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Multiple Effects of Withania Somnifera: A Review Article

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ABSTRACT

Withania somnifera (WS) belongs to family "Solanaceae" is a highly valuable medicine plant. It has tremendous effects in promoting physical as well as used for various disorders of human being. It is a natural source of withanolides (Withaferin A & Withanolide A), which are steroidal lactones and are used for various ailments. This review explains botanical description, photochemistry, pharmacological studies and metabolite profiling of *Withania somnifera.*

Key words: *Withania somnifera*, Photochemistry, Medicinal plants, Withanolides

1. INTRODUCTION

Withania somnifera also known as “Ashwagandha”, has twenty-three known species.

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Among these species, *Withania somnifera*is economically important because of their therapeutics effects [1]. Beside all its uses it has a drawback, when cultivated commercially, it is related with two main problems. The first problem is variation of plants between each other because of soil fertility and having less quantity of chemical constituents. Secondly and the major problem is planting and harvesting, which is about 4 to 5 years [2].

Botanical Description of *W.somnifera*

S.No.	Description	*Withania somnifera*(L.) [3]
1	Habitat	Undershrub
2	English name	Winter cherry, Indian ginseng
3	Vernacular name	Ashwagandha
4	Leaves	Alternate, sub-acute, entire margins, broadly ovate
5	Flowers	Hermaphrodite
6	Calyx	Persistent, gamosepalous, 5sepals enlarges with fruit, enclosing the fruit partially or completely
7	Corolla	Campanulate greenish yellow with 5 petals
8	Androecium	Broadly ovate anthers(1.2mm)
9	Gynoecium	Ovide ovary
10	Style	Filiform
11	Stigma	Two lamellate
12	Fruit(berry)	Spherical and enclosed in calyx
13	Seed	Spherical

1.2. PHYTOCHEMISTRY

Several studies on the chemistry of Withania species shows that they are rich of many flavonoids, alkaloids, tannins and steroidal lactones has been isolated from *Withania somnifera* [4]. Approximately more than 138 withanolides, 13 Alkaloids and some of the sitoindosides have been isolated from the roots and aerial parts of withania species [5]. Withanolides are the main chemical constituent of withania

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species, that are present almost in a concentration of 0.001-0.5 of total dry weight [4]. The structure of withanolides are formed from C28-Steroidal lactones, which is oxidized at carbon no.22 and carbon no.26 to form ring structure (lactone rings)[6]. The withanolides skeleton is belong to steroidal lactone, 22-hydroxyfurost-26-oic acid γ-lactone. By changing side chains, we can get different structures of anolides. Withanolides and ergostane-type steroids contain a C8 or C9 side chain with a five or six membered of lactone or lactol ring that fused to the carbocyclic core via a C–C bond or an oxygen bridge [7,6].

Withaferin A and a unique thio-dimer called ashwagandhanolide is the major chemical constituent of *W.somnifera.* [8]. From roots of *W.somnifera* isolate five new withanolides derivatives with fourteen known compounds. Recently, a new withanolide has been find out from *W.somnifera.* The nomenclature of this chlorinated withanolide is 6a-chloro-5b,17a-di-hydroxywithaferin-A[9].

Figure1. Leaves of W.somnifera

Seeds of W.somnifera

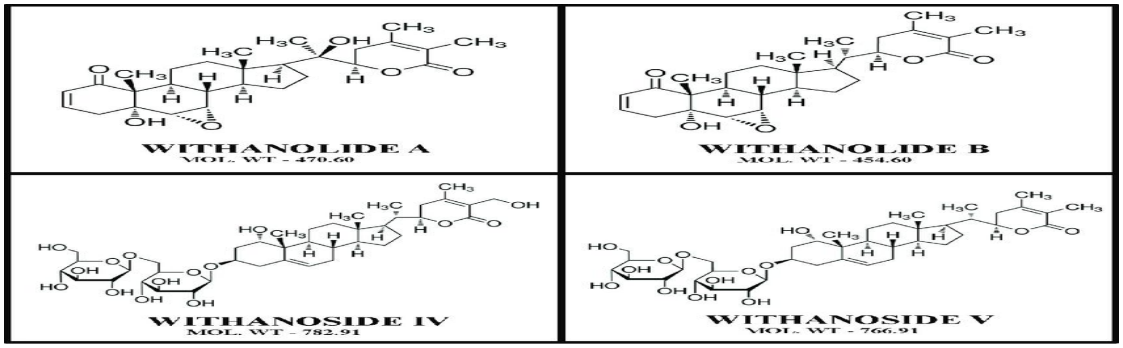

Figure 2. Chemical Compounds of Withania somnifera

2. METHODOLOGY

Search engine, Google scholar and PubMed were searched for data collection. During the searching of search engines, sixty (60) research papers were found and

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among all searched, only forty five (45) were included in the current study. The remaining fifteen (15) were excluded due to improper information regarding the *Withania somnifera.*

3. Pharmacological Potential of Withania Somnifera

The chemical constituents extracted from *Withania somnifera* possess a great importance because of their extensive use. These biologically active chemical constituents are Alkaloids like cuscohygrine, ashwagandhine, anahygrine, tropine. Some steroidal compounds of *W.somnifera*are "ergostane-type steroidal lactones, withasomniferols A-C, withaferin A, withanolides A-Y, withasomniferin A, withanone, withasomidienone [10]. The main active chemical withanolidal are Withaferin A (4-beta,27-dihydroxy-5-beta,6-betaepoxy-1-ocowitha-2,24-dienolide) and withanolide A (5α,20α dihydroxy 6α,7α-poxy-1-oxowitha-2,24-dienolide) are isolated from plant. Chemically they are similar but have different chemical constituents [11].

3.1. Anti-inflammatory Effects

Several workers studied the anti-inflammatory effect of *W.somnifera.* Anbalagan and Sadique conducted a comparative of hydrocortisone (anti-inflammatory) and *W. somnifera* that explained that *W. somnifera* possesses anti-inflammatory activity.

Begum and Siddique (1987) studied the effects of *W.somnifera* on glycosaminoglycan synthesis in the granulation tissue of carrageenan-induced air pouch granuloma. A comparative study of hydrocortisone, phenylbutazone and root powder of *W.somnifera*(administered 1000 mg/kg orally). This study shows that sample of *W.somnifera* significantly reduced glycosaminoglycan as comparative to phenylbutazone and hydrocortisone[12].

Al-Hindawi *et al.*, (1992) conducted a study that methanolic extract of *W.somnifera* shows significant anti-inflammatory effects compared with hydrocortisone sodium succinate. The anti-inflammatory activity is due to the high concentration of Withaferin A [13].

3.2. ANTICANCER AND CHEMO PROTECTIVE EFFECTS

Various research studies explained that *Withania somnifera* has anticancer effect [14-17]. A study done by (parkash *et al.*,2002) shows that the root extract of

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*W.*somnifera shows significant decline in average number of skin lesions in skin cancer in mice [17]. A study of palyi et al, in 1969 showed that withaferin A also inhibit the growth of roots of Allium cepa by arresting the cell division at metaphase. *W.somnifera* also shows anticancer effect of lungs adenoma in albino mice induced by urethane [18].

3.3. HEPATOPROTECTIVE ACTIVITY

Mohanty *et al* conducted a study in 2008 that explain the Hepatoprotective effect of root powder of *W.*somnifera by influencing the levels of lipid per oxidation [19]. In 2009, verma *et al* conducted a study on aqueous root extract of *W.somnifera* which contains different flavonoids and neurotransmitters have beneficial effects on hepatic cells of Clarias batrachus by stimulating the neuroendocrine system which leads to hyperactivity of endomembrane which causes exocytosis. [20].

3.4. IMMUNOMODULATORY ACTIVITY

(Bahr and Hansel, 1982) studied the immunomodulatory effects of Withaferin A. It shows that Withaferin A have both immunoactivating as well as immunosuppressive activity. Immunosuppressive activity is seen against antigen recognition and proliferative capability of lymphocytes B and lymphocytes T [21].

3.5. ANTI FUNGAL AND ANTIBACTERIAL ACTIVITIES

Withanolides extracted from Ethanolic extract of whole plant shows Anti-fungal and anti-bacterial activity. The oral administration of methanolic extract of plant shows increase survival rate and less bacterial load against Salmonella infections in mice [22]. A study done by (Arora *et al.*,2004) reveled that menthol hexane and diethyl ether extract of roots and leaves of *W.somnifera* shows antibacterial effects against Salmonella typhimurium and E.coli by agar plate disc-diffusion assay [23].

3.6. HYPOCHOLESTEROLEMIC AND HYPOLIPIDEMIC ACTIVITIES

It has been reported that root powder of *W.somnifera* decreased cholesterol, triglycerides nd total lipids in hypercholesteraemic animals [24]. *W.somnifera* increases the bile acid synthesis which in turn increases the elimination of body cholesterol [25].

3.7. CENTRAL NERVOUS SYSTEM ACTIVITY

Withania somnifera and their species are commonly used in various nervous system

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disorders like epilepsy, catalepsy, sleep, anxiety and depression [26,27]. The plant extract has the ability to modulate neurotransmitters. In hippocampus, it suppresses the corticosterone level and increasing the cholinesterase activity, which in turn increases the level of serotonin. The relevant study revealed that withanolide A and withanoside 4 are capable of promoting new neuronal projections [28]. Sehgal *et al.*, explained in 2012 that semi-purified root extracts of *W.somnifera* have some significant effects on different brain aliments by increasing LDL related protein in micro vasculature of liver and brain. It has capability to reverse some behavioral defects, β-amyloid peptide accumulation, plague pathology, and accumulation of oligomers in middled-aged Alzheimer's disease mice [29].

3.8. FREE RADICAL SCAVENGING ACTIVITIES

In 1998,Dhuley conducted a study on lipid per-oxidation activity on stress induced rabbits and mice. The oral administration of *W.somnifera* aqueous root extract decreases lipid per oxidation activity by scavenging free radical [30].

4. DISCUSSION

Withanolides are the principal chemical constituents of the WS. Withaferin A & Withanolide A are the derivatives of withanolides. There are many scientific evidence-based studies were performed that explain that WS have anticancer, anti-inflammatory, antifungal, hypo-cholestrolemic, antioxidant, antibacterial, immunoregulatory and hepatoprotective effects [31]. Moreover, the phytochemical compounds of WS have antidiuretic, cytotoxic, sedative, antitussive, leishmanicidal activity [31].

Singh *et al* explained the anticancer activity of WS that withaferin A induces the reactive oxygen species (ROSs) and causes mitochondrial dysfunction that triggers apoptosis in the cancer cells [32]. The COX-1 and COX-2 convert arachidinic acid to prostaglandins (PGs) which causes inflammation in the body tissues. Jayaprakasam & Nair reported that withanolides inhibit the COX-2 enzyme and stop the prostaglandins which causes inflammatory response [33]. Pramanick *et al* reported in 2008 that *W.somnifera* contain "withanolide Z" which has inhibitory effects against DNA topoisomerase I, therefore, withanolide Z has leishmanicidal activity against Leishmania donovani [34].

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5. CONCLUSION

The plants, animals and minerals are the most common sources of the drugs. Among these sources, the plants are the abundant source of the medicine (crude drug). Metabolic pathway produces primary and secondary metabolites in the plants. These metabolites are alkaloids, terpenes, isoterpenes, phenols, flavonoids, terpinoids, saponins and glycoside. These metabolites or bioactive natural products having various pharmacological activities and has the ability to prevent different diseases. *Withania somnifera* contains primary and secondary metabolites used against various diseases. Chemical constituents of *Withania somnifera* are withanolides, withaferin A, withaferin B, isopelletierine, anaferine, Sitoindosides (sitoindosides VII-X), cuseohygrine, anahygrine, 5-dehydroxy withanolide-R, withasomniferin-A and acylsterylglucosides. These bioactive molecules are useful for various ailments such as parkinson's, osteoarthritis, arteriosclerosis, huntington's, arthritis, alzeimer's disease, rheumatoid, hypertension, neuronal disorders (diabetes) and cancers.

6. FUTURE PROSPECTIVE

W.somnifera is highly valuable plant, and contains many important chemical constituents. These compounds have important role in various diseases and can be used in pharmaceutical industry because of its wide range of use. Further evaluation are needed to explore the various aspects such as identification, isolation and structure elucidation, mechanism of action, side effects and contraindications of the phytochemicals of *W.somnifera*.

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