A Review on Phytochemistry and Pharmacological Activity of *Asparagus racemosus*

By

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A thesis submitted to the Department of Pharmacy in partial fulfillment of the requirements for the degree of
Bachelor of Pharmacy (Hons.)

Department Of pharmacy
Brac University
December 2020

Declaration

It is hereby declared that

1. The thesis submitted is my own original work while completing degree at Brac University.
2. The thesis does not contain material previously published or written by a third party, except where this is appropriately cited through full and accurate referencing.
3. The thesis does not contain material which has been accepted, or submitted, for any other degree or diploma at a university or other institution.
4. I have acknowledged all main sources of help.

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Approval

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Ethics Statement

This study does not involve any kind of animal or human trial.

Abstract

Medicinal plants play a significant role in formulation of medications. *Asparagus racemosus* is one of the ancient medicinal plants with a lot of therapeutic values. This is a traditional medicinal plant belongs to the plant family Liliaceae. This review article focuses on the pharmacological activity and therapeutic potential of the plant *A. racemosus*. Phytochemicals of these plants have shown important therapeutic activities such as; antiulcer, antioxidants anticancer, antimicrobial, anti-inflammatory, anti-toxic, diuretic gastroprotective and many other activities. Moreover, this plant extract plays a significant effect in male & female reproductive systems. This review is basically a comprehensive overview of traditional applications, current knowledge on the phytochemistry, pharmacology, various formulations and adverse effect of *A. racemosus.*

Keywords: *Asparagus racemosus;* Saponins; Phytochemicals; Antiulcer; Antioxidant; Phytoestrogen

Dedication

Dedicated to my parents and family members for their enormous support till the end.

Acknowledgements

I would like to express my deep and sincere gratitude to my research supervisor Ma'am, Dr. Farhana Alam Ripa, Assistant Professor, Department of Pharmacy, Brac University, for giving me the opportunity to do research and providing invaluable guidance throughout this research. I am also deeply thankful to our Chairperson Dr. Eva Rahman Kabir Ma'am, academic coordinator Dr. Hasina Yasmin Ma'am and all the respected faculty members of the Department of Pharmacy at Brac University for their invaluable help and support. I also gratefully acknowledge the support of the library staffs & laboratory assistants of Brac University for their cooperation in keeping us updated with the arrival of new materials. I am mindful and thankful to all my friends of my University for their cooperation at every stage which assisted me to overcome the hurdles. Finally, gratitude goes to my beloved parents for their uncountable love & support throughout every stage of my life.

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List of Acronyms

MAO	Monoamine Oxidase
GABA	Gamma-Aminobutyric Acid
FST	Forced Swim Test
TST	Tale Suspension Test
OFT	Open Field Test
EMP	Elevated Plus Maze
AST	Aspartate Aminotransferase
ALT	Alanine Aminotransferase
DEN	Diethyl nitrosamine
KA	Kainic Acid
SSRI	Selective Serotonin Reuptake Inhibitor
SNRI	Serotonin-norepinephrine reuptake Inhibitor
DDT	Dichlorodiphenyltrichloroethane
GSH	Glutathione
GPx	Glutathione peroxidase
HCT116	Human Colon cancer cell lines
DMBA	7,12-Dimethylbenz[a]anthracene

Chapter 1

Introduction

1.1 Medicinal Plants

The roots, bark, seeds, leaves or any other part of a plant exerts beneficial pharmacological effect and is used for therapeutic, purgative, tonic or any other health related purposes. A significant source of drug is obtained from plant and plant products since ancient times. Initially, the use of medicinal plants was instinctive, as is the case for animals. Ever since ancient civilizations, people have been using plants as remedies for diversified diseased condition. People are mainly dependent on plants for their own life. In the beginning, the use of plants was limited to food, therapeutic use and building house but with the progression of time, the benefit of plants has been investigated for a variety of other purposes. Thus, their reliance on plants has increased both consciously and implicitly. The World Health Organization (WHO) describes medicinal plants as plants containing therapeutic properties or compounds that can be used for therapeutic purposes or for the development of useful drugs by synthesizing metabolites. Modern medicines are seen to be progressively using plant-derived active compounds, and these compounds show a significant connection between their modern medicinal application and the conventional use of source plants (Balandrin, Kinghorn, and Farnsworth 1993).When scientists had grasped the connections between medicine and therefore the body, it became potential to synthesize natural compounds by chemistry. Science and custom have diverged in the 1st edition of the American Pharmacopoeia collection revealed in 1820, where 70% of medicines were plant-based. Within the 1960 version, 5.3% were of plant origin. In comparison with modern medicine, traditional medicines possess a great amount of benefit than modern medicines. Firstly, Traditional medicines tend to sell at lower costs in comparison with the modern medications.

This can be most likely due to the low price of analysis, testing, selling and different production processes. Secondly Herbs have a tendency to own reduced side effects in comparison with the modern medicine. This is often as a result that most medicines are well tolerated by the patients. Another important advantage of herbal medicine is that they have a tendency be additionally reliable and effective for sophisticated and resistant health complications. In cases like arthritis, medicine like Cox-2 inhibitor, Vioxx was used for the treatment and was recalled because it can cause cardiovascular complications; medicinal plants tend to become successive choice. Furthermore, the supply of medicinal plants more compared to the modern medicines**.** *A. racemosus* is a plant inherent to India, Nepal, Sri Lanka, Australia, Africa and East Europe. It prefers to grow in moist, humid and arid conditions. Its surroundings are common in shade at low altitudes and in tropical climates. There are many species of Asparagus seen to be grown in Indian subcontinent. *A. racemosus* is most typically utilized in native medication (Hasan et al. 2016).

1.2 Botanical Description

The plant can grow in a place up to 1500 m of altitude range and present in tropical and subtropical regions. The plant is under-shrub and rise up to 3 meter in height. It is an herb that bears spine like numerous luscious short rootstocks. The roots are stretched, tuberous brown in color with tapering ends at both sides which is 1-2 cm in thick and 25-90 cm long that appears ash silver white color both inside and outer surface. The plant is a woody climber known as liana bearing brown or may be whitish to grey colored and small protective spines (Choudhary and Sharma 2012). The leaves resemble like pine needles and the flowers are uniform and small in size which looks white in color having small spikes. The flower is hermaphrodite in nature and mainly pollinated by Bees. The flowering occurs in month of February-March and by the end of April the flowers exert a great aroma with a mild fragrance Fruits are often seen with enticing red berries. Its fruits are little, spherical in form and

changes from green to red color on maturity (Sachan et al. 2012). Further knowledge on microscopic morphology added that there is an elliptical or oval section in the transverse section of the root. Moreover, 5-6 layers of compact unit of the root are called periderm which consists of tangentially elongated phloem. A single layer of phelloderma is accompanied by about 2-3 peripheral layers of cork cells. 6-7 layers of cortical cells follow the phelloderm. In the middle, vascular bundles are arranged and form a circular ring. Protoxylems are arranged toward the center; toward the outer side the metaxylem region is found. There is a broad secondary phloem zone consisting of sieve channels, cells of the companion and parenchyma of the phloem. The secondary phloem is accompanied by a large zone of secondary xylem consisting of vessels, tracheids and xylem parenchyma. Numerous epidermal hairs are found in the epidermal layers (Ahmad et al. 2017).

Figure 1: Plant parts of A. racemosus (MS et al. 2018).

1.3 Taxonomy and Local Names

The plant species called *A. racemosus* is belong to plant kingdom and mainly is a member of Liliaceae or Asparagaceae plant family. The genus Asparagus contains more than 250 species

distributed throughout the world out of which 22 species of Asparagus has been found in India.

Table 1: Scientific Classification of A. racemosus (R K Goyal, J Singh, and Harbans Lal 2003)

Kingdom	Plantae
Division	Magnoliophyta
Class	Liliopsida
Order	Asparagales
Family	Asparagaceae; Liliaceae
Genus	Asparagus
Species	Racemosus

This plant species has various local names in various regions.

Table 2: Vernacular Names of A. racemosus

Region	Name
Bangladesh	Shatamuli
English	Wild Asparagus
Hindi	Shatavari
Gujrat	Shatawari
Nepal	Kurilo
Madhya Pradesh	Narbodh or Satmooli

1.4 History and Traditional Uses

The geographical location, weather and soil condition of south Asian countries, some places of Africa and Europe mainly tropical and subtropical regions are preferable condition for cultivation of various plants including *A. racemosus*. This herb is regionally known as

Shatavari or Shatamuli which means “person with hundred spouses”. The name clearly justifies the ability in wide range of health complications. The herb *A. racemosus* was documented as a useful remedy for certain health complications in Ayurvedic and some other systems of medication like Unani, Siddha etc. *A. racemosus* has been recorded in various documents of Ayurvedic systems as an effective remedy in treatment of madhur rasam, madhur vipakam, som rogam, seet veram, chronic fever and internal heat (Frawley and Jain 1989). Traditional medicine sources enlisted this plant as an effective medication to treat complications like diarrhea, dyspepsia, ulcer, dysentery, tumor, nervous disorders, hepatic and cardiovascular disorders. Similarly, it was regarded as a rejuvenative tonic that improves the internal function of the body like boost immunity, increase stamina, increase longevity, enhance mental function and increase fertility in females. It is regarded as a vigorous tonic for female as it is highly effective in treating various health complications related to female reproductive system thus increasing fertility and vitality in women. Additionally, Ayurveda confirmed this plant’s contribution in lactation after pregnancy and in spontaneous abortion which is justified by modern researches. Moreover, it was noticed to assist in spontaneous abortion. The contribution this plant has brought in female health and reproduction is recorded in two documents of ayurvedic medicine ‘Charak Samhita’ and ‘Asthang Hridyam’ written by Charak and Vaghbata. This plant is claimed to revive body and soul also motivates love and enthusiasm. For this reason, it is recorded as ‘’Queen of herbs’’ in Ayurveda. Numerous researches are performed in current era of technology to ensure the justification of previous usage of different plants including *A. racemosus*. This brings significant advancement in phytopharmacology and creates opportunity to isolate and develop unique compounds for medication with better and greater therapeutic value. Many laboratory researches performed on plant extract of *A. racemosus* brings justification of traditional usage (Karim et al. 2017)**.**

1.5 Rationale of This study

A. racemosus is a plant blessed with a lot of pharmacological activity and also affects the functioning of different organs. There are several studies conducted by researchers to access the phytochemical constituents and pharmacological potential of the plant. Traditionally this plant is enlisted as one of the top remedies in Ayurveda because it has been used to treat several health conditions from ancient times. This plant is blessed with pharmacological activity like anti-microbial, anti-oxidants, anti-ulcer, immune system enhancing, anti-diarrheal, analgesic, anti-inflammatory, antidiabetic and so on. This wide range of activity attracted the researchers to gather more knowledge on the plant pharmacology. Additionally, the chemical compounds that are isolated from this plant like steroidal saponins, carboxylic acid, polycyclic alkaloid and many others indicate the justification of its various pharmacological activities. This review focuses on the knowledge of the plant phytochemistry and pharmacology.

1.6 Aim of the study

This aim of this review is to incorporate a detailed overview on traditional applications, current knowledge on the phytochemistry, pharmacology and toxicology of *A. racemosus*.

1.7 Objective of this study

The objective of this study includes the following:

I. Gathering knowledge on the plant's characteristics, botany, history and traditional application.
II. Enlisting the phytochemical constituents and minerals that are isolated from the plant.
III. Enlisting the Pharmacological activity and adverse effects of the plant parts.
IV. Summarizing the protective activity of the plant on different organs.
V. Include the formulations made by the various plant extracts.

Chapter 2

Phytochemicals

A. racemosus is a plant blessed with wide range of phytochemical constituents including Steroidal Saponins, Carboxylic Acid, Polycyclic alkaloid along with some trace elements.

2.1 Steroidal Saponins

Steroidal saponins are one of the important active constituents of *A. racemosus* and known as shatavarin I and shatavarin IV. These compounds are usually found in the roots of this plant. The group of compounds which consist of steroid alkaloids, triterpennoids and glycosylated are known as saponins. These compounds are also a secondary metabolite and usually found in different type of medicinal plants. These compounds are called saponin because they result in formation of foam in aqueous medium. Steroidal saponins have some roles in human body like they regulate cell cycle, the production of hormones and work as a source of steroids. Moreover, they help in the absorption of protein and the replication of cell. However, the glycosides of asparasaponin are shatavarins having two types of skeletons named spirostanols rhamnose and furostanols.

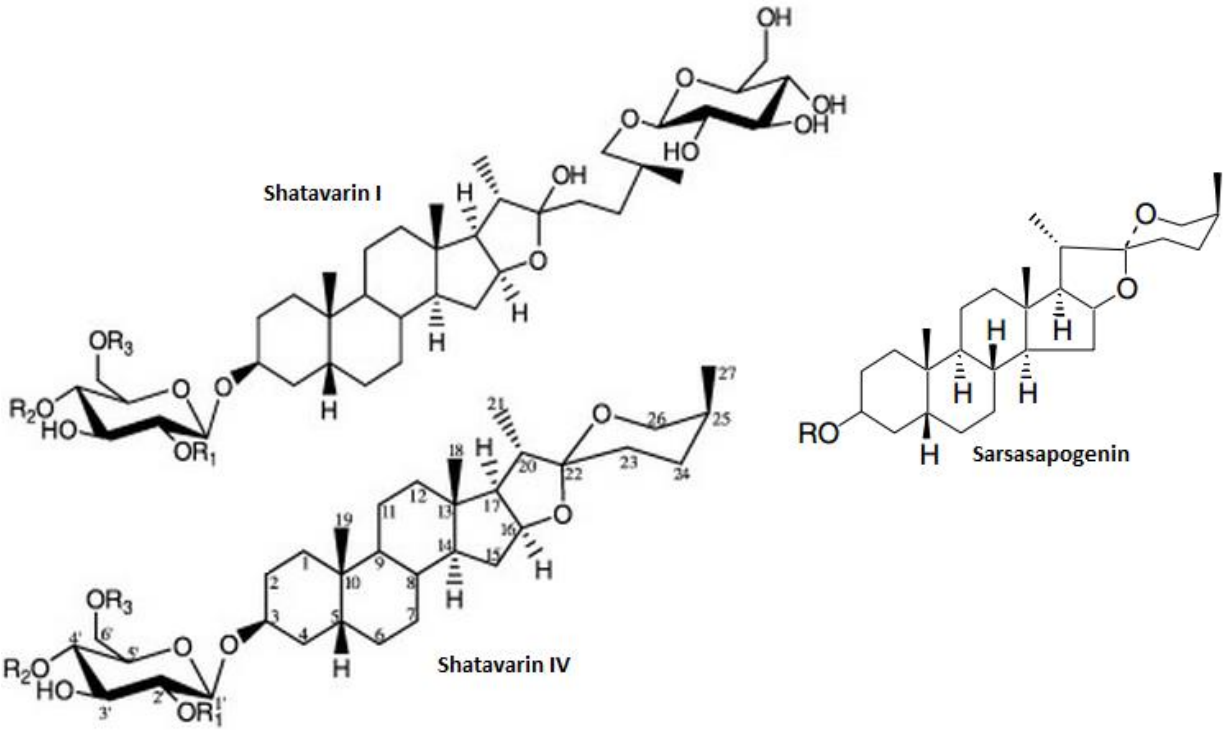

Figure 2: Steroidal Saponins (Gohel et al. 2015)

2.2 Asparagusic acid

Asparagusic acid, IUPAC name: 1, 2-dithiolane-4-carboxylic acid, is a pentacyclic compound containing sulphur. Since the other dithiolane derivatives have been identified in non-food species, it appears to be unique for *A. racemosus*. It prevents fungal growth and has the ability to repel insect attack. It also possesses a considerable nematocidal activity thereby resisting the entry of invading parasitic nematodes into the exposed growing tissues (Mitchell and Waring 2014).

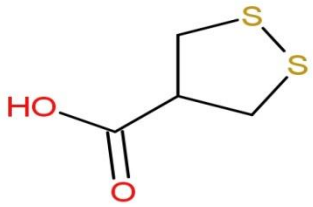

Figure 3: Asparaguisic Acid (Mitchell and Waring 2014)

2.3 Flavonoids

Flavonoids are a category of natural substances with varying phenolic structures derived from grains, bark, berries, fruits, roots, stems, flowers, wine and tea. In a number of types of pharmaceutical, medical and cosmetic uses, flavonoids are currently considered an integral ingredient. These are the compounds that have been linked to anti-mutagenic, anti-inflammatory, anti-oxidative and anti-cancer properties coupled with their ability to modulate the activity of main cell enzymes. The Rutin and Quercetin flavonoids are polyphenolic compounds derived from *A. racemosus* and some other herbal medicinal plants. Rutin is a bioflavonoid and antioxidant and soluble in H_2O that is converted into quercetin after reaching in the blood stream.

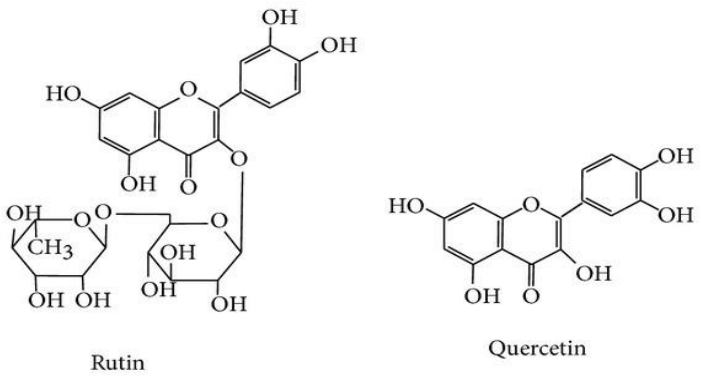

Figure 4: Rutin and quercetin structure (MATERSKA 2008)

There are also a group of flavonoids known as isoflavones are also obtained from *A. racemosus* with a variety of pharmacological activities such as anticancer, antioxidant and potential antidiabetic properties.

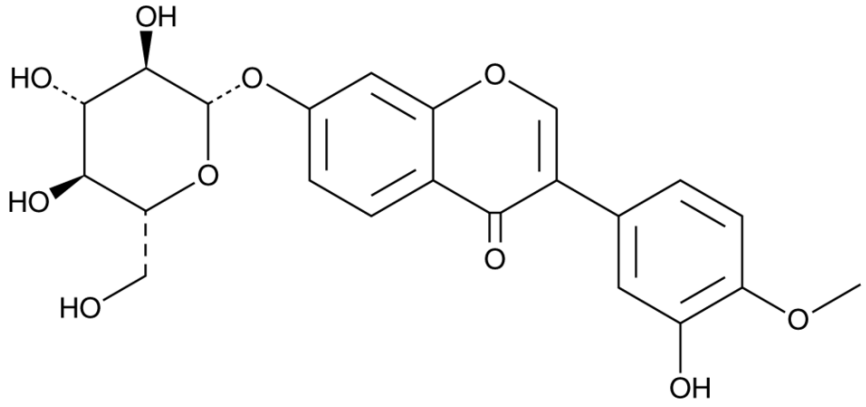

Figure 5: Isoflavone (8-methoxy-5, 6, 4-trihydroxy isoflavone-7-0-beta-D-glucopyranoside) (Saxena and Chourasia 2001)

2.4 Alkaloids

Alkaloids belong to the group of organic N-containing bases which are normally found in the nature. They are a wide range of phytochemicals isolated from plants and some other living organisms. There are various physiological effects of alkaloids on us and animals. Some important alkaloids are ephedrine, nicotine, quinine, morphine and strychnine. A polycyclic alkaloid named Asparagamine A which is in stereochemistry, a new alkaloid of cage-type that is found the roots of *A. racemosus*. This new derivative of polycyclic pyrrolizidine is also the alkaloid which was separated from this genus for the first time which has carbon substituents at C-5 and C-8. Studies have confirmed that this compound has anti-oxytocin properties through in vitro analysis.

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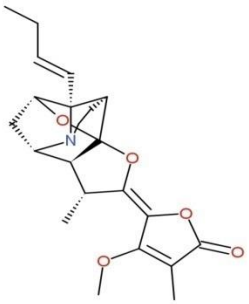

(5Z)-5-{(4R,5S,6S,8R,9R,13S)-9-[(1E)-1-Buten-1-yl]-4-methyl-2,14-dioxa-10-azapentacyclo[6.5.1.01,5.06,10.09,13]tetradec-3-ylidene}-4-methoxy-3-methyl-2(5H)-furanone

Figure 6: Asparagamine A (Ruangrungsi et al. 1994)

2.5 Furan Compounds

Five membered aromatic heterocyclic substances like furan show many types of biochemical activities and they are claimed as essential active constituents. The furan derivatives showed several biological activities such as anti-nociceptive, antiseptic, bactericidal, antioxidant, nematocidal, antifungal, antiviral, anti-inflammatory properties. Roots of *A. racemosus* are are the source of racemofuran, which has antioxidant property and also significant anti-inflammatory properties.

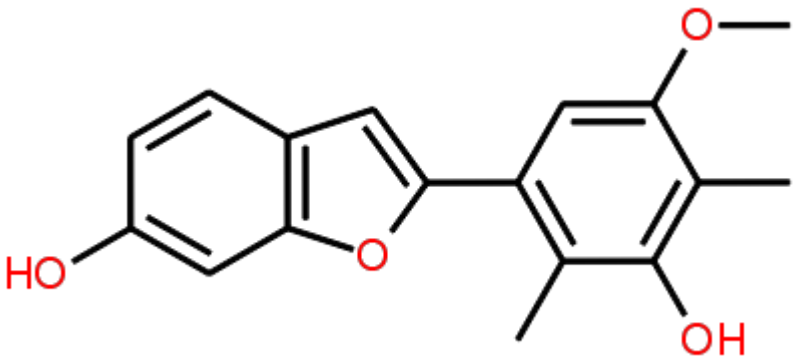

Figure 7:The structure of Racemofuran (Wiboonpun, Phuwapraisirisan, and Tip-Pyang 2004)

A list of major phytochemical constituents isolated from different parts of the *A. racemosus* is given below:

Table 3: Phytochemical compounds isolated from plant parts of A. racemosus

Group name	**Active constituents**	**Plant parts**
Steroidal saponins,	Shatavarin I-IV	Root
Carboxylic acid	Asparagusic acid (1,2-dithiolane4-carboxylic acid)	Root
Oligospirostanoside	Immunoside	Root
Polycyclic alkaloid	Asparagamine A	Root
Isoflavones	8-methoxy-5, 6, 4-trihydroxy isoflavone-7-0-beta-D-glucopyranoside	Root
Cyclic hydrocarbon	Racemosol, Dihydrophenantherene	Root
Furan compound	Racemofuran	*Root*
Carbohydrates	- Polysacharides, mucilage	*Root*
Flavanoids	Glycosides of quercitin, rutin and hyperoside	Flowers and fruits
Sterols	sitosterol, 4,6- dihydryxy-2-O(-2-hydroxy isobutyl) benzaldehyde and undecanyl cetanoate	Root
Trace minerals	Zinc, Manganese, Copper, Cobalt, Magnesium, Calcium, Potassium, Selenium, Iron	Roots, Leafs, Stem
Kaepfrol		Woody Portions of Tuberous Roots
Miscellaneous	Gamma linolenic acid, Vitamins A, B1, B2, C and E, Folic acid, Diosgenin, Arginine, tyrosine, Resin, Tannin	Roots, Leafs, Stem

The Trace elements isolated from *A. racemosus* is given below in table below (Negi et al. 2010).

Table 4: Trace elements isolated from A. racemosus

Metal	Root (mg/kg)	Leaves (mg/mg)
Zinc	44.0±0.2 to 148.0± 1.2	53.0±0.2 to 165.0±3.2
Copper	14.0±0.1 to 23.0±0.3	15.0±0.6 to 34.0±0.5
Manganese	5.0±1.4 to 62.0±2.5	14.0±0.4 to 84.0±0.7
Iron	211.0±0.5 to 1493.0±0.2	505.0±0.2 to 2040.0±0.3
Cobalt	84.0±0.3 to 122.0±1.5	85.0±0.3 to 88.0±0.2
Sodium	199.0±0.5 to 490.0±20	127.0±0.6 to 745.0±0.3
Potassium	2652.0±0.4 to 13260.0±3.5	5460.0±0.2 to 10842.0±2.5
Calcium	961.0±0.6 to 2115.0±3.2	1346.0±0.3 to 6153.0±1.6
Lithium	18.0±0.2 to 58.0±3.8	28.0±0.6 to 48.0±1.6

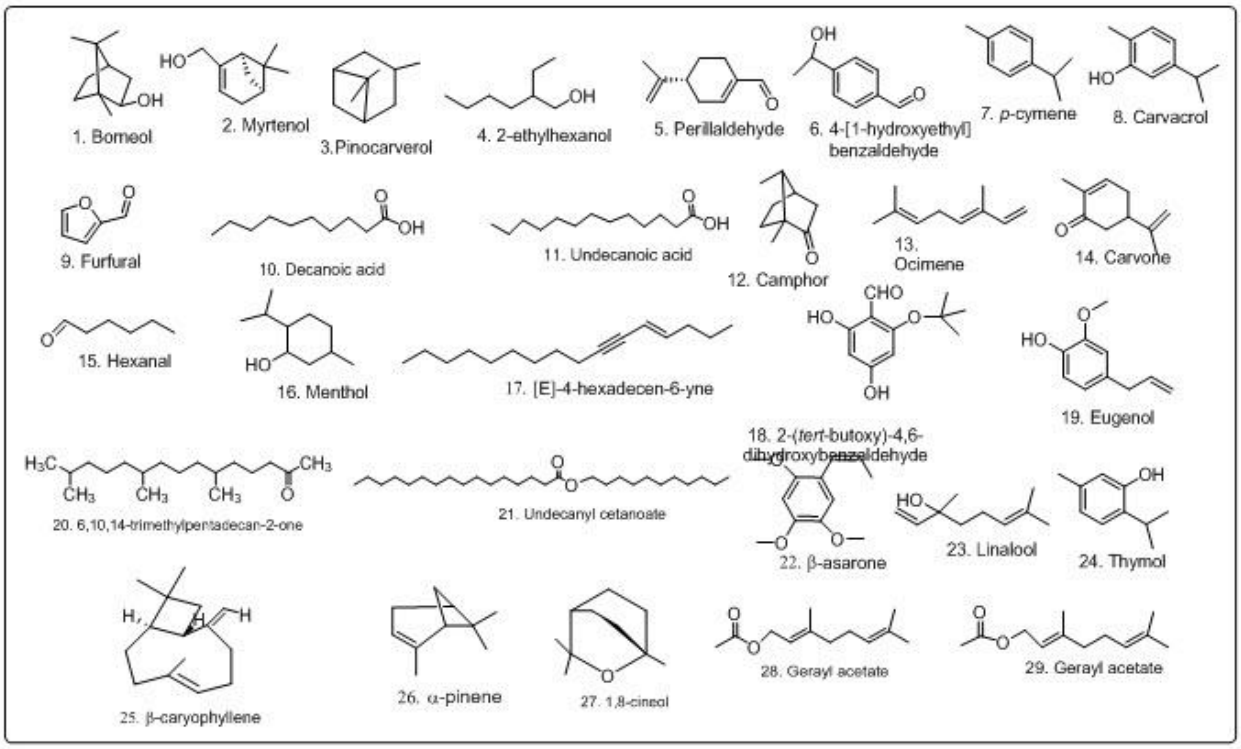

Figure 8: Structure of volatile compound isolated from A. racemosus (Selvaraj et al. 2019)

Chapter 3

Pharmacological Effects & Activities

A. racemosus possess a wide range of pharmacological effect on the human system. These are discussed here:

3.1 Antioxidant Activity

Antioxidant is a term employed for any substance that inhibit oxidation by suppressing some weak and unstable molecules termed as free radicals which damage cell organelles like DNA, cell membranes, and other parts of cells. These unstable free radical molecules lack electrons therefore; draw electrons from other molecules and consumes those molecules in the process. Free radicals are harmful molecules for cells and can break a cellular reaction and affect other components of the cell. Antioxidants losses some of their own electrons and neutralizes free radicals so that it can't steal electrons from important molecules of the cell. By donating electron, they consume these molecules. Hence, antioxidants are called natural "Switch Off" for free radicals. Hence, the term antioxidant doesn't reflect only specific nutritional property rather a chemical property (Pisoschi and Pop 2015). *A. racemosus* shows antioxidant properties in several studies. One study showed that crude extract as well as aqueous extract of *A. racemosus* exerted an antioxidant effect in mitochondria of mice liver. Oxidative damage of mice liver mitochondria was done using gamma radiation in those rays of 75-900 grey in rat liver mitochondria. Application of gamma rays induced lipid peroxidation which was further assessed by the formation of substances that react with thiobarbituric acid and lipid hydroperoxides. Both crude and purified aqueous extract was observed to inhibit oxidation of protein and lipid peroxidation remarkably. Thus, follows antioxidant action. The activity of this plant extract was compared with established standard antioxidants; glutathione and ascorbic acid and similar effects was recorded (Kamat et al. 2000). In another Study,

toxicity was induced in mice using kainic acid injections in between hippocampus and striatum region which causes excitotoxic lesions in mice brain. Methanolic root extract of *A. racemosus* were applied to the mice and observed the action of plant extract against KA induced damage. Results showed enhanced glutathione peroxidase (GPx) activity followed by increased glutathione quantity (GSH). Hence indicates glutathione like antioxidant activity (Karuna et al. 2018). Yet another study, Action of *A. racemosus* plant extract was investigated in vitro against several free radicals like anionic superoxide, hydroxyl, hydrogen peroxide and nitric oxide along with metal chelation & reducing power. These free radicals participate in occurrence of various diseases and cause aging. Results showed the consumption of various free radicals and impart iron chelating and reducing activity. The following study further demonstrated the presence of compounds like polyphenols, flavonoids, ascorbic acid in high amount in *A. racemosus* therefore ensured its antioxidant activity. Following researches summarizes the overall activity of *A. racemosus* as a natural antioxidant and can be used in prevention of various diseases (Mag et al. 2007).

3.2 Antidepressant & Antianxiety Activity

Antidepressants are medications that help relieve from symptoms of depression and anxiety like worthlessness, insomnia, mental confusion and treat some chronic pain condition. Antidepressant medications correct the chemical imbalance of neurotransmitters in brain by keeping influence on how different neurotransmitters especially serotonin and norepinephrine work in the brain. Antidepressants like SSRI's, SNRI's and tricyclic antidepressant work by inhibiting the reuptake of these neurotransmitters to presynaptic neuron and ensure the neurotransmitters will be remaining in the synaptic cleft. Hence, the presence of more neurotransmitter in the synapse indicates the signal is received and depression is reduced (Maj, Przegalinski, and Mogilnicka 1984). Methanolic extract of this plant interact with

adrenergic, dopaminergic, serotonergic and GABAergic system and significant antidepressant activity was observed following the inhibition of MAO-A and MAO-B. The methanolic extract of *A. racemosus* seeds demonstrated a decrease in immobility time in forced swim test (FST) and tail suspension test (TST) in mice, which was comparable to imipramine and observed rise in the levels of dopamine in vitro (Dhingra and Kumar 2007). Methanolic extract of root of *A. racemosus* demonstrated significant antianxiety effect in open field test (OFT), hole-board, and (EPM) tests in rats, the activity being comparable to that of standard drug, diazepam. The levels of serotonin and norepinephrine were seen to be elevated in the amygdala along with an increase in the expression of 5-HT2A receptors. Moreover, the anxiolytic effect of *A. racemosus* in OFT, hole-board, and EPM tests, was found to be attenuated by flumazenil, indicating GABAA -mediated action. However, no sedation had been observed in OFT and EPM tests as compared to diazepam. Thus, the anxiolytic response of *A. racemosus* is believed to be mediated by GABA-ergic and serotonergic mechanisms (Garabadu and Krishnamurthy 2014).

3.3 Anti-ulcer activity

Anti-ulcer agents are used for both treatment and prevention of ulcers happens in duodenum and stomach. It additionally mitigates acid reflux, esophagitis and intestinal discomfort. Antiulcer agents mainly inhibit gastric acid production, neutralize gastric acid and protect the gastrointestinal mucosa from acid injury. *A. racemosus* root extracts showed significant antiulcer activity in several studies. In one study, ulcer was developed in stomach and duodenum using acetic acid, cysteamine, cold restraint stress, aspirin & pylorus ligation. Methanolic extract of *A. racemosus* root showed significant protection against acute gastric ulcers. Moreover, other root extracts of *A. racemosus* also studied for antiulcer activity in mice, rabbits and guinea pigs. Contraction of smooth muscles of stomach, duodenum and ileum were observed in those studies whereas no change in peristaltic movement was seen in

animals. It was also observed that the action produced by this plant was similar to that of acetylcholine and drugs like atropine can block the action which suggested a cholinergic mechanism of action (Sairam et al. 2003).

3.4 Anti Dyspepsia Effect

Indigestion also termed as Dyspepsia is difficulty, pain and disturbance in digestion which occurs accompanied by the symptoms such as discomfort in stomach, nausea,vomiting, heartburn etc. The herb *A. racemosus* has been found to be prescribed by practitioners since ancient times for discomforts regarded digestion. The plant extract reported to give similar therapeutic effects as Metoclopramide. This is a dopamine agonist which binds with dopamine receptor (D-2) basically reducesthe gastric emptying time and used in the treatment of dyspepsia. In this report, normal healthy male volunteers were treated with 2 g-powdered roots of *A. racemosus* and effects were compared with 10 mg of Metoclopramide tablet which turned out to be similar in some pharmacokinetic parameters including the gastric emptying halftime. *A. racemosus* is documented as a mild dopamine agonist and supports the claim of usage of this medication as an anti-dyspeptic drug. This study doesn't elaborate the mechanism of action of shatavari in dyspepsia rather proves the effectivity of this plant on the basis of its pharmacokinetic and pharmacodynamic properties (Dalvi, Nadkarni, and Gupta 1990).

3.5 Immunomodulatory& Immunoadjuvant Action

Immunomodulators are chemical agents that modifies the of response and have an effect on the functioning of the immune systems in numerous ways in which like stimulating antibody formation or by inhibiting white blood cell action. Studies have confirmed some chemical constituents of *A. racemosus* works as immunomodulators that modifies the immune reaction by increasing phagocytosis and proliferation of lymphocytes. In a study, *A. racemosus* root

extract considerably inflated percent phagocytosis and proliferation of lymphocytes in mice once incorporated with milk was administered in mice. This ensures it's immunomodulatory action (Arora et al. 2014). In another study, aqueous root extract of *A. racemosus* was evaluated in experimental animals vaccinated with diphtheria, tetanus, pertussis (DTP) immunogen. The impact of this plant on vaccinated animals was evaluated using serological and hematologic parameters. Vaccinated animals were divided into two groups and treated with *A. racemosus* and some were untreated with plant extract. *A. racemosus* root extract at a dose of 100mg/kg was administered for 15 days after infecting with disease causing agent *B. pertussis* strain. The *A. racemosus* extract was administered orally 100mg/kg per day for fifteen days. The plant extract was evaluated on several parameters including degree of illness, paralysis and occurrence of death in experimental animals. Results had showed a positive effect in antibody production against induced infection. Moreover, decreased mortality and overall health improvement was observed in treated group with *A. racemosus* compared to untreated control. However, intra cerebral and increase in concentration of antibody protein compared to untreated animals; therefore showed a significant immunoprotection by assisting the antibody production (Gautam et al. 2004). Yet another study, the consequences of *A. racemosus* root extract on general Th1/Th2 immunity of SRBC sensitized animals was observed. The result showed a significant increase of CD3+ and CD4/CD8+ percentages indicate vital up-regulation of Th1 (IL-2, IFN-g) and Th2 (IL-4) cytokines suggesting its Th1/Th2 adjuvant activity. Thus, the study justified *A. racemosus* extract, together with LPS, Con A or SRBC, created a major proliferation suggesting impact on T lymphocyte activation. In another study, the effect of standardized *A. racemosus* root aqueous extract on systemic Th1/Th2 immunity of SRBC sensitized animals was observed (Gautam et al. 2009).

3.6 Antibacterial Activity

A. racemosus showed antibacterial activity in several studies. The chemical constituent isolated from root extract of *A. racemosus* exerts antibacterial activity by inhibiting protein synthesis which mimics the activity of Chloramphenicol which binds with the 20S and 50S subunit of bacterial ribosomes and inhibits the action of enzyme peptidyl transferase which takes part in bacterial protein production. The plant extract also exerts similar effect like penicillin and amoxicillin. In one study, the antibacterial activities of the methanolic root extract of *A. racemosus* against several organisms including Gram Positive *Staphylococcus aureus* and Gram-Negative Proteus species, *Vibrio cholerae*, *Pseudomonas alkaligenes*, *Escherichia coli*, *Shigella species*, *Salmonella typhi*, *Klebsiella pneumonia* at the concentration of 10000 µg/ml, 1000 µg/ml, 100µg/ml, 10 µg/ml and 1 µg/ml were evaluated. *A. racemosus* at the concentration of 10000 µg/ml showed highest activity against all bacterial strains ranging from 26±1.41 (proteus species) to 14±141 (Salmonella typhi) (Uddin et al. 2012). In another study, the methanolic root extract showed in vitro antibacterial property in different concentrations including 50, 100, 150 mg/mL against some bacterial strain of *E. coli*, *Shigella dysenteriae*, *Pseudomonas putida*, *Shigella sonnei*, *Salmonella typhimurium*, *Shigella flexneri*, *Vibrio cholerae*, *Bacillus subtilis*, *Salmonella typhi* and *Staphylococcus aureus*. The effects produced by the plant extract was compared with Chloramphenicol (Mandal, Nandy, et al. 2000).

3.7 Antifungal Activity

The in vitro anticandidal activity of *A. racemosus* roots and tubers extract was investigated against *Candida albicans, Candida tropicalis, Candida krusei, Candida guillermondii, Candida parapsilosis* and *Candida stellatoida,* which are isolated from vaginal thrush patients. *A. racemosus extract* exerted high degree of inhibition in vitro against some of these strains of *Candida*. The effects further studied and compared with several standard

antifungals for similar activity which couldn't be identified thus M/A against fungal strains are unknown (Uma, Prabhakar, and Rajendran 2009).

3.8 Antidiabetic Action

A. racemosus was observed to give antidiabetic actions in several studies. In a study ethanolic extract of this plant roots were noticed to decrease serum glucose level in type 2 diabetic patients whereas not any mentionable effect was observed in case of type 1 diabetic patients. This indicates that the active constituents of the plant take part in enhancing insulin action and improving insulin secretory capability of the beta cells of pancreas. Thus, the study assessed the antihyperglycemic property and revealed the mechanism of action of *A. racemosus* in lowering blood glucose level. These findings additionally indicate that antihyperglycaemic activity of *A. racemosus* is partially initiated by inhibition of sugar digestion and absorption, along with improvement of hormone secretion and action within the peripheral tissue (Hannan et al. 2012). In another study, the action of *A. racemosus* was assessed using cell lines in vitro and observed to give insulinotropic effect. The mixture of ethanolic extract with either of aqueous, butanol, chloroform, hexane or ethyl acetate fractions of this plant were applied against cell lines of rat pancreas, islets, insulin secreting cells. Stimulation in the production of insulin was observed in vitro for mixture of ethanol extract with any three (ethyl acetate, butanol and aqueous) of the following fractions where aqueous fraction exerted less effect in insulin secretion. This further demonstrated that Non polar fractions of the plant exert more action on insulin production and secretion rather aqueous one (Hannan et al. 2007).

3.9 Anti Diarrheal activity

A. racemosus occupies moderate anti-diarrheal activity. In a study, ethanolic extract of *A. racemosus* inhibited & prolonged the onset of diarrhea in mice which was induced by castor

oil. When administered orally,this castor oil gets mixed with pancreatic enzyme which exerts ricinoleic acid from the triglycerides. In intestine, this ricinoleic acid converts to ricinoleate salt by reacting with the sodium and potassium present in the intestinal lumen. Ricinoleate salt stimulates the intestinal epithelial cell's adenylyl cyclase whichresults in the increase of water and electrolyte excretion. Ethanolic extract of *A. racemosus* inhibit the ricinoleate salt formation thus inhibit or delays the onset of diarrhoeal action which was then compared with standard drug Loperamide (Venkatesan et al. 2005).

3.10 Antiurolithiatic Activity

The term Urolithiasis indicates the solid non-metallic minerals in the urinary tract. This process is very complex. When any imbalance occurs between promoter & inhibitor in the kidney, it results in urolithiasis. It is also called Kidney stones. There are several types of kidney stones among which the most common are calcium oxalate stones. Ethanolic extract of *A. racemosus* exerted antiurolithiatic activity in experimentally induced urolithiasis in rats. Urolithiasis was induced by ethylene glycol or combination of ethylene glycol and ammonium chloride. The rats are treated with 0.75% EG and 2% AC for 10 days. *A. racemosus* decrease the concentration of urinary salt in urinary tract and increase secretion of salts in the urine thus interrupt the formation of saturated crystallizing salt (Jagannath et al. 2012). Though the best possible solution for kidney stones treatment is surgery, medical therapy and lifestyle changes are important as there is more chance of recurrence of stones without it.

3.11 Analgesic Activity

A. racemosus shows mild analgesic activity. In several studies, acetic acid induced pain has been used to evaluate the analgesic activity of *A. racemosus* in mice. Acetic Acid induces pain sensation by triggering the immune response. It liberates endogenous substances which

gradually excite the pain nerve endings. When PGE_2 and PGF_{24} level increased in the peritoneal fluid, it creates pain sensation which was induced by acetic acid. In one study the aqueous methanolic extract of *A. racemosus* at both doses 250 and 500 mg/kg bodyweight caused significantly reduction in abdominal constrictions and jerking. Release of prostaglandin and other pain mediators exerts inhibitory effect that imparts analgesic activity (Ahsan et al. 2019). In another study, ethanolic extract of *A. racemosus* produced significant pain inhibition comparable to the standard drug Diclofenac Sodium. Nevertheless, some active constituent of *A. racemosus* like Flavonoids, plays an important role in analgesic and antioxidant activity. Alkaloids are widely known for their ability to pain perception. Tannin, another constituent of *A. racemosus* shows anti-nociceptive activity and also work against bacterial infections.

3.12 Anti-inflammatory Activity

A complex reaction associated with cardinal signs like fever, pain etc. and causes some incidents like increased vascular permeability, membrane alteration and protein denaturation are usually referred as inflammation. Various Studies has confirmed the anti-inflammatory activity of *A. racemosus*. In one study, ethanolic extracts of *A. racemosus* showed anti-inflammatory action against paw edema of rats where inflammation was induced using carrageenan. Chemical mediators like leukotriene, prostaglandin, PAF and cytokines are found to be responsible for the hypersensitivity reaction. It also showed antiarthritic activity in Freund's adjuvant induced arthritis by simply reducing the paw volume and decreasing arthritic score (Mittal and Dixit 2016). Another study proved that some *A. racemosus* liposomes have been observed to give anti-inflammatory activity. These liposomes were prepared by several techniques including thin-film hydration (TF), reverse-phase evaporation (REV) and polyol dilution (PD) and delivered in topical or transdermal route that exerted anti-inflammatory activity (Plangsombat et al. 2016). Furthermore, ethanolic leaf extract of

A. racemosus showed noticeable anti-inflammatory activity at a dose of 600 mg/kg. it has been observed to cause inhibition of almost 46 % paw edema in rats which was exerted using carrageenan. This is further justified by Phytochemical screening of the extract of ethanol from the leaves of *A. racemosus.* It has been hypothesized sterols and flavonoids and some other class of compounds might possibly account for the anti-inflammation activity of the plant extract (Battu, Kumar, and Battu 2010).

3.13 Antipyretic Activity

A. racemosus is a traditional medicine used in ailments that caused fever. In folklore, extract of 100 g fresh tuber of *A. racemosus* mixed with 100 ml of boiled water is consumed lukewarm (Vijayan, VB, and John JV 2007).Fever is a complex physiological reaction that is caused by aseptic stimuli or infections. As the concentration of prostaglandin E2 (PGE2) increases within portions of the brain, the body temperature increases. Most antipyretic drugs are involved in inhibiting their action by inhibiting cyclooxygenase's enzymatic activity and thereby reducing PGE2 levels within the hypothalamic region, thereby exerting their antipyretic action. In one study, the rat model of yeast-induced hyperpyrexia was used to investigate the antipyretic function of ethanolic extract of the roots of *A. racemosus*. Pyrexia caused by yeast is called pathogenic fever, which is due to the development of prostaglandins (PGE2) that set a higher temperature for the thermoregulatory core. This plant's ethanol extract had a more definitive effect on the reduction of hyperthermia than the aqueous extract. After 3 hours of administration, it was also observed to have an effect close to that of the standard medication Paracetamol (Vasundra Devi and Divya Priya 2013).

3.14 Adaptogenic Activity

A. racemosus is a plant enlisted in ‘Rasayana’, a category of plant medicinal products that other than improvement of the body's protection mechanisms also help physical and mental wellbeing, longevity and long life. Adaptogens are compounds that allow any organism to overcome any stress like physical, chemical and biological. These are the agents which increase the non-specific resistance of organisms to battle different stress. Ethanolic extract of *A. racemosus* was studied against cisplatin mediated side effects such as Gastric emptying and normalizing hypermotility of the intestines. *A. racemosus* reversed cisplatin's effect on gastric emptying, and even normalizing cisplatin mediated intestinal hypermobility. One herbal remedy made with *A. racemosus* named Siotone produces significant action against persistent, erratic but mild stress-induced behavioral disturbances, glucose metabolism, suppressed male sexual behavior, immunosuppression, and albino rat cognitive dysfunction. This formulation of herbs which has substantial adaptogenic behavior has chronic reversal biochemical, physiological and behavioral stress-inducing disruptions. Methanolic extract from fresh *A. racemosus* rhizomes showed considerable protection against acute gastric ulcers caused by cold restrain stress, acetic acid, pylorus ligation, aspirin plus pylorus ligation and duodenal ulcers caused by cysteamine.

3.15 Diuretic Activity

Diuretics are substances defined as any medicine that improves urinary production. Diuretics help eliminate excess fluids, salts, toxins, and stored metabolic products, such as urea, from the body. They serve to rid the body of excess fluid (edema) which accumulates in the tissues due to different disease conditions. In a study, aqueous extract of *A. racemosus* was evaluated for its diuretic potential in albino rats of Wistar strain. The pharmacological response was compared against furosemide which is regarded as loop diuretics. Like other loop diuretics, Furosemide works by inhibiting the luminal Na-K-Cl cotransporter in the thick ascending

limb of Henle 's circle, by binding to the chloride transport channel, resulting in urinary depletion of sodium , chloride and potassium (Davies and Wilson 1975). The rats showed diuretic responses to all doses of the extract. Particularly at the dosage of 3200mg/kg showed significant diuretic activity in compared to furosemide. Thus potassium, phosphate and chloride excretion were significant with high doses of the extract. The reason for this diuresis may be due to saponins such as Shatavarin I, II, III, IV that are found in steroidal asparagus saponins and isoflavones (MC Satish Kumar, K Sammodavardhana, UP Rathnakar, Udapa Shvetha).

3.16 Anti Tussive effect

The root juice of *A. racemosus* was used against cough in traditional medicine in various regions of India including West Bengal, Bankura and Tribal regions of Khatra. Cough is induced by stimulation of the cough reflex arc composed of the vagal nerves of the airway, the cough core of the medulla, and the nerves of the efferent. It can be anticipated that inhibiting it at any position of the arc would cause antitussive effect. Antitussive drugs acting centrally operate by inhibiting the cough core in the brain, increasing the coughing threshold. The precise method by which they do this is still not well known (Woo, 2008). In one study, Methanolic root extract, dose 200 and 400 mg / kg put out important antitussive behavior on sulfur dioxide induced cough in mice. The cough inhibition of 40% and 58.5% respectively was equivalent to that of 10-20 mg / kg codeine phosphate, where 36% and 55.4% respectively were observed in the inhibition (Mandal, Kumar C.K., et al. 2000).

3.17 Anti Proliferative activity

Antiproliferative action is the ability of a compound to inhibit cell formation. This implies that it does not cause the cells to replicate easily. Compounds that inhibit the growth of cancer cells are antiproliferative agents. Steroidal constituents such as Shatavarin I-IV are

isolated from *A. racemosus* attached to the cell line of cancer. They've been given at different concentrations within each line. Level of mortality and the viability of cells were monitored in parallel in a given series of intervals. During the course of the study two methods are used such as the Sulforhodamine B cytotoxicity test and M30 Cyto Death ELISA was used to assess cell viability and apoptosis rates in the carcinoma cell line. The estimation of the cell mortality rate was based on accumulation of caspase-cleavage chemical activity and Cytokeratin 18 (ccCK18) in cells used in culture media. Almost all cells of HCT116 have cytotoxic activity that involves saponins extracted from *A. racemosus* but the rest of the sugar aglycone present in sarsasapogenin did not indicate such activity. Shatavarin IV in all Shatavari compounds tested; shows the full capacity to limit cell viability and mortality rate (Singh et al. 2018).

3.18 Anti-cancer Activity

A. racemosus plant extract has shown anticancer activity in several experiments. In one of the experiments, several hormones influence the development and growth of 7, 12-dimethylbenzanthracene (DMBA)-induced mammary tumors in rats. It specifically indicates the exposure of virgin female rats to Asparagus-root-extract-diet prior to administration of DMBA assists in a drop in mammary tumor incident. Besides when the animals are primed with estradiol, the occurrence of mammary tumors was further decreased with Asparagus-root-extract-diet prior to their introduction to DMBA. (Rao 1981) Another research was performed to determine the anticancer activity of major shatavarins (shatavarin IV) from the AR-2B fraction of *A. racemosus* roots. In vitro cytotoxicity tests using MCF-7, HT-29, and A-498 cell lines demonstrated potent activity with AR-2B (5.05 percent shatavarin IV) as well as its isolated AR2B-shat IV compound (shatavarin IV) (Mitra, Prakash, and Sundaram 2012).

3.19 Aphrodisiac Activity

Aphrodisiacs are the substances that applied to enhance sexual activity and assists in fertility by increasing sexual urges, sexual satisfaction or sexual activity. Sexual urges are an ineluctable part of life. Aphrodisiac agents are accustomed to modify the impaired sexual functions of people in general. There are quite a variety of herbs and nutrients that are wonderful aphrodisiacs. Aqueous extracts of the roots of *A. racemosus*, *C. borivilianum* and *C. orchioides* were collected and lyophilized. These lyophilized extracts were studied for sexual behavior effects in male albino rats and compared with untreated control group and evaluated based on various parameters of sexual behavior. Administration of these extracts at a dose of 200mg/kg observed to cause an anabolic effect following by weight gains of body and reproductive organs. Several parameters of sexual behavior were observed like decrease in mount latency, post ejaculation latency whereas a rise in mount frequency. Furthermore, increase in penile erection as well as decreased hesitation time was also reported. This indicates development of sexual urges in treated mice. The observed effects seemed to be because of the testosterone-like activity of the extracts. The current results, therefore, support the traditional knowledge claim for the utility of those herbs and supply a scientific basis for his or her putative ancient usage (Thakur et al. 2009). The lyophilized aqueous extract was also seen to increase pendiculatory activity in male Wistar rats and in vitro sperm count, thereby providing further evidence for aphrodisiac activity of *A. racemosus* (Thakur and Dixit 2007). Powder of *A. racemosus* was noticed to produce a significant increase in mounting behavior of male Wistar rats, which was comparable to action produced by standard drug, sildenafil citrate (Wani, Achur, and Nema 2011).

3.20 Phytoestrogenic effects

A plant compound that exerts similar effect as ovarian and placental oestrogens and their active metabolites in structure and function are outlined as Phytoestrogens. These compounds

produce an effect on the regulation of ovarian and oestrogen cycles in female mammals and therefore these compounds promote growth, differentiation and physiological functions of the female genital tract, pituitary, mammary and some other organs and tissues in both male and female (Whitten and Patisaul 2001). *A. racemosus* is renowned for its phytoestrogenic actions as well as endocrine modulating action which was found to exert its action by binding directly with the estrogen receptors. However it doesn't elevate the internal oestrogen level in the body (Banks et al. 2003). Estrogenic property of *A. racemosus* was demonstrated a long ago in one study where the alcoholic plant extract was noticed to increase the mammary gland weight as well as uterine weight in laboratory rats thereby additionally attributed in corticosteroids and prolactin release (Sabnis, Gaitonde, and Jetmalani 1968). In another study, *A. racemosus* exerted a noticeable mammotropic & lactogenic effect on both normal and oestrogen primed rats, therefore imparting the mammary epithelium resistant to the DMBA induced mammary carcinoma. The root powder extract prepared using chloroform and methanol in similar ratio (1:1), applied in different concentration (0.25%, 0.5%, 1% or 2) into the laboratory rats prior to the administration of DMBA resulted in decrease of tumor occurrence as well as decline in tumor progression on both normal and oestrogen primed rats (Rao, 1981). Similarly, recent studies have also proved its effect on female mammary and reproductive organ. In a more recent study, the alcoholic extract of *A. racemosus* rootstalk was administered orally for 15 days at a dose of 30mg/100g body weight to pregnant female albino rats. Effects on reproductive organs and mammary glands were observed and phytoestrogenic activity was confirmed (Pandey et al. 2005). The Phytoestrogenic activity of this plant was found to be utilized in a polyherbal formulation called Menosan which contains 110 mg *A. racemosus* extract per tablet. This formulation was studied and observed to increase uterine weight as well as uterine glycogen without affecting serum estrogen and

progesterone levels in immature rats. Moreover, ‘Menosan’ has also been observed to give positive effects the treatment of post-menopausal symptoms (Singla and Jaitak 2014).

3.21 Galactogogue Action

A. racemosus is one of the traditional plant medicines used extensively in ancient systems of medicine like Ayurveda and other folk medicine as a galactogogue. The impact of asparagus on milk production and secretion has been studied and established in humans and different animals. Research on these demonstrated galactogogue effects like increase in milk secretion, growth development of mammary gland and alveolar tissue in rats, buffaloes, goats and humans (Barry 1991; Patel et al. 2013; Patel and Kanitkar 1969). Administration of alcoholic extract of *A. racemosus* caused these significant galactogogue actions. This might be due to the similar action as Metoclopramide which is a dopamine receptor antagonist and demonstrated an increased release of prolactin which contributes in lactation. The justification of this effect of *A. racemous* is the similarity in action with a dopamine receptor antagonist, metoclopramide which is an antiemetic and used to treat dyspepsia as well as ensures lactogenic property. However, any other the antidopaminergic activity wasn't determined (Dalvi et al. 1990). It’s a claimed galactogauge since old times as previous researches proved that intramuscular administration of the plant root extract caused an elevation in weight of mammary glands as well as uterus in post-partum estrogen primed rats. There was a rise in weights of adrenals in addition to depletion of water-soluble vitamin suggesting the discharge of adrenocorticotrophic hormones obtained from pituitary gland. The growth of lobuloalveolar tissue and increased milk secretion in the estrogen primed rats is because of the action of released corticosteroids or prolactin (Sabnis et al. 1968).Various Ayurvedic companies had launched herbal formulations containing *A. racemosus* regarding galactogogue action. Recalex, Payapro etc are considered few between these.

Chapter 4

Protective Activity in Organs and Systems

4.1 Hepatoprotective Activity

A. racemosus has demonstrated vital hepatoprotective effect in several ways. This classic herb has proved to be effective against hepatotoxicity, hepatocarcinogenesis (production of cancer cells in liver) and liver cirrhosis in several researches. In researches related to hepatotoxicity, hydro alcoholic extracts of this plant has demonstrated hepatoprotective effect by inhibiting CCl_4 induced hepatotoxicity in liver of rats (Fasalu Rahiman, Musambil, and Shejina 2015). Similarly ethanolic root extract was observed to work against hepatotoxicity induced by isoniazid in treated rats (Palanisamy and Manian 2012). Furthermore, aqueous extract of this plant has reduced the toxicity produced by lead (Pb) in Swiss albino mice (Sharma, Verma, and Sharma 2012). In researches related to hepatocarcinogenesis, this herb was observed to prevent formation of tumor in liver of Wister rats in one histopathological study of hepatic tissues. Tumor was tried to induce in both pretreated rats with aqueous root extract and normal rats using DEN (200mg/kg) followed by a tumor promoter DDT (0.05% in diet) for 2 weeks. After observation for 18 days, immunohistochemical staining of hepatic cells were done. Results showed presence of cluster of tumor cells in normal rats whereas absence of tumor cells in pretreated rats with plant extract. This indicates aqueous extract of this plant work against DEN induced hepatocarcinogenesis (Agrawal et al. 2008). Moreover, this plant was proved to be effective against liver cirrhosis another analogous study, where *A. racemosus* root powder was found to significantly reduce the elevated serum hepatic marker enzymes like aspartate amino transferase (AST), alanine amino transferase (ALT) and alkaline phosphatase (ALP). Increasing level of hepatic marker indicates inflammation of liver cells further develops into liver cirrhosis (Om et al. 2011).

4.2 Neuroprotective effect

A. racemosus was claimed to be effective in various nervous system related disorders in Ayurveda. This plant was observed to protect the brain against neuronal damage caused by toxic substances. In one study; excitotoxic lesions in rat brain were produced by intra hippocampal and intra-striatal injections of kainic acid. Oxidative damage was also observed as kainic acid injection decreased glutathione peroxidase (GPx) activity and reduced glutathione (GSH) content by acting as a nucleophilic scavenger for harmful compounds like free radicals. Methanolic extract of *A. racemosus* which was found to produce antioxidant activity earlier, showed an enhancement in GPx activity and GSH content and reduction in membranal lipid peroxidation and protein carbonyl content thus work against the striatial and hippocampal damage and eradicate the lesions in brain(Parihar and Hemnani 2004). Similarly ethanolic plant extract give considerable neuroprotection against oxidative stress and behavioral dysfunction caused by ethanol in brain (Uddin and Asaduzzaman 2016). Excitotoxic lesions and oxidative stress are vital causes of damage of neurons. These can eventually lead to nervous disorders like Parkinson's disease and Alzheimer's disease. Furthermore, *A. racemosus* root extract was observed to significantly increase the normal cell count in various regions of hippocampus in mice with no significant change in behavioral test results. In the same study, memory retention and recall test were administered in mice treated with *A. racemosus* extract and significantly higher test scores were seen compared to the control group. This again demonstrates neuroprotective action of *A. racemosus* (Saxena et al. 2007). An Indian polyherbal formulation containing *A. racemosus* named Mentat is used to reduce alcohol withdrawal symptoms like convulsions, tremor, anxiety and hallucinations in patients trying to quit alcohol (Kulkarni and Verma 1993).

4.3 Effects on cardiovascular system

A. racemosus showed cardioprotective activity as well as caused cardiac problems in several researches. Mechanism of action of *A. racemosus* extracts on heart has been identified as studies confirmed that *A. racemosus* induced positive ionotropic and chronotropic effect on frog's heart which indicates the stimulation of beta 1 adrenergic receptors. Increased heart rate and increased contractility was observed due to this. However, higher doses resulted in cardiac arrest. Similarly, another study was performed where *A. racemosus* successfully treated hypotension in cats and created similar effect like atropine which is an anti-cholinergic and suppressed cholinergic pathways. Furthermore, *A. racemosus* extract managed cause congestion; regulate hemostasis and normal blood flow in mesenteric vessels of rats. No effect on clotting time whereas slight increase in bleeding time was observed (Selvaraj et al. 2019). Moreover, root powder of this plant was found to reduce serum lipid and serum cholesterol levels thus plays a vital role in prevention of hypercholesterolemia, atherosclerosis and some coronary artery diseases. Administration of root powder extract of *A. racemosus* reduced lipid peroxidation which resulted reduction in overall lipid contents including LDL & VLDL, total cholesterol and triglycerides in plasma as well as liver of rats. From these studies it has been determined that *A. racemosus* prevent hypercholesterolemia as this tend to stop the accumulation of exogenous cholesterol in serum and liver as well as accelerate the conversion of stored cholesterol into bile acid (Visavadiya and Narasimhacharya 2005). A herbal preparation named Abana which is a tablet containing 10 mg of *A. racemosus* root extract has been demonstrated as a cardio protective agent. Studies have confirmed a severe hypocholesterolemia caused by this formulation in rats indicates the decreased cholesterol and lipid content thus beneficial to cardiovascular health (Khanna, Chander, and Kapoor 1991).

4.4 Effect on Reproductive system

A. racemosus is claimed as a remedy for female reproductive health since ancient times and laboratory researches have revealed this herbs action on reproductive systems to some extent. Firstly, the root extract was observed to increase serum FSH level in immature rats in one study. Thus, accelerates folliculogenesis and ovulation. Root extract of *A. racemosus* is also proved as a useful uterine muscle relaxant. In this regard, one study showed methanolic root extract of the plant was able to relax the uterine muscle of pregnant rats than the non-pregnant one. This is because this plant extract can successfully reduce the contraction induced spontaneously by high potassium depolarization and oxytocin. Mechanisms involved were both calcium-dependent and -independent pathways. A polyherbal formulation containing *A. racemosus*, similarly showed decreased spasmogen-induced contraction in rats. Plant phytochemicals contain steroidal compounds those are observed to exert similar effect like estrogen on uterus. Moreover, it has also been shown to be effective in the treatment of dysmenorrhea and abnormal uterine bleeding. *A. racemosus* also contributes in male reproductive health as it exerted testosterone like effect in laboratory tests as well as used as proved as an aphrodisiac in several studies.

4.5 Effect on respiratory system

A. racemosus was demonstrated as a bronchodilator as higher doses of the alcoholic extract caused a mild dilatory effect on bronchial muscles of rats in one research. However, it failed reduce the histamine induced bronchoconstriction. Moreover, the alcoholic extract has also demonstrated a respiratory depression in one study with cats (In et al. 2014).

4.6 Effects in healing injury

The aqueous root extract of *A. racemosus* was seen to produce significant improvement in the epithelialization period, remarkable enhancement of wound contraction rate and an

increased skin breaking strength in incision and excision wound models in rats, thereby enhancing wound healing.

4.7 Parts of plant in different Pharmacological activities

A. racemosus is a plant with numerous amounts of pharmacological properties. The table below associates between the plant parts and pharmacological activities.

Table 5: Plant part associated with various pharmacological activities

`Roots	Immunomodulators, Estrogenic, Galactagogue, Anti dyspepsia, Anti-inflammatory, Antiallergic, Anticancer, Antidiabetic, Antioxidant, Antitussive, Anti diarrheal, Anti-ulcer, Antibacterial, Antilithiatic, Hepatoprotective(Joshi, Rakesh, and Joshi 2016)
Shoots	Diuretic, Anti diabetic, Anti-inflammatory
Leaves	Cholinesterase, Antiparasitic
Whole Plant	Nephroprotective, Hepatoprotective, Antimicrobial (Sachan et al. 2018)
Aerial Part	Antiasthmatic, Hypolipidemic, Urolithiasis and Antifertility
Flowers	Diuretic
Seeds	Antiparasitic

4.8 A Wonderful Female Tonic

This traditional herb is blessed with numerous pharmacological properties which cure many health-related issues of female including complications in reproductive systems. Phytoestrogenic property of this plant indicates the development of the growth of uterus and mammary glands. The herb also works against complications like infertility because it accelerates ovulation. Furthermore, complications related to menstruation like abnormal

bleeding in uterus, dysmenorrhea, pre-menopausal syndrome (PMS) as well as prevention of some menopausal symptoms can be achieved using *A. racemosus* plant extracts. Moreover, it is a useful tonic in pregnancy as it prevents miscarriage, relax the muscles of uterus while conceiving and increase lactation afterwards. Complications occur during pregnancy like pre-eclampsia associated with pregnancy induced hypertension (PIH) can also be treated using *A. racemosus* root extracts.

Chapter 5

Adverse effect and toxicological reports

Adverse effect, additionally noted as ADR is any unexpected health complications followed by a harmful reaction in body experienced during the use of a prescribed medication. Dose reduction, alternative medications, change in treatment procedure might be attributed to solution of this circumstances. Hence**,** accurate dosing of any medication is important to exert proper therapeutic effect and avoid adverse effect which relies on several factors like age, patient's health, route of administration, some environmental factors etc. This is applicable for both plant products as well as synthetic medicines. Medicinal plants usually observed to impart less harmful effects compared to modern medications. Similarly, for *A. racemosus*, it's ethanolic and aqueous extracts was found to impart no harmful or toxic effect in higher doses (50 mg/kg-1gm/kg). Further study on aqueous extract with higher doses up to 3g/kg body weight confirmed no toxic effect and fatality (Kumar et al. 2010). Furthermore, the plant methanolic extract also observed to impart no toxic effect in yet another study where elevated dose of plant extracts up to 2gm/kg body mass was applied to rats. No symptoms of toxicity or harmful reaction have been noticed. Additionally, no changes in conditions including mortality, physiological & biological parameters as well as no occurrences of hemorrhage or necrosis in the tissues were observed after administration in higher doses (Kumar et al. 2010). *A. racemosus* has been described as completely safe for long-term use, even during pregnancy and lactation in traditional records of medications. However, methanolic extract was observed to impart partial teratogenic effects in one study. Oral administration of plant extract (100mg/kg body mass) for 60 days on pregnant charles foster rats resulted in complications like higher fetal resorption followed by decreased fetus size, retardation of fetus growth, malformation in fetus that gradually develops swelling in legs in post-partum

period. For this reason, *A. racemosus* is not suggested to intake continuously during pregnancy as it might bring damage to the newborn (Goel et al. 2006). Moreover, in few studies, alcoholic root extract of *A. racmosus* was found to increase heart rate and contractility in frog's heart. However, higher dose resulted in cardiac arrest and bronchodilation was also observed in experimental animals (R K Goyal et al. 2003).

Chapter 6

Polyherbal Formulations

Polyherbal formulations are prepared using various plant extracts in one medicine. The concept is found in Ayurvedic and other traditional medicinal systems where multiple herbs in a particular ratio may be used in the treatment of illness. Polyherbal formulation containing *A. racemosus* was proved to be effective in veterinary medications. In one study with Karan-Fries crossbred cows, polyherbal preparation supplementation containing *Withania somnifera*, *A. racemosus*, *Emblica officinalis*, *Ocimum sanctum*, *Tinospora cordifolia*, *Tribulus terrestris*, and *Nigella sativa* were observed to boost immunity and udder health in periparturient period of the cows. 19% (w/w) of *A. racemosus* root powder is used to prepare the polyherbal formulation in this study. This plant is very well known in this subcontinent due to the traditional application which has been practiced from ancient times till now. Similarly, in Bangladesh, *A. racemosus* is cultivated as traditional medicinal plant. Usually, their roots are used to found in the local markets occasionally. Several polyherbal formulations are prepared using *A. racemosus* by various pharmaceutical companies around India. However, an herbal formulation containing 500 mg of *A. racemosus* root powder named E- Green is sold by the ERGON Pharmaceuticals in Bangladesh.

Table 6: Various polyherbal formulations containing A. racemosus

EveCare	This is herbal preparation that contains 32 mg of *A. racemosus* extract per 5 ml of liquid. It was observed to treat different complications regarding menstruation and threatened abortion. The formulation was developed by Himalaya Drug Co., Bangalore, to treat various menstrual disorders and threatened abortion. Additionally, this formulation was reported to treat Dysfunctional uterine bleeding (DUB).
Menosan	Polyherbal formulation Menosan comprises of 110 mg of *A. racemosus* extract each tablet and applied in case of female reproductive system complications and was reported to increase uterus growth and uterine glycogen without affecting serum estrogen and progesterone level in immature rats.
Mentat	Mentat is a psychotropic herbal formulation containing *A. racemosus* has been seen to reduce the symptoms of alcohol withdrawal like anxiety, tremor, hallucination, convulsion in researches which proves its effect like anticonvulsive agent.
Abana	Abana is a herbal formulation containing *A. racemosus* is found to mediate cardioprotective activity and significant hypocholesterolaemic effect in rats and therefore established as potential cardioprotective agent.
Geriforte	Polyherbal preparation containing *A. racemosus* cures ageing,

(Table-6 continued)

	arteriosclerosis and has restorative effect in elderly people. It is known to induce cellular regeneration, prevent arteriosclerosis, increase hormone utilization, enhance protein and carbohydrate metabolism and induce hypocholesterolemia. Besides, it has been useful clinically by producing a feeling of well-being, increasing mental activity, lessening fatigue increasing appetite and sexual functions in the aging.
Siotone	Polyherbal preparation Siotone has been prepared from extracts of *Withania somnifera, Ocimum sanctum, A. racemosus, Tribulus terristris* Siotone comprises adaptogenic activity and has been proved effective in reduction of stress by reversing stress mediated biochemical and physiological pathways. Psychological disturbance accompanied with these stresses were treated as well.
Satavari Mandur	Prepared using root extract of *A. racemosus* and has tradition application in treatment of peptic ulcers. It treated gastric ulcers produced via pyloric ligation in laboratory animals thus indicates the presence of mucosal defensive factors and showed significant protection against pyloric ligation induced gastric ulcers. Involvement of mucosal defensive factors like increased mucous secretions suppresses the acid & pepsin production and secretion. Thus, assists in the activity of allopathic drug Ranitidine in gastric ulcer.

Chapter 7

Discussion and Conclusion

The ancient and recent research on the plant *A. racemosus* has confirmed that this plant is blissful with immense health benefits and pharmacological activities. Traditional sources of medicine like Unani, Ayurveda and Siddha have recorded this plant as a remedy of several health complications that were not easily curable in ancient times. Similarly, this plant has also brought a remarkable contribution its modern pharmacy practices through assuring justification of those traditional uses in numerous researches. Regardless of this, there is still more limitations between traditional knowledge and modern practices. Further studies and researches are required to take advantage of the potential of this plant in nervous disorders and psychiatric problems. One vital limitation is the existence of this plant is increasingly under threat due to inadequate harvesting practices, losing sustainability of the nature followed by decreasing soil fertility. Therefore, for its further utilization and future application, conservation is greatly necessary. For this reason, there's a requirement for the development of atmosphere friendly artificial system for conservation of its active compounds which can reduce the dependency on this plant. Researchers, nowadays, are looking forward to formulate new medications from natural resources. Systemic development of utilization, conservations and research methods for medicinal plant including *A. racemosus* can bring greater value in health, economy and medical therapy in our country.

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