ejpmr, 2023, 10(1), 345-354

SJIF Impact Factor 6.222

EUROPEAN JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH

www.ejpmr.com

Case Study

ISSN 2394-3211

EJPMR

EFFECT OF PHYTOCHEMICALS FROM WITHANIA SOMNIFERA(ASHWAGANDHA) ON LIVER ENZYMES

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Article Received on 04/11/2022 **Article Revised on 25/11/2022** **Article Accepted on 15/12/2022**

ABSTRACT

*Withania somnifera (*Ashwagandha) - one of the most essential medicinal herb of Ayurveda. It possesses broad spectrum actions and importance against various disorders such as hepatic, neurological, gastric, immunological etc. liver is an essential organ for various metabolic functions. But it gets damaged due to prolonged exposure to various toxic chemicals, infectious agents, overdose etc. The objective of this review paper is to analyze the effect of phytochemicals obtained from Ashwagandha *(Withania somnifera)* on liver marker enzymes providing hepatoprotective action.

KEYWORDS: Ashwagandha *(Withania somnifera),* toxic chemicals, infectious agents.

INTRODUCTION

Liver is considered as body's largest organ. Liver (hepatocytes) performs important role in various organisms (humans and animals both) (Mani et al.,2014). Liver is considered as the major site for various metabolic and excretion process. It is the largest endocrine gland in the body which performs more than 500 biochemical functions (Pundir et al.,2009). It is considered as chief chemist of the body. It has highly vascularized structure receiving blood from artery and vein (hepatic artery and portal vein). It plays an essential role in metabolism of various types of exogenous and endogenous compounds. It secretes bile juice. It can store Vitamin A, Vitamin B complex and glycogen too. Liver is capable of synthesizing albumin fibrinogen and clotting factors. Plays vital function in detoxification of the drugs from the body. Also performs functions like conjugation of toxic substances, steroid hormones. Esterifies free fatty acids and hemopoiesis (Eurrel et al.,2013). It possesses tremendous capacity of regeneration [Osgood et al.,2016). It is essential because it performs various biochemical; metabolic functions but continuous exposure to various toxic chemicals can lead to different types of liver injuries. As discussed earlier, liver being the chief chemist of the body has to perform a variety of important functions but its functioning is badly affected because of our changing life styles. It became prone to various diseases. So it is very important that liver's health remains intact. Liver - vital organ for the metabolic and detoxification processor for xenobiotics. Toxic chemicals known to elevate the levels (liver marker enzyme) such as aspartate aminotransferase (AST) and alanine aminotransferase(ALT) (Yang et al., 2007) (Widodo et al., 2007). Liver does lot of functions to keep our body healthy. Also, it converts nutrients into chemicals as per body requirement for performing metabolic processes. It filters toxins and poisons develop by high levels of ROS. Turns food into energy too. But if it doesn't work well whole body gets affected.

Liver is prone to various infections such as in case of viral infection it can suffer from Hepatitis A, Hepatitis C, and Hepatitis B. Immune system related infections are Primary biliary cholangitis, Primary selerosing cholangitis, Autoimmune hepatitis. Cancer and tumors can be Liver Cancer, cancer of bile duct, Liver cell adenoma. Inherited diseases are Hemochromatosis, Hyperoxaluria, Wilson disease, a-1AD (Alpha -1 Antitrypsin Deficiency) & other diseases of liver infection are Alcoholic liver, Drug overdose, NAFLD (non alcoholic fatty liver disease), ALF (Acute Liver Failure), cirrhosis. (Webmed.com/hepatitis/liver-and-hepatic-diseases) *Withania somnifera* (Ashwagandha) belongs to *Solanacea* family is a potent medicinal herb in Ayurveda(Khazir et al., 2012).This herb is regarded as the 1st class tonic(adaptogenic) in the world's greatest herbal medicinal range. In Ayurveda Ashwagandha is classified as a rasayna(rejuvenator); promotes health(Mental and Physical) and enhances longevity. *Withania s.* broad range activity is used to treat almost all disorders that harm human body. The practitioner of traditional medicine system i.e. the Vaids named *Withania s.* as "Indian Ginseng" (Kulkarni et al., 2008). This shrub is found in the dry subtropical region of India

especially in Maharashtra and West Bengal. It is also found in countries like Spain, Island, Morocco, Jordan, Easter Africa, Sri Lanka etc (Kumar et al., 2017). Popularly known by various names in India wiz. Punir(Hindi), Aksan(Punjabi), Ashvagandha(Bengal) , Ammukira(Tamil) (Kulkarni et al.,2008). It is considered as one of the most important herbal medicine in the botanical kingdom which has wide spectrum action in various diseases by performing pharmalogical actions.It can be used as whole plant or as well as specific parts can be used such as roots, stem and leaves as per requirements. Ashwagandha comprises of wide spectrum Phytochemicals which have broad range of biological functions. *Withania s.* demonstrates many Biological functions namely hepatoprotective. (Subramanian et al., 2008), anti-cancer(Widodo et al., 2007), anti-microbial (Kumar et al., 2017), anti-stress(Dhuley et al., 2000); (Ziauddin et al., 1996), and anti-hyperglycemic (Bhattacharya et al., 2000), anti – inflammatory and immunomodulatory properties (Mishra et al., 2020); "Charaka samhita" uses *W.somnifera* in the treatment of various liver disease. Mainly 35 withanoloids, 12 alkaloids and many sitoindosides were extracted and their structure were explicated (Mishra et al., 2000); (Matsuda et al., 2001),(Sharma et al., 2020). The extract of Ashwagandha contain many phytochemicals such as withanolides (Withanolide D & Withaferin A and obtained from roots and leaves respectively), Alkaloids etc. *Withania somnifera* used in the traditional medicinal system for treatment of many diseases. Also withaferin A reports shows that it inhibits angiogenesis and hence provides protection in various types of cancer (Verma et al., 2010).

A number of alkaloids like withanine and somniferine are obtained from *Withania somnifera* which posses medicinal properties along with sugar(reducing) phytoestrol, ipurandl and mixture of (saturated and unsaturated) acids are present in different parts of plant (Bharti et al., 2016). Leaves of Ashwagandha contains withanolides E, F, G, H, I, J, K, L and M, steroidal Lactones, somnital glucose, inorganic salt and withanone. Roots contain pyrazole alkaloid withasomine. Leaves contain dihydroxy kaempferol-3 rutinoside; 3-6 rutinoside and rutinoside-7 glucoside (Javaid et al., 2018) (Kandil et al., 1994). Seeds contain Withanolide C-28 and withanolid WS-1. Bark contains withanolid (withasomnilide, Somniferanolide, Somnifera-withanolide, Withasomniferanalide and somniwithanolide) (Verma et al., 2010).

Being a multipotent medicinal herb it performs many functions in treating various diseases. This plant act as marvelous tonic, stimulant; prolonged medication of *Withania somnifera* helps improve weight gain, liver weight and anti-stress effect (Uddin et al., 2012). It shows analgesic activity (Sahni et al., 1995) due to 5-hydroxy-tryptamine and also protects from the activation of GABA inhibitory receptors (Mehta et al., 1991); (Kulkarni et al., 1996). Used to combat anxiety and depression; immunostimulatory properties (Bhattacharya et al., 2000). High levels of cytochrome P-450 and cytochrome b5 posses' hepatoprotective effect.

S.No.	Part of the *Withania somnifera* plant	Phytochemical obtained	Reference
1.	Stem	Tannins, flavonoid	(Azhar et al., 2014)
2.	Leaves	Withanolide, alkaloids , Fatty acids	(Alagesan et al., 2019), (EL-Hefny et al., 2020)
3.	Root	Pyrazol, alkaloid,Tannins	(Quadri et al., 2020), (Saraf et al., 2020)
4.	Bark	Withasomnilide, somniferanolide, free amino acids	(Ansari et al., 1997)
5.	Shoot	Crude protein, calcium, scopoletin	(Qamar et al.,2012)

SYMPTOMS OF DISEASES

Hepatitis refers to liver inflammation majorly it is caused of viral infection. During hepatitis various degenerative processes occur such as fatty degenrations, necrosis etc. hepatitis is either infectious; non-infectious or toxic (Mehta et al., 2020) Hepatitis A type of liver disease is caused by (HAV) hepatitis A virus. It spreads when unvaccinated person injests contaminated food or water with feaces of an infected person with poor sanitary conditions. Symptoms can range from mild to severe; which includes pyrexia, anorexia, diarrhoea, nausea, malaise, abdominal discomfort, jaundice, dark colored urine. The severity of this disease is more prevalent in old age groups and adults as compared to children (Liang et al., 2009)."Hepatitis A." *StatPearls [Internet]* (2020)]. Hepatitis B virus: it is caused by HBV (hepatitis B virus) common cause for various liver diseases and liver cancer. In this condition the patient shows signs and symptoms of fatigue, nausea, jaundice and rarely to acute liver failure (Liang et al., 2009). Hepatitis C: it is caused by Hepatitis C virus. Chronic hepatitis C is many a times asymptomatic but it can cause damage to the liver upto high extent acutely symptomatic can suffer from fever, fatigue, nausea, vomiting, erythema, spider nevi, parotid enlargement, gynaecomastia, temporal muscle wasting, hepatosplenomegaly, ascites, (Modi et al., 2008). Hepatitis D: chronic hepatitis is aggressive type of viral hepatitis which increases the risk of cirrhosis of the liver cells, liver decompensation and hepatocellular carcinoma, anorexia,fatigue,lethargy (Farci et al., 2012). Hepatitis E: infection with HEV leads to an acute self limiting infections which are generally asymptomatic. Majorly it includes symptoms like jaundice, anorexia, hepatomegaly, pruritus, arthralgia, nausea, malaise, vomiting, abdominal pain,rare cases of acute liver failure (Kamar et al., 2014). PBC- is a cholestatic, chronic &

autoimmune. Clinical features of Primary biliary cholangitis includes pruitus, fatigue, osteopenia, osteoporosis, xanthelscema, hypercholesterolemia, cirrhosis and in harsh conditions can lead to failure of the liver (Sylvestre et al., 2003). primary sclerosing cholangitis (PSC) can cause chronic cholestatic fibroin flammatory liver disease characterized by progressive and multifocal fibrosis of the biliary system; which can lead to fibrotic liver disease and cirrhosis; IBD(Inflammatory bowel disease). It can increase the risk of cholangiocarcinoma(CAA), hepatocellular carcinoma (HCC), Gallbladder carcinoma(GBC), colorectal carcinoma(CRC) (Fricker et al., 2019). Liver cancer: is the 7th common type of cancer diagnosed & is considered as the (3rd leading cause) of death (Yan et al., 2020). It is common malignant tumor. Primary liver cancer is associated with liver cirrhosis; aflatoxin; viral hepatitis; and other environmental factors. Clinical features observed during liver cancer are; severe pain in abdominal region, weight loss, weakness, hepatomegaly. Bile duct cancer: bile duct tumors are also known as extra hepatic biliary tract tumors. It can be classified majorly into 2 types intrahepatic tumors and extrahepatic tumors. Distal and peripheral BDT (bile duct cancers) can cause BTO (biliary tract obstructions); jaundice; abdominal pain; pyrexia; weight loss; pruritus (Farnell et al., 2013) Liver cell adenoma: is a type of benign epithelial liver tumor. It is an encapsulated liver tumor which lacks bile ducts. Symptomatic patients can be with pain in the upper right quadrant; also bleeding inside the liver is being observed and these are attributed to cholecystitis. LFTs can be abnormal; necrosis can be observed. During the condition of liver cell adenomatosis levels of alkaline phosphatase gets elevated (Barthelmes et al., 2005) Hemochromatosis- is a genetic or acquired disorder in which amount of iron gets overloaded. In this condition individual can be both symptomatic or asymptomatic; symptoms can be general or organ related. Also problems like arthralgia and fatigue; arthritis or fibromylgia. Also if this problem is not diagnosed soon; iron can accumulate in high amount which can lead to hyperglycemia, hyperthyroidism, abnormal liver function, pain in abdomen, loss of sexual desire or libido, heart palpitations, weakness, hyperpigmentation(i.e. slightly grey coloration is being observed in the skin), hairloss (Allen et al., 2010). Hyperoxaluria: primary hyperoxaluria, is an (autosomal) rare disorder which is observed by deficiency in vitamin B6 dependent hepatic peroximal enzyme. It is categorized by nepheolithiasis; renal damage; pain in groin region, nausea, blodd in urine, vomiting, pain while urinating, fever/ chills, smells bad or cloudy while urinating (Bhasin et al., 2015). Wilson's disease (hepatolenticular degeneration), is an autosomal recessive disorder caused by ATP7B gene mutation. It is a disorder of copper(Cu) metabolism. Symptoms observed are impaired motor movements; involuntary movements, peristalsis, cone dystrophy, tremors, oropharyngal dysfunction, mental retardation, liver dysfunction, chronic hepatitis, chirrhosis, hepatic encephalopathy; fulminant hepatitis (Liu et al., 2017). Alpha -1 antitripsin deficiency: is a genetic disease caused by homozygocity of Z mutant. Z mutant Gene regulates Z protein (in liver); which gets abnormal during biogenesis and gets accumulated intracellularly Due to accumulation of Z protein in the hepatocytes various problems can be observed such as liver injury, hepatocellular carcinoma, cirrhosis, chronic hepatocellular apoptosis, regeneration, end organ injury (Teckman et al., 2014). ALD (Alcoholic Liver disease): primary site of ethanol metabolism is liver. Over consumption of alcohol in the body leads to severe tissue damage of the liver; which can further give rise to hepatic lesions; hepatitis; fibrosis/cirrhosis ; statosis; steatohepatitis(inflammation in the liver cells). Due to Alcoholic liver disease (ALD), Reactive oxygen species (ROS) levels increases in the body; shortage of protective mediators, excess production of cytokines (Basra et al 2011). Drug overdose- During impairement in the liver functions there is need for medication. Drug should be consumed in adequate amount at adequate intervals because due to improper consumption liver can get adversely affected. It can cause analgesia, constipation, sedation and sudden encephalopathy, sedation and sudden encephalopathy in patients with liver failure (Hassan et al .,2016). ALF: hepatic failure is observed by jaundice; hepatic encephalopathy; abrupt onset in absence of pre exist liver disease. ALF (this term is used during the development of severe hepatic dysfunction with six months of the onset of symptoms) is characterized in patients suffering from viral hepatitis (Shakil et al., 2000). Acute liver failure is the condition from jaundice to encephalopathy along with cerebal oedema (Bernal et al., 1999) NAFLD (Non alcoholic fatty liver disease) is a range of liver conditions which act on people who drinks little to no alcohol; and extremely high fat gets stored in the liver cells. NAFLD when gets aggressive can lead to nonalcoholic steatohepatitis (NASH) which is diagnosed by liver inflammation, liver cirrhosis and liver failure. Symptoms it includes are Fatigue, abdominal swelling (ascites), enlarged spleen, red palms, jaundice, pyrexia,large blood vessels, discomfort in right abdomen, fibrosis (Kellerman et al., 2018).

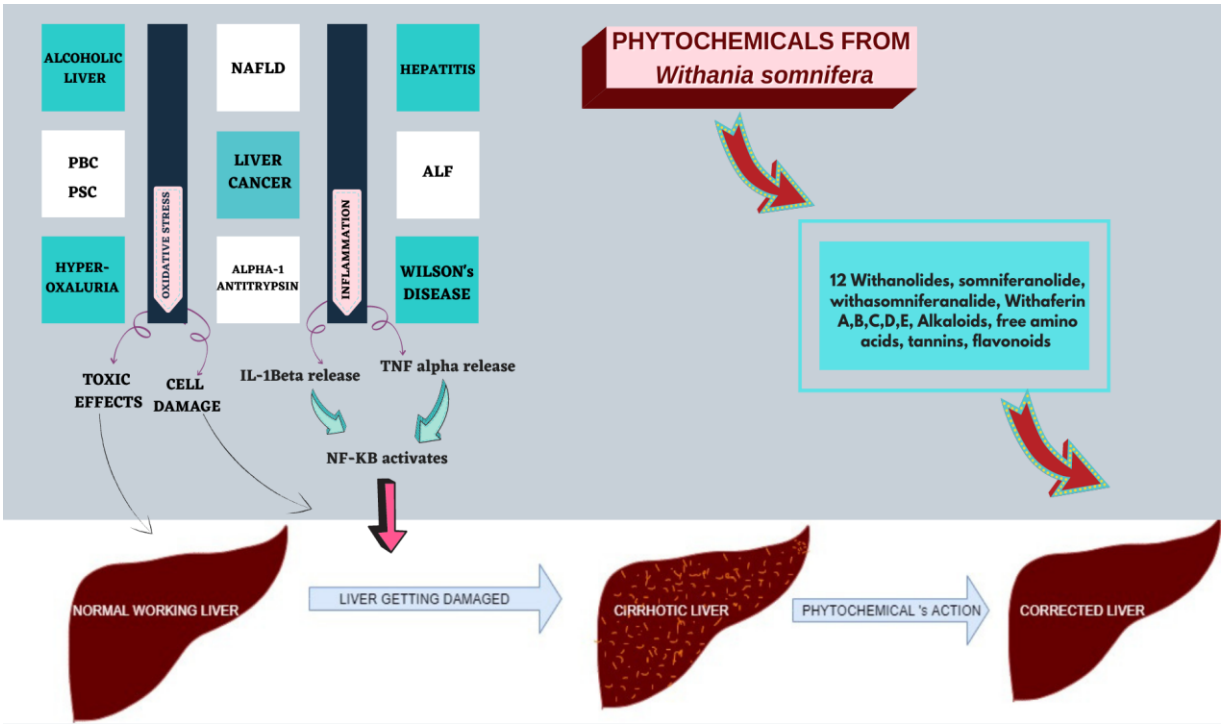
PATHOLOGICAL MECHANISM

Due to several biochemical reactions results in highly reactive free radicals(ROS –Reactive oxidative species). ROS attacks the membrane lipids which causes lipid peroxidation; alters permeability thus in turn causes tissue injuries. Due to hepatic tissue damage liver functions gets affected which shows deleterious effects on human length. This management of liver disease is the major challenge to modern society but use of antioxidants have been proposed as theirapeutic agent in order to counteract liver damage. Although, our body has naturally inbuilt antioxidant as SOD (superoxide dismutase), CAT (catalase), and tissue gluthione(GSH) protects tissues of the body from damage of free radicals the excessive release of reactive oxidative species (ROS)

overcome this inherit system which leads to liver damage due to which external supplementation is required through phytochemicals (Wang et al., 2015). Cirrhotic liver is the culminating pathologies outcome of various liver diseases. Cirrhosis of liver is fulfilled by convoluted network (signaling pathways mediated by cytokines) which in turn regulates fibrogenesis and HSCs (Hepatic stellate cells) (Schuppan et al., 2008). PDGF (Platelet-derived growth factor) is the powerful mitogen to HSCs (Hepatic stellate cells). These are of 4 types PDGF (A,B,C and D) (Martin et al., 2013) PGDF receptors are overexpressesive in tissues which are fibrous; activity increases with increase in liver fibrosis Different types of damages to hepatocytes can induce kuffer cells which in turn secreates PDGF. PDGF activates various signaling molecules and transcription factors which activates genes. It upregulates MMP(2,9), TIMP-1 expression. It inhibits collagenase activity. PDGF(B,D) are important isoforms in PDGFR (PDGF receptor), in hepatic stellate cells(beta signaling), Platelet derived growth factor beta autophosphorylates and activates ERK½ (extracellular signal- regulated kinase), JNK (C- JunN- terminal kinase), MAPK (p38 mitogen- activated protein kinase); PK (protein kinase) B/A kt pathways . PDGF-D activates Hepatic Stellate Cells and bring mitogenic and fibrogenic effects into play; thus plays crucial role in remodeling of the matrix during liver fibrosis (Zhoug et al., 2014) TGF-b is powerful inducer in hepatic fibrosis known. It is formed by myofibroblasts LSECs, Kupffer Cells and hepatocytes. It initiates and maintains liver fibrosis. The TGF-b1 level increases in liver (fibrotic) and reaches maxima at cirrhosis. The primary effect of TGF-b 1 is that it stimulates the activation of HSCs which provides supportive feedback for the progression of liver fibrosis. Also it induces apoptosiis acceptable for loss of tissue and for the progression of liver fibrosis. Also it induces a decreases liver size in cirrhosis (Zhou et al., 2014) Tumor necrosis alpha factor it is mainly produced by monocytesmacrophages, Hepatic Stellate Cells and Kupffer Cells. It has proinflammatory activites and cytotoxic effects. Its major role is in activation of HSCs [Connolly et al., 2009). Also it synthesizes ECM. It reduces the spontaneous apoptosis which activates Hepatic Stellate Cells by upregrading the antiapoptic factor such as NF-kB, BCL-XL and p21

Hepatic Stellate Cells by lowering glutathione and inhibiting pro-collagen alpha 1 expression.

Interferon are soluble extracellular signaling molecule.



IFN-alpha and beta are synthesized by leukocytes in response to various infections whereas IFN-y is secreated by T cells various antigens and mitogens. Inter feron gamma receptor led to low production and collagen deposition, fibronectin, laminin,& pro- collagen type-1 in liver (Wang et al., 2017). TNF a signaling – precursor form & soluble form of TNF a can transmit downstream signal through joining TNFR 1 and TNFR 2 is activated by precursor form (Naismith et al., 2000). TNFR 1 in cytoplasm contains death domain & TNFR 2 locks mtif. Trimeric TNF a binds to TNFR 1 leadas to trimerization of the receptor. Complex 1 is being formed by TNFR1 – TRADD, several E3 ligases, Receptor interactivr kinase 1 (RIP 1), TNFR linked factor 2 and 5, cellular inhibitor of apoptosis ½ (cIAP ½) and dimeric linear ubiquitin chain aseembly complex(LVBAL). In complex 1, the Lys 63(K 63)- linked polyubiquitnation of R1P1 by CI APS induces the recuirment of the TGF-b (transforming growth factor beta) TAK 1 (activated kinase 1)- TAK 1- through TAB 2 it recruits Ik B kinase (IKK) complex

containing two catalytic alpha and beta subunits also referred as NF-kB essential Modulator (NEMO). TAK 1(activated) phosphorylate IKKBeta & then phosphorylates and degrades IkB alpha. NF-kB homo or heterodimerase released from NF-KB-IKB alpha complex and translocates into nucleus phosphorylated TAK 1 activates MAPK pathways phosphorylation-dependent manner. TRAF 2 and RHP1 are required for TNFR 1- mediated JNK (C-Jun N-terminal Kinase) activation. Complex –I components like A20 cylindromatosis (CYLD) induces disassembly of complex-1and then cytosolic complex 2 at or complex 2 b is formed. Complex 2 a comprises TRADD, FADD (FAS- associated death domain protein), caspase- 8 and RIP 1, which activates various cascades, lead to apoptosis (Yang et al., 2015).Cytokines group (interleukins) expressed by leukocytes, also can be observed in CD4 T lymphocytes, macrophages, endothelial cells, monocytes. They play major role in liver fibrogenesis.They are secreted in larger concentrations during various types of immune responses and inflammatory reaction is in accordance with cytokines productions (Tacke et al., 2014). Interleukin 6 – is an proinflammatory cytokines associated with inflammatory disorders. Serum and intrahepatic levels of IL-6 elevates in chronic liver disease (Tacke et al., 2009). It gets directly bind to hepatocytes. It promotes JAK pathway JAK1 and JAK2 and tyrosines. It plays important role in liver cancer. It protects during hepatic fibrogenesis. Accordingly to research systematic IL-6 injection and transplantation of mesenchymal stem cells(MSCs) which is intrahepatic helps in reduction of hepatocyte apoptosis and liver fibrogenesis after CCl4 treatment (Nasir et al., 2013). Interleukin 13 is a Th 2 effector cytokine provides protection against allergic disorders. It is linked with fibrosis progression and produces TGF beta, collagen etc and other fibrosis associated genes (Tacke et al., 2014)

THERAPEUTIC APPROACHES

Withania somnifera contains various types of phytochemicals steroidal lactones {Withanolides), withaferins, withaferin-A, Withasomnidienone, withasomnierose(A-C), withanones} alkaloids(isopelletierine, anaferine, Cuseohygrine, anahygrine) , (Sankar et al., 2007). Ashwagandha contains active nutraceutical plant based ingredient protandium which activates Nuclear factor erythoid-derived 2-like 2(Nrf) (Scalzo et al., 2014). NAFLD is a progressive disorder arises due to lipid accumulation in hepatocytes (Satapathy et al., 2015). Nearly,1/3rd of the patients with non-alcoholic steatohepatitis(NASH) i.e. inflammation and cirrohosis (Finelli et al., 2013). studies indicate that reactive oxidative species(ROS) and electrophoresis are linked with NASH pathogenesis which leads to induction of Nrfthus prevents and treats NAFLD (Masarone et al., 2018). The major therapeutic function of Nrf2 is that it activates osteocalcin which in turn improves NAFLD by decreasing ROS levels (oxidative stress) and inhibits Janus-N-Terminal pathway (Zhang et al., 2016). The activites of AST(Aspartate aminotransferase),ALT(Alkaline phosphatase) in serum When observed significantly increased in acetaminophen treated groups in comparison with normal groups. The increased levels of liver marker enzymes can lead to hepatic cell damage but *Withania somnifera* prevents alteration (Sabiba et al., 2013). Antiinflammatory & Antioxidant activites of *Withania s.* is mediated through subduing of the TNF-a, Cox-2 , IL-b and iNOS in order to protect liver (Kandhare et al., 2016). The chemical compounds of *Withania somnifera* is capable for making this plant as anti-biotic and hepato-protectant in atmosphere. This can be assured by GC-MS (Gas chromatography and Mass spectrometry). Also phytochemical obtained from Ashwagandha are responsible for multi-therapeutic approaches in various disorders such as liver cirrhosis (Mishra et al., 2020). Study by Sultana et al., 2012 shows that root extracts of *Withania somnifera* on (liver marker enzymes) such as Aspartate aminotranferase and ALT in gentamicin induced toxicated rats. This study was conducted between year July 2010 to June 2011 in SSMC, Dhaka. In this Hepatic damage was shown in wistar male rats which were treated with gentamicin and the levels of serum AST(Aspartate aminotranferase) ,ALT(Alanine Transaminase) and BIL were elevated. Also, the weight of liver was higher but in rats which were pretreated by *Withania somnifera* root extract and gentamicin it significantly lowers levels of serum AST and ALT which shows hepatoprotective action against gentamicin induced toxicity. Withaferin A at 10mg/Kg shows effective protective action against CCL4-induced hepatotxicity in rats (chaudhary et al., 2020), (Rastogi et al., 1998).

Study conducted by Nile, Shivraj Hariram et al.2019 the withaferin A shows highest anti-oxidant; cancer cell cytotoxicity and inhibitory activity of enzyme as compared to others. It also act as angiogenesis potent inhibitor with anti-cancer activity (Yang et al., 2013). It also shows that with withanolides obtained from ashwagandha are considered to have hepatoprotective action. The liver gets damaged due to high levels of serum enzyme such as ALT, AST these are observed in paracetamol treated mice which damages the structure of the liver. It has been observed that the root extract of *Withania somnifera* helps in lowering the levels of increased levels of serum marker enzymes (AST,ALT,ALP and bilirubin levels). Also, Ashwagandha possess antioxidant properties (Pandey et al., 2013).Production of reactive oxidative species(ROS) and glutathione reduction are major players in Acetaminophen(AAP) induced toxicity (Olaleye et al., 2010). This is obtained from the depletion of antioxidant status i.e. catalase, superoxide dismutase, reduced glutathione, and glutathione-S-Transferase of paracetamol intoxicated rats. Here, Ashwagandha restores the levels of antioxidant which provides protective action in Acetoaminophen(AAP) mediated liver injury. This was conformed by obtaining

histopathological results and hence *Withania somnifra* provides promising hepatoprotective and anti-oxidant action(Sabiba et al., 2013) In *Withania somnifera* leaf extract treated group; significant decrease is being observed in the levels of AST and ALT as compared to infected group from Table 4- (El-Boshy et al., 2013).The AST and ALT increases in infected non-treated groups to other groups which indicates about speticemic effect of bacteria; these results are in accordance with hepatic infection induced in animals and hence for table 4 it was observed that there is no significant change in (biochemical) parameters, BIL T, total protein, Albumin cholesterol, Globulin, in groups treated with *Withania s.* No side effect or toxicity was present and is thus safe for use in human(s) for various acute treatments and chronic treatments (El-Boshy et al., 2013).

S.No.	NAME OF THE PHYTOCHEMICAL	TYPE OF STUDY	OUTCOME	REFERENCE
1.	Withaferin A	In vitro	Anti cancer activity	Yang et al., 2007
2.	Alkaloids	In vitro	Lowers the levels of AST,ALT and hepatoprotective action	Sultana et al., 2012.
3.	Withania somnifera extract	In vivo	Prevented hepatic cell damage	Sabiba et al., 2013.
4.	Root extract	In vitro	Lowers the levels of AST,ALT	Malik et al., 2013.
5.	Leaf extract	In vitro	Antioxidant properties	Khalil et al., 2011.

SUMMARY

From the above description we summarized that various phytochemicals obtained from *Withania somnifera* such as Withaferins, Withanoloids, Flavonoids, Tannins, Alkaloids, Amino acids etc. provides hepatoprotective action especially in case of liver cirrhosis by correcting liver marker enzymes(AST,ALT). Along with that it provides immunomodulatory and antioxidant properties. Thus improves overall health of the liver.

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