intestinal weakness, antihelmintic, *grahani rog*, in hiccups. It is a very good medicine for hepatic disorders because of the presence of phytoconstituent piccrorhizine in it.[14] The famous Ayurveda formulation *Aarogyavardhini vati* which is a well-known hepatoprotective product, works because *kutki* is a major ingredient in this formulation.

Administration of picroliv, a standardized fraction of alcoholic extent of *Picrorhiza kurroa* showed significant protection against hepatic damage in Mastomys natalensis. The increased levels of serum glutamate oxaloacetate transaminase (GOT), glutamate pyruvate transaminase (GPT), alkaline phosphatase, lipoprotein-X (LP-X) and bilirubin in the infected animals were marked reduced by different doses of picroliv. In the liver, picroliv decreased the levels of lipid peroxides and hydroperoxides and facilitated the recovery of superoxide dismutase and glycogen.[15]

Nephrotoxic drugs: The incidence of drug-induced nephrotoxicity has been increasing with the ever increasing number of drugs and with easy availability of over-the-counter medication viz. nonasteroidal anti-inflammatory drugs (NSAIDs), antibiotics etc. Drug-induced acute renal failure (ARF) accounted for 20% of all ARF in an Indian study; of which aminoglycosides accounted for 40% of total cases.[16]

Aminoglycosides, Gentamycin, Vancomycin(antibiotic), rifampicin(anti-tubercular), NSAIDs, cisplastin (anti-neoplastic agent), ACE inhibitors(antihypertensive), acyclovir(antiviral), ampicillin, allopurinols, captopril(thrombolytic) are some of drugs which causes nephrotoxicity.

Possible mechanism of drug induced nephrotoxicity[17]

- Crystals of some drugs like sulphadiazines transmit through tubular lumen they cause local abrasion and chemical irritation of collecting duct epithelium followed by peritubular haemorrhage, tubular necrosis and obstruction at any level from collecting duct to bladder

which results in asymptomatic crystalluria and microhematuria, gross hematuria, oliguria to anuria and post-renal ARF.

- Acyclovir's low solubility leads to intratubular precipitation with symptoms of obstructive uropathy and hematuria.

- NSAID's causes chronic kidney diseases. also known as "analgesic nephropathy". It is chiefly a chronic interstitial nephritis associated with capillary sclerosis of the vessels of renal pelvis and renal papillary necrosis followed by calcification. It is due to medullary ischaemia induced by loss of vasodilatory effects of prostaglandins on vasa recta. Long term toxicity of individual drugs is unknown.

- ACEInhibitors cause a sudden decline in GFR due to loss of efferent arteriolar tone. In bilateral obstruction of renal arteries (> 70%); efferent arteriolar tone is necessary for maintaining GFR. Therefore, ACEI in such cases can cause renal failure.

- In cisplastin, Nephrotoxicity is by acute tubular necrosis or tubulointerstitial process with symptoms of azotemia and fluid loss.

Ayurveda herbs to detoxify nephrotic system

***Craeteva nurvela* Buch.-Ham. (*Varun*):** It belongs to family capparidaceae. It is widely used as diuretic, in oedema, in renal calculi. In renal disorders, its root bark is used with *gokshur, punarnava & yavakshar*. Its formulation *varunadi kwath* is used as nephroprotective & in renal calculi.[18]

Several studies have explained its nephroprotective action. It protects from cisplastin induced nephrotoxicity. Cisplatin induced renal injury was evidenced by the elevated biochemical markers such as blood urea and serum creatinine and by the histopathological features of acute tubular necrosis. Petroleum ether extract of *C. nurvala* stem bark significantly decreases the raised blood urea and serum creatinine. It increases the glutathione level and catalase activity and decreases the concentration of thiobarbituric acid reactive substances (TBARS) in the kidney cortex. Hence the possible mechanism of nephroprotection by lupeol extracted from petroleum ether extract of *C. nurvala* stem bark may be attributed to its antioxidant and free radical scavenging properties.[19]

***Boerhavia diffusa* Linn. (*Punarnava*):** It belongs to family nyctaginaceae. It is *punarnava* in *Sanskrit* which means which gets rejuvenated every year & rejuvenates the whole body by producing new cells & tissues, removing old, dead cells & tissues & also by removing toxins from body. Its name also clarifies its work, detoxification of body. From the ancient times, it is being used as anti-ageing, in oedema, diuretic, spleenomegaly etc. For anti-ageing purpose, its root is used. Its formulations like *punarnavarishta, punarnavashtak kwath, punarnava swaras* are used as nephroprotective.[8]

It protects from acetaminophen induced nephrotoxicity. Administration of acetaminophen to rats induced marked detritions of renal function, characterized by a significant increase in blood urea nitrogen, serum creatinine along with depletion of super oxide dismutase (SOD), catalase (CAT), glutathione peroxidase (GPx) activities and reduced glutathione (GSH) levels, however pre-treatment with *B. diffusa* aqueous extract protected against these changes. Acetaminophen also caused histopathological changes like tubular necrosis, degeneration of epithelial cells, glomerular damage and congestion which was reversed with *B. diffusa*. The results suggest that *B. diffusa* has the potential in preventing the acetaminophen-induced nephrotoxicity.[20]

***Bauhinia verigata* Linn. (*Kaanchnar*)**

Traditionally it is being used in goitre, cyst, any extra growth in body, in prolapse of anus, in haematologic disorders, in piles, in urinary tract infections etc. Its flowers decoction is used in UTI. In haematologic disorders, powder of flowers is used with honey. Its famous formulation *kaanchnar guggulu* is used in goitre, or in any extra growth in body.[8]

It has nephroprotective action also which is widely accepted by modern researches. It protects from gentamycin induced nephrotoxicity. Nephrotoxicity is identified by estimating the raised levels of bio markers like serum creatinine, Blood Urea Nitrogen (BUN) and uric acid. It is due to the necrosis of nephrons. GFR is also reduced in the patients who are suffering with nephrotoxicity. Methanolic leaf extract of Bauhinia variegata shows significant effect on the nephrons due to its antioxidant effect. This antioxidant effect may be due to the presence of tannins and saponins in the plant. the plant has significant nephroprotective activity. Methanolic leaf extract has reduced the increased creatinine levels & other biomarkers.[21]

***Aerva lanata* Juss (*Gorakshaganja*):** It is used in urinary tract infections, renal calculi, splenomegaly etc. Its decoction of root is used in UTI. In renal calculi, hot infusion of flowers is used.[14]

The Aerva lanata plant is reported to have α-amyrin, campesterol, β-sitosterol, its palmitate, chrysinand flavonoid glucosides63. Canthin-6-one and β-carboline alkaloids were isolated from Aerva lanata. Four new alkaloids viz., aervine, methylaervine, aervoside and aervolanine were isolated. The plant was reported for various activities such as diuretic, hepato protective.The ethanolic extract of Aerva lanata possesses marked nephroprotective activity with stripped toxicity because of the flavonol glycoside like kaempferol-3-rhamnoside & kaempferol-3-rhamnogalactoside which supplied a promising role within the treatment of acute nephritic injury caused by nephrotoxins like cisplatin and antibiotics.[22]

***Pedelium murex* Linn. (*Brihad Gokshur*)**

It is used as nephroprotective, in urinary tract infections, diuretic, in renal calculus, aphrodisiac. In enuresis, hot infusion of fruits is given. Decoction of fruit is used with liquorice & nut grass in burning micturition. It is used with *Commiphora mukul* (Hooks.ex.Stocks)Engl.(*guggulu)*.[8] Its formulations like decoction of fruits, *gokshuradi guggulu* are used as nephroprotective.

The ethanolic extract of dried fruits of *Pedalium murex* Linn was evaluated for its nephroprotective activity. Nephrotoxicity was induced in Wistar rats by intraperitoneal administration of Cisplatin 5mg/kg. Effect of concurrent administration of *Pedalium murex* ethanolic extract at a dose of 250 mg/kg given by oral route was determined using serum creatinine and blood urea and change in body weight as indicators of kidney damage. Cystone was used as standard drug. The extract significantly decreased the cisplatin induced nephrotoxicity. The results showed that the ethanolic extract of dried fruits of *Pedalium murex* has an excellent nephroprotective activity as compared to cystone.[23]

Neurotoxic drugs: Neurotoxicity mostly caused by immunosuppressant's, antibiotics, chemotherapeutic agents etc. neurotoxicity from calcineurin inhibitors mostly immunosuppressants occurs in 7-22% for severe toxicity such as change in mental status, dysarthria, seizures, mutism, leukoencephalopathy, central pontine myelinolysis & coma. Less severe complications such as tremors, peripheral neuropathy, mood changes, headache, insomnia in 20-60 % patients. Incidence of adverse neurologic effects may be as high as 70%

in patients on high dose of steroids. Ciprofloxacin & norfloxacin causes common CNS side effects in 1-22% of patients.[24]

Amiodarone(antiarrythmic), chlorpromazine(sedative), ciprofloxacin, norfloxacin(common antibiotics), 5-flourouracil(chemotherapeutic agent), cyclosporine(immunosuppressant), cisplastin(antineoplastic), zidovudine(antiviral) etc. produce neurotoxicity.

Possible mechanism of drug induced neurotoxicity[25]

Direct neurotoxicity. Because some of the drugs used for treatment of neurologic disorders target receptors in the nervous system, there remains the possibility of direct neurotoxic effect. E.g.

Disturbances of brain energy metabolism

- ATP synthetase inhibition, eg, oligomycin
- Uncoupling, ie, dissociation of oxidative phosphorylation, eg, by barbiturates
- Disturbances of oxygen consumption
- Enzymatic dysfunction, eg, theophylline leading to convulsions by inhibiting adenosine
- Selective vulnerability of the central nervous system

Sequelae of disturbances of brain energy metabolism

- Ca2+ ion entry in the cell
- Oxygen free radical formation
- Excitatory amino acids

Ion channel disturbances

- Mitochondrial dysfunction, eg, zidovudine-induced mitochondrial myopathy
- Neurotransmitter disturbances, eg, atropine produces memory impairment by reducing acetylcholine
- Metabolite-mediated toxins, eg, MPTP neurotoxicity to dopamine cell in the substantia nigra.

Disturbance of the proteome

- Alterations of individual protein structure by drugs leading to loss of neuronal function.

Secondary drug-induced neurologic disorders. The central nervous system is affected by changes in other organs. Many of the neurologic disorders are secondary to diseases of other

organs. Similarly, the nervous system is affected by adverse drug reactions affecting other body systems. e.g.

- Drug-induced cardiac arrhythmias can lead to dizziness, syncope, and cerebral ischemia.
- Drug induced Coagulation disorders can lead to cerebral hemorrhage or thrombosis.
- Drug induced Respiratory disorders can lead to decreased ventilation and cerebral hypoxia.
- Drug-induced hyponatremia and hypoglycemia can lead to convulsions.
- Hyponatremia can produce cerebral edema.
- Drug-induced vitamin deficiency can lead to peripheral neuropathy.
- Drug-induced hypothyroidism can lead to decline of mental function, ataxia, and seizures.
- Hyperthyroidism can produce tremor and myopathy.

Ayurveda herbs to detoxify nervous system

***Bacopa monnieri* (Linn.) Wettst. (*Brahmi*)**

Bacopa monnieri (Linn.) Wettst. is extensively used since times immemorial in traditional Indian medicine as a nerve tonic and thought to improve memory. *Brahmi ghrita* is used in hysteria, schizophrenia, obsessive compulsive disorder. Leaf powder is used in mental weakness & in stress conditions.[8]

Several studies suggest that BM is a potential cognitive enhancer and neuro protectant.[26] The chemical constituent responsible for the effect of BM on learning schedules was identified as a mixture of two saponins designated as bacosides A and B. They also enhanced protein kinase activity and produced an increase in protein in hippocampus.[27] BM extract protects against Alzeimer's diseases(AD), it protects neurons from beta-amyloid-induced cell death. This neuroprotection is due to its ability to suppress neuronal oxidative stress and the AChE activity.[28]

***Centella asiatica* (Linn.) Urban (*Mandukparni*)**

Traditionally it is being used as anti-ageing, brain tonic, memory enhancer & in nervous disorders. For memory enhancing purpose, its powder is used with milk.[8]

The scientific studies have reported a variety of biochemical components in CA which include flavonoids, terpenoids, essential oils, alkaloids, carbohydrates, amino acids etc.[29] Since the ancient time, CA is used to enhance intelligence and improve cognitive function. And now it is experimentally proved in 28 human samples that CA enhance working memory

and improve self-mood.[30] Asiatic acids isolated from CA showed enhanced learning and memory properties in male Spraque–Dawley rats.[31] It also showed to improve brain function in juvenile and young mice when aqueous extract of CA is administered at a dose of 200 mg/kg.[32] One of the major findings of CA is that it can inhibit AChE, the hydro alcoholic extract of the plant was tested *in vitro* against AChE, which is the key enzyme in the pathogenesis of AD. Since deficit in the level of acetylcholine (ACh), which is hydrolyzed by AChE, has been identified in the brains of AD patients, inhibition of AChE as well as its sister enzyme butyrylcholinesterase (BChE) has become a rational target for drug development against AD.[33] The extract was found to inhibit AChE with 50% of inhibition rate at 150 μg/mL concentration *In vivo* studies in rats, have shown evidence that CA has a remarkable antioxidant effect and has the potential to decrease in melondialdehyde (MDA) and an increase in glutathione and catalase levels. It has anti convulsant property also.

***Celastrus paniculatus* Willd. (*Jyotishmati*)**

It is a very good medicine for nervous disorders. CP seeds are diaphoresis, cognitive enhancer, nerve tonic. *Jyotishmati* oil is used in ascites, locally applied in rheumatoid arthritis. For memory enhancing purpose, this oil is mixed with eight times of butter & then applied on head. Decoction of seeds is used in RA, gout, nervous disorders.[14]

Phytochemical studies show the presence of evoninoate, sesquiterpene, alkaloids paniculatine A, paniculatine B and wifornine F, celastrine, celapanine, celapanigine, celapagine, polyalcohol (malangunin, malkanginnol, malkanguniol and paniculatadiol), triterpenoids (pristimerin), sterols (β- amyrin and β-sitosterol).[30] Pre-treatment of neuronal cells with CP seed oil significantly attenuated glutamate-induced neuronal death. CP seed significantly and reversibly inhibited whole-cell currents activated by N-methyl- D-aspartate. The results suggest that water soluble extracts of CP seed (CPWSE) protected neuronal cells against glutamate induced toxicity by modulating glutamate receptor function. CPWSE (200 mg/kg body wt. for 14 days) showed an improvement in learning and memory & stimulated a significant decrease in the brain levels of malondialdehyde (MDA), with simultaneous significant increases in levels of glutathione and catalase.[34]

***Acorus calamus* Linn. (*Vacha*)**

Acorus calamus roots and rhizomes have been used in Indian system of traditional medicine for the hundreds of years and it is highly valued as a rejuvenator for the brain and nervous

system and as a remedy for digestive disorders. It is used with honey or milk in nervous disorders.[14]

Recently it is scientifically proved that AC rhizome constituents, particularly α and β-asarone, possess a wide range of pharmacological activities such as sedative, CNS depressant, behavior modifying, anticonvulsant, acetylcholinesterase (AChE) inhibitory and memory enhancing activities.[35] AC also shows neuroprotective effect against stroke and chemically induced neurodegeneration in rats.[36]

***Withania somnifera* Dunal (*Ashwagandha*)**

WS is depressant, diuretic, good nerve tonic. The major biochemical constituents of *Ashwagandha* root are steroidal alkaloids and steroidal lactones in a class of constituents called withanolides.[37] Much of *Ashwagandha*'s pharmacological activity has been attributed to two main withanolides, withaferin A and withanolide D. WS have antioxidant effect in the brain. WS extract can prevent increases in lipid peroxidation (LPO).[38] Biochemical investigation reflected significant increase in major free-radical scavenging enzymes, superoxide dismutase, catalase and glutathione peroxidase levels in the rat brain.[39] Administrated orally (50-200mg/kg orally) both sitoindosides IX and X compounds also produced significant anti-stress activity in albino mice and rats. They also augmented learning, acquisition and memory retention in both young and old rats.[40] The experimental studies have revealed that after oral administration in mice, withanoside IV is metabolized into sominone, which induces marked recovery in neuritis and synapses and also enhance axonal and dendritic out growth and synaptogenesis.[41]

***Nardostachys jatamansi* DC (*Jatamansi*)**

Traditionally it is used in digestive disorders, strengthner, nerve tonic, cognitive enhancer, for bringing consciousness, analgesic, rejuvenator. In hysteria, its oil is used. In nervous disorders, hot infusion is used.[42]

Ample quantity of scientific data supports the traditional use of *NJ* in nervous system disorder. It was observed that NJ reversed the neurodegenerative loss by enhancing the biogenic amines and reducing the dopaminergic D2 receptors in the striatum part of brain.[43] Being an antioxidant, it produced significant beneficial effects on GSH, CAT, SOD and some other related enzymes and catecholamine.[44] It has antidepressant effects also as it causes inhibition of GABA & monoamine oxidase (MAO).[45] It has anticonvulsant effects also. It

was effective in maximum electric shock model (MES) and increased the seizures threshold.[46] Methanolic extract of NJ reversed the amnesia and learning impairment induced by scopolamine and diazepam indicating that NJ could be a useful agent for restoration of memory in elderly people or in dementia. Neuroprotective effect of *Nardostachys jatamansi* DC. in rats was observed by using middle cerebral artery (MCA) occlusion to induce cerebral ischemia.[47] In the study, MCA model cause reduced GSH, thiol group, catalase and Na-K ATPase activities. All the alterations done by MCA model were attenuated by pre-treatment with hydro alcoholic extract of *NJ* for 15 days. This finding was also supported by histopathological studies which show decrease in neuronal cell death following MCA and reperfusion.

Jatamansone was found to be most active therapeutic agent as neuroeffective drug. Comparative studies against D-amphetamine, chlorpromazine in hyperkinetic children showed that Jatamansone reduces the aggressiveness, stubbornness, restlessness and insomenia.[48]

CONCLUSION

Drug-induced toxicity is a major cause of health problems now a day as drugs are being used generously & continuously for getting quick results & to relieve ailments. ADRs may result on single dose administration or on prolong use as in chronic pains and other long standing diseases. Some of these side effects may not be directly mortal but the damage done to the body organs may make life difficult. Ayurveda provides solutions to this problem by healing these organs. Ayurveda is so vast that it not only provides treatment to various diseases but also provide ways to save ourselves from toxins induced by continuous use of allopathic drugs. Ayurveda uses the inherent power of natural herbs to bring about wonderful results on the human body. These herbs are natural, safe & detoxify each & every organ of the body. Thus the body organs injured due to ADRs of Modern medicine can be effectively healed and rejuvenated with the help of Ayurvedic herbs.

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