Phytochemical and Pharmacological Potential of Crotalaria L. – A Review

By

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A thesis submitted to the Department of Pharmacy in partial fulfillment of the requirements for the degree of
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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

The thesis/project titled "Phytochemical and Pharmacological Potential of Crotalaria L.- A Review" submitted by Sumayea Kabir Saba (ID-13146068) of Spring, 2019 has been accepted as satisfactory in partial fulfillment of the requirement for the degree of Bachelor of Pharmacy on 29th May 2019

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Ethics Statement

The study does not involve any kind of animal trial and human trial.

Abstract

Medicinal plants are important source of therapeutic drugs. This review article focused on the Crotalaria genus. The objective of this research was to find out the potential therapeutic activities of some of the important species of Crotalaria genus. It is a large family of plants containing over 600 plants having various ranges of activity for numerous disease conditions. Phytochemicals of these plants have shown important therapeutic activities such as; anticancer, antitumor, antimicrobial, anti-inflammatory, anti-toxic, gastroprotective activity etc. However, the plants of this family also contain toxic alkaloids such as pyrrolidazone which is present in 60% of the plants of this family. This alkaloid was observed to cause death in several animal species but also was found to have potential against mutagenic growth. Methodology of this review article was literature review from different authentic sources of journals. The result of the study is that species of crotalaria genus can be a promising area of therapeutics.

Dedication

Dedicated to my parent & supervisor Dr. Hasina Yasmin

Acknowledgement

First of all, I express my greatest gratitude to Almighty Allah for endowing me with health, patience, protection and faith in all aspect of my life.

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Chapter 1

Introduction

1.1 Medicinal plants

Various plants have been utilized in conventional medication for a long time. Some do appear to work in spite of the fact that there may not be adequate logical information (twofold visually impaired preliminaries, for instance) to affirm their viability. Such plants ought to qualify as medicinal plants. The term 'crude medications of common or natural source' is utilized by drug specialists and pharmacologists to portray entire plants or parts of plants which have therapeutic properties (Sofowora, 2008).

As far back as antiquated times, in the exploration for the cure of their illness, the general population searched for medications in nature. The beginnings of the therapeutic plants' utilization were instinctual, just like the case with animals (Stojanoski, 1999). In perspective of the way that at the time there was not adequate data either concerning the explanations behind the diseases or concerning which plant and how it could be used as a solution, everything depended on exploration. In time, the explanations behind the use of explicit therapeutic plants for treatment of specific illnesses were being found; subsequently, the therapeutic plants' utilization continuously isolated the empiric structure and progressed toward becoming established on instructive information. Until the approach of iatrochemistry in the sixteenth century, plants had been the wellspring of treatment and prophylaxis (Kelly, 2009). However, complications associated with synthetic drugs and their limitations to tackle the ever-growing number of diseases make it important to look for solution in natural medicine.

The general population of various societies and countries around the world, especially in Iran, China, Egypt, and Greece has assumed, synthetic drugs are productive to treat maladies and

facilitate this procedure, prescription suggesting these drugs were growing. However, any synthetic drugs having therapeutic properties have been exhibited to cause symptoms. Thus, the general population has learned to utilize therapeutic herbs with negligible reactions (Bahmani, Zargaran, & Rafieian-Kopaei, 2014). In such a manner, various researches have studied the impact of herbs for aversion and treatment of neurological, gastrointestinal, and respiratory illnesses. Other than the impacts of plants on neurological clutters, wounds, an assortment of pain, headache, chilly, diabetes, hypertension, hyperlipidemia, skin issues, peptic ulcer, dysmenorrhea, and regenerative framework have been investigated (Delfan et al., 2014). Traditional systems of medicine continue to be widely practiced on many accounts. Population rise, inadequate supply of drugs, the prohibitive cost of treatments, side effects of several synthetic drugs and development of resistance to currently used drugs for infectious diseases have led to increased emphasis on the use of plant materials as a source of medicines for a wide variety of human ailments (Zahid,2016).

Recently, WHO (World Health Organization) estimated that 80 percent of people worldwide rely on herbal medicines for some aspect of their primary health care needs. According to WHO, around 21,000 plant species have the potential for being used as medicinal plants (Sen & Samanta, 2014).

Over the past 100 years, the improvement and mass production of synthetic drugs have changed health care in around the word. However, many people of rising countries depend on natural medicines for their primary care. In Africa, about 90% and in India, 70% of the population be contingent on natural medication to meet their health care necessities. In China, natural drugs are responsible for around 40% of medicines used and more than 90% of general hospitals in China have divisions for natural drugs (WHO 2005). However, the use of natural drugs has also

increased in developed countries. In the United States, in 2007, about 38% of adults and 12% of children were receiving derivatives of natural drugs (Ernst, Schmidt and Wider, 2005). National Center for Complementary and Alternative Medicine (Barnes, Bloom and Nahin, 2008) found that traditional drugs were most widely taken alternative drug therapy (18.9%).

A study piloted in Hong Kong in 2003 stated that 40% of the people participating expressed faith in natural medicine (Chan et al. 2003). In a survey of 21,923 adults in the United States, 12.8% took at least one natural drug (Harrison et al. 2004) and in another survey (Qato et al. 2008), 42% of participants took nutritional supplements, with multivitamins and minerals most normally used.

The most common reasons for using traditional medicine are that it is more affordable, more closely corresponds to the patient‘s ideology, allays concerns about the adverse effects of chemical (synthetic) medicines, satisfies a desire for more personalized health care, and allows greater public access to health information. The major use of herbal medicines is for health promotion and therapy for chronic, as opposed to life-threatening, conditions. However, usage of traditional remedies increases when conventional medicine is ineffective in the treatment of disease, such as in advanced cancer and in the face of new infectious diseases. Furthermore, traditional medicines are widely perceived as natural and safe, that is, not toxic This is not necessarily true, especially when herbs are taken with prescription drugs, over-the-counter medications, or other herbs, as is very common (Canter & Ernst 2004; Qato et al. 2008; Loya, Gonzalez-Stuart& Rivera 2009; Cohen & Ernst 2010).

These herbal products today are the symbol of safety in contrast to the synthetic drugs that are regarded as unsafe to human being and environment. Although herbs had been priced for their medicinal, flavoring and aromatic qualities for centuries, the synthetic products of the modern

age surpassed their importance, for a while. However, the blind dependence on synthetics is over and people are returning to the naturals with hope of safety and security. It‘s time to promote them globally (Zahid, 2016).

1.2 Phytotherapy

The term was introduced by the French physician Henri Leclerc (1870-1955). He had published numerous essays on the use of medicinal plants, most of them in La Presse Medicale, a leading French medical journal. Phytotherapy is a field of medicine that uses plants either to treat disease or as health-promoting agents. It is often referred to as herbalism in Western medicine. Traditional use of phytotherapies generally preserves the original composition and integrity of the source plant, so that either the whole plant or thedesired percentage of its minimally adulterated components is used for medicinal purposes (Falzon & Balabanova, 2017).

1.3 Phytochemicals

Phytochemicals (from the Greek phrase phyto, meaning plant) are biologically active, naturally going on chemical compounds determined in plants, which furnish health benefits for humans similarly than those attributed to macronutrients and micronutrients. They shield flora from disease and damage and make contributions to the plant‘s color, aroma and flavor. In general, the plant chemicals that shield plant cells from environmental risks such as pollution, stress, drought, UV publicity and pathogenic assault are referred to as phytochemicals (Nafiu, Alli & Aniah, 2016). Recently, it is actually recognized that they have roles in the protection of human health when their dietary intake is significant. More than 4,000 phytochemicals have been cataloged and are classified via a defensive function, physical characteristics and chemical traits and About one hundred fifty phytochemicals have been studied in detail. In wide-ranging dietary phytochemicals are located in fruits, vegetables, legumes, complete grains, nuts, seeds, fungi,

herbs and spices. Broccoli, cabbage, carrots, onions, garlic, entire wheat bread, tomatoes, grapes, cherries, strawberries, raspberries, beans, legumes, and soy ingredients are frequent sources. Phytochemicals accumulate in specific parts of the plants, such as in the roots, stems, leaves, flowers, fruits or seeds. Many phytochemicals, particularly the pigment molecules, are regularly targeted in the outer layers of the quite a number plant tissues. Levels differ from plant to plant depending upon the variety, processing, cooking and developing stipulations (Muglia & Prando, 2015). Phytochemicals are also handy in supplementary forms, but evidence is lacking that they supply the same health benefits as dietary phytochemicals. These compounds are known as secondary plant metabolites and have biological houses such as antioxidant activity, antimicrobial effect, modulation of detoxing enzymes, stimulation of the immune system, minimize of platelet aggregation and modulation of hormone metabolism and anticancer property. There are greater than thousand regarded and many unknown phytochemicals. It is universal that vegetation produces these chemicals to guard themselves, however current researches display that many phytochemicals can additionally guard human towards illnesses (Liu et al., 2000).

1.3.1 Classification of Phytochemicals

The particular taxonomy of phytochemicals may have no longer been finished so far, due to the significant variety of them. In latest year Phytochemicals are categorized as foremost or secondary constituents, based on their position in plant metabolism. Primary materials include the common sugars, amino acids, proteins, purines and pyrimidines of nucleic acids, chlorophyll‘s et Crotalaria Secondary elements are the last plant chemicals such as alkaloids, terpenes, flavonoids, lignans, plant steroids, flavonoids and glucosides. Literature survey shows

that phenolics are the most standard and structurally different plant phytoconstituent (Moses, 2012).

Phenolics

Phenolic phytochemicals are the predominant member of phytochemicals and the most substantially spread in the plant kingdom. The three most extensive groups of dietary phenolics are flavonoids, phenolic acids, and polyphenols. Phenolic is hydroxyl crew (-OH) having type of chemical compounds where the (-OH) bonded without delay to an aromatic hydrocarbon group. Phenol (C_6H_5OH) is deliberated as the simplest class of this crew of herbal compounds. Phenolic compounds are a significant and composite team of chemical materials originated in plants. They are plant secondary metabolites having a significant role as protective compounds. Phenolics exhibit several residences high-quality to humans and its antioxidant residences are integral in defining their section as protecting agents against free radical-mediated ailment routes. Flavonoids are the largest group of plant phenols and the most premeditated. Phenolic acids structure a team that includes the substantially dispersed hydroxybenzoic and hydroxycinnamic acids (Khoddami, Wilkes, & Roberts, 2013).

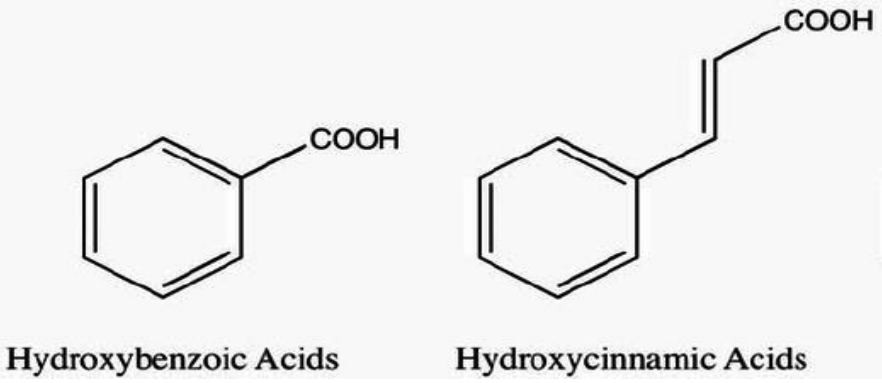


Figure 1: The basic structure of phenolics (Khoddami, Wilkes, & Roberts, 2013)

Phenolic acids

The term ―phenolic acids", in general, designates phenols that possess one carboxylic acid functional group. Naturally occurring phenolic acids comprise two different carbon frameworks: the hydroxycinnamic and hydroxybenzoic structures. Hydroxycinnamic acid compounds are produced as simple esters with glucose or hydroxy carboxylic acids (Huang, 2016).

Flavonoids

Flavonoids are polyphenolic compounds that are ubiquitous in nature. More than 4,000 flavonoids have been documented, many of which appear in vegetables, fruits and beverages like tea, espresso and fruit drinks. The flavonoids appear to have a key position in efficacious medical management of antique periods, and their exercise has continued up to today. Flavonoids are pervasive among vascular flowers and appear as aglycones, glucosides and methylated derivatives. More than 4000 flavonoids have been described so far within the parts of plants typically taken via human beings and approximately 650 flavones and 1030 flavanols are recognized. A minor amount of aglycones (i.e., flavonoids barring connected sugar) are many times extant and not often denote a relatively considerable quantity of the whole flavonoid compounds in the plant. Figure 1.2, represents the foremost flavonoids‘ structures (Panche, et al., 2016).

Tannin

From a chemical point of view, it is difficult to define tannins due to the fact that the time period encompasses some very various oligomers and polymers. It may be said that the tannins are a heterogeneous team of excessive molecular weight polyphenolic compounds with the capability to shape reversible and irreversible complexes with proteins (mainly), polysaccharides (cellulose, hemicellulose, pectin, etc), alkaloids, nucleic acids and minerals, etc . On the foundation of their

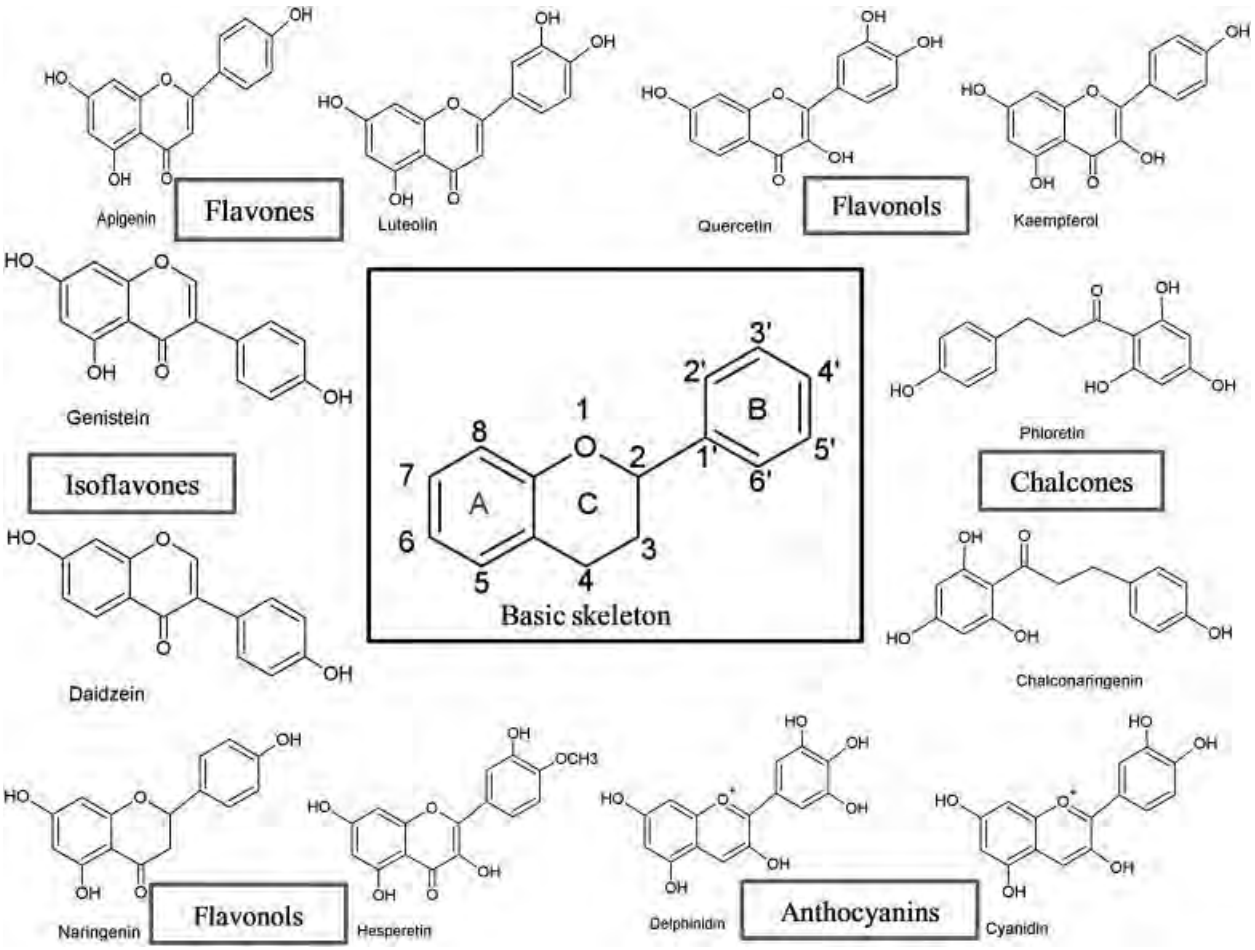


Figure 2: Flavonoids and their classes (Panche et al., 2016)

structural traits it is consequently possible to divide the tannins into four major groups: Gallotannins, ellagitannins, complex tannins, and condensed tannins. Gallotannins are all those tannins in which galloyl units or their meta-depsidic derivatives are bound to various polyol-, catechin-, or triterpenoid units. Ellagitannins are those tannins in which at least two galloyl units are C–C coupled to every other, and do now not incorporate a glycosidically linked catechin unit. Complex tannins are tannins in which a catechin unit is certain glycosidically to a gallotannin or an ellagitannin unit. Condensed tannins are all oligomeric and polymeric proanthocyanidins formed by means of linkage of C-4 of one catechin two with C-8 or C-6 of the subsequent monomeric catechin (Bianchi, 2016).

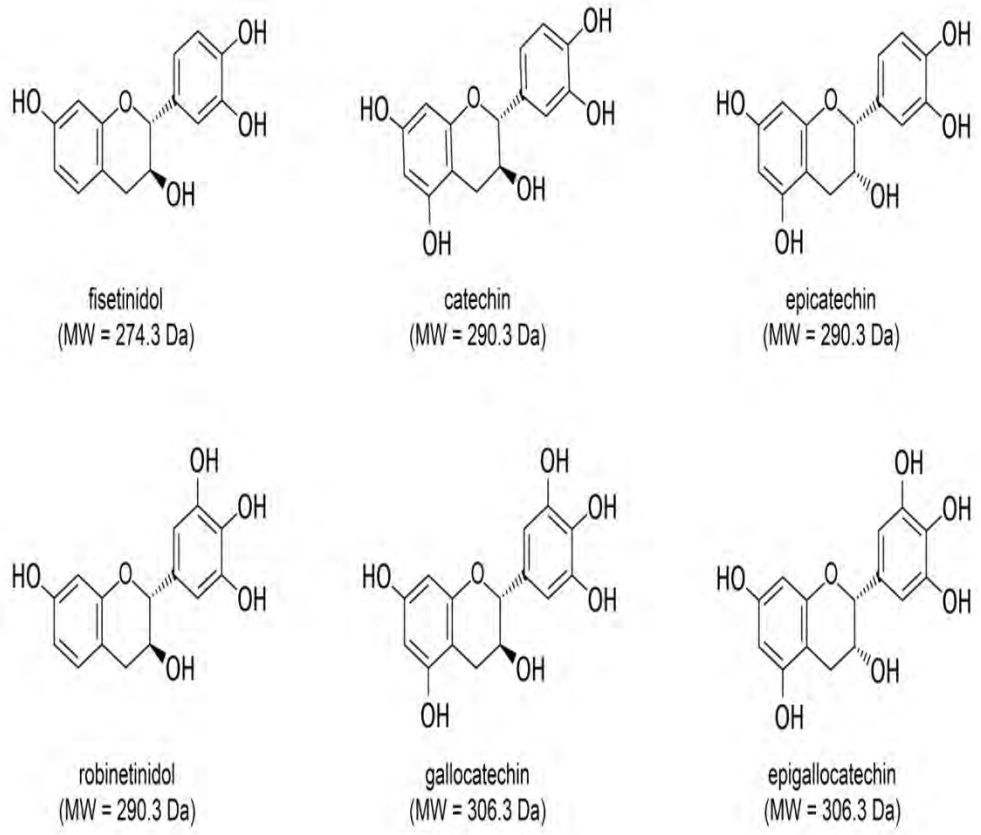


Figure 3: Structure of condensed tannins (Bianchi, 2016)

Alkaloids

Alkaloids are herbal product that carries heterocyclic nitrogen atoms, are fundamental in character. The title of alkaloids derives from the ―alkaline" and it was once used to describe any nitrogen-containing base. Alkaloids are naturally synthesis with the aid of massive numbers of organisms, along with animals, plants, microorganism and fungi. It was observed that they had been nitrogen-containing bases which formed salts with an acid. Hence they had been recognized as the vegetable alkalis or alkaloids and these alkaloids are used as the local anesthetic and stimulant as cocaine (Zhao, Wu, & Wang, 2014). Almost all the alkaloids have a bitter taste. The alkaloid quinine, for example, is one of the bitterest tasting elements known and is extensively

bitter (1x10-5) at a molar concentration. Alkaloids are so numerous and involve such a range of molecular structure that their rational classification is difficult. However, the fantastic method to the trouble is to team them into families, relying on the kind of heterocyclic ring device present in the molecule (Zhao, Wu, & Wang, 2014). The names of character contributors are, therefore,

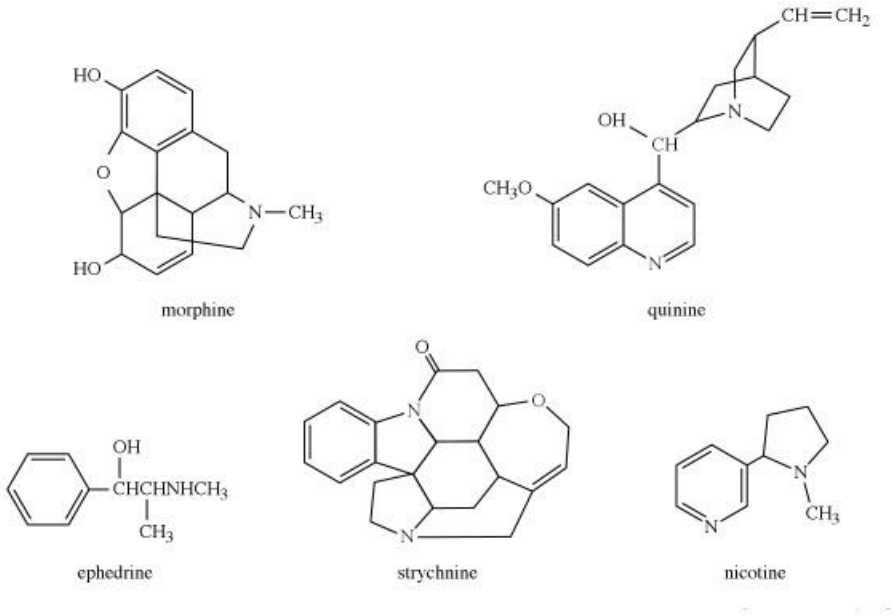


Figure 4: Different Alkaloids (Zhao, Wu, & Wang, 2014: Britannica, 2018)

normally derived from the title of the plant in which they occur, or from their attribute physiological activity. The more than a few classes of alkaloids according to the heterocyclic ring system they include are listed below. Pyrrolidine alkaloids: they comprise a pyrrolidine (tetrahydropyrrole) ring system. E.g Hygrine found in Erythroxylum coca leaves and cuscohygrine. Pyridine alkaloids: they have piperidine (hexahydropyridine) ring system. E.g Coniine, piperine and isopelletierine. Pyrrolidine-pyridine alkaloids: the heterocyclic ring system existing in their alkaloids is Pyrrolidinepyridine.E.g Myosmine, Nicotine alkaloid observed in tobacco (Nicotiana tabacum) plant. Pyridine-piperidine alkaloids. This family of alkaloids contains a pyridine ring device join to a piperidine ring system the easiest member is Anabasine

alkaloid remoted from poisonous Asiatic plant anabasis aphyllan. Quinoline Alkaloids: These have the basic heterocyclic ring system quinoline .E.g Quinine occurs in the bark of cinchona tree.It has been used for centuries for the treatment of malaria. Synthetic pills such as primaquine have generally exchange quinine as an anti-malarial. Isoquinoline alkaloids: They comprise heterocyclic ring system isoquinoline. E.g Opium alkaloids like narcotine, papaverine, morphine, codeine, and heroine (Britannica, 2018).

Terpenoids

The terpenoids are a category of natural products which have been derived from five-carbon isoprene units. Most of the terpenoids have multi cyclic constructions that vary

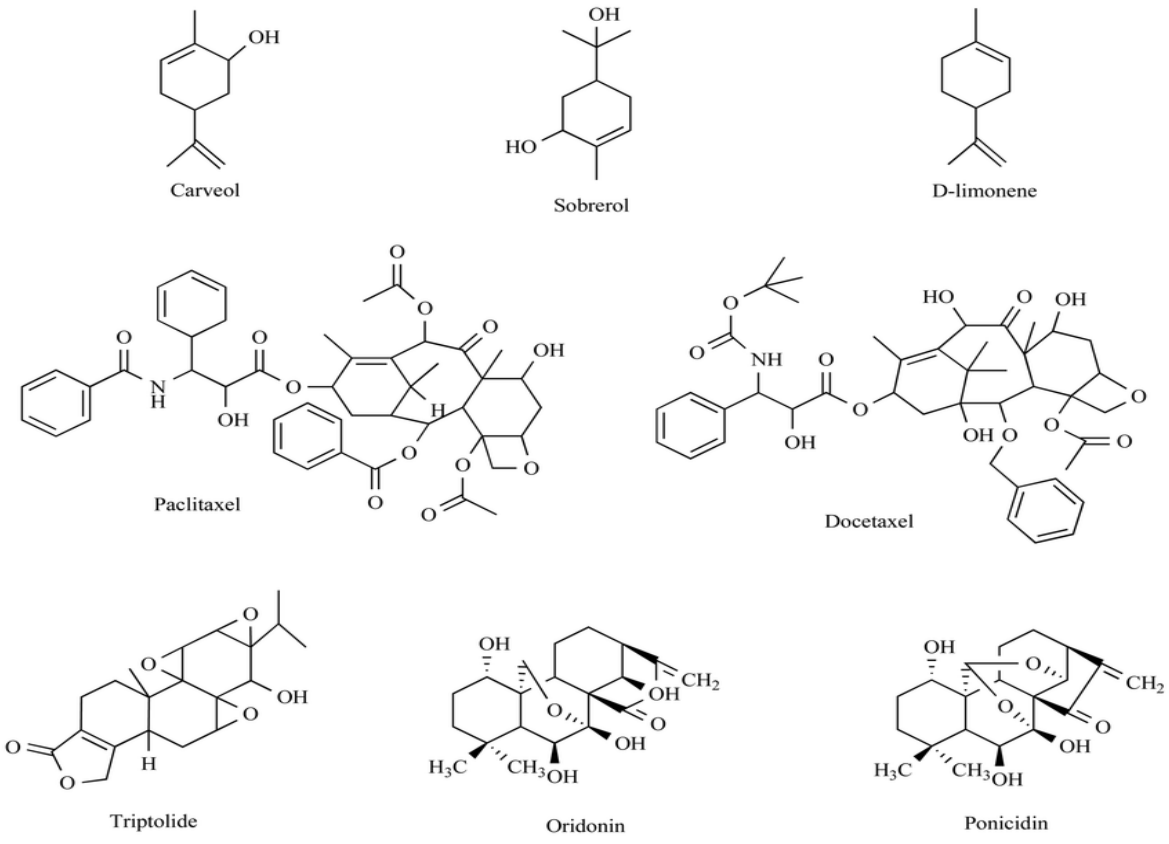
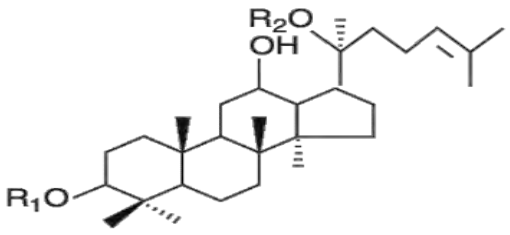


Figure 5: Chemical structures of monoterpenoids and diterpenoids (Yang & Dou, 2010)

from one every other with the aid of their useful groups and primary carbon skeletons. These types of natural lipids can be found in each classification of living things, and consequently viewed as the greatest group of natural products. Many of the terpenoids are commercially fascinating due to the fact of their use as flavors and fragrances in foods and cosmetics examples menthol and sclareol or due to the fact they are vital for the nice of agricultural products, such as the flavor of fruits and the heady scent of flora like linalool. Terpenes are considerable in nature, broadly speaking in vegetation as ingredients of crucial oils (Zhao, Wu, & Wang, 2014). Their building block is the hydrocarbon isoprene, $CH_2=C(CH_3)-CH=CH_2$. Terpene hydrocarbons consequently have molecular formulation (C_5H_8) n and they are categorized in accordance with the variety of isoprene gadgets (Yang & Dou, 2010).

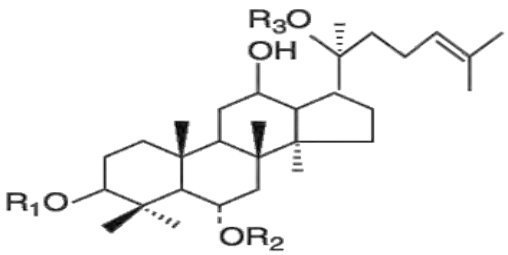
Saponin

Saponins are a group of secondary metabolites discovered considerably distributed in the plant kingdom. They form consistent foam in aqueous options such as soap, for this purpose the name ―saponin". Chemically, saponins as a group consisting of compounds that are glycosylated steroids, triterpenoids, and steroid alkaloids. Two essential kinds of steroid aglycones are know spirostan and frost derivatives. The predominant triterpene aglycone is a derivative of oleanane. The carbohydrate section consists of one or larger sugar moieties containing glucose, galactose, xylose, arabinose, rhamnose, or glucuronic acid glycosidically linked to a sapogenin (aglycone). Saponins that have one sugar molecule attached at the C-3 function are recognized as monodesmoside saponins, and these that have a minimal of two sugars, one attached to the C-3 and one at C-22, are called bidesmoside saponins (Saxena et al., 2013).



Protopanaxadiol-type

	R1	R2
Rb1	O-G-G	O-G-G
Rb2	O-G-G	O-G-Ap
Rb3	O-G-G	O-G-X
Rc	O-G-G	O-G-Af
Rd	O-G-G	O-G
Rg3	O-G-G	O-H
Rh2	O-G-G	O-H
Aglycone(PD)	O-H	O-H



Protopanaxatriol-type

	R1	R2	R3
Re	O-H	O-G-R	O-G
Rf	O-H	O-G-G	O-H
Rg1	O-H	O-G	O-G
Rg2	O-H	O-G-R	O-H
Rh1	O-H	O-G	O-H
Aglycone(PT)	O-H	O-H	O-H

Figure 6: Saponins derived from ginseng (Zhao, Wu, & Wang, 2014)

1.4 Biological Activities of Phytochemicals

The phytochemicals present in flowers are accountable for preventing ailment and promotion health have been studied notably to set up their efficacy and to understand the underlying mechanism of their action. Such studies have protected identification and isolation of the chemical components, establishment of their organic efficiency each with the aid of in vitro and in vivo studies in experimental animals and via epidemiological and clinical-case manipulate studies in man (Frumkin & Thun, 2001). Study findings advocate that phytochemicals can also minimize the hazard of coronary heart sickness by preventing the oxidation of low-density lipoprotein (LDL) cholesterol, lowering the synthesis or absorption of cholesterol, normalizing blood pressure and clotting, and enhancing arterial elasticity. Phytochemicals might also detoxify materials that cause cancer. They appear to neutralize free radicals, inhibit enzymes that spark off carcinogens, and prompt enzymes that detoxify carcinogens. For example, according to information summarized with the aid of Meagher and Thomson, genistein prevents the formation of new capillaries that are needed for tumor increase and metastasis. The physiologic homes of

extraordinarily few phytochemicals are properly understood and more many types of research have focused on their viable role in stopping or treating most cancers and heart disorder (Moses, 2012). Phytochemicals have additionally been promoted for the prevention and remedy of diabetes, high blood pressure, and macular degeneration. While phytochemicals are categorized by way of function, a compound may also have greater than one biological feature serving as each an antioxidant and antibacterial agent (Frumkin & Thun, 2001).

Chapter-2

Crotalaria Genus

2.1 Introduction

Crotalaria L. (Fabaceae) is one of the largest genera of Papilionoideae consisting of about 700 species. These species are extensively allotted in the various continents. The greatest wide variety occurs in tropical and subtropical regions. This genus belongs to the legume family and is made up largely of herbaceous plants (Okuda, Yoshida& Hatano, 1992). These species contain phytochemicals such as alkaloids, tannins, saponins. Among all the species, *Crotalaria pallida* was found to be the most used plant. Good medicinal value was found in the treatment of skin infection, fever and ulcer. Crotalaria species are also widely used in traditional veterinary pharmacy in preventing liver disease. 60% species of this genus contain pyrrolidazone alkaloid. Though Pyrrolidazone is toxic to cattle but adequate concentration of this compound can induce significant anti-metastatic activity. Other species most typically used are *Crotalaria usaramoensis Baker, Crotalaria anagyroides H. B. K., O. juncea, and Crotalaria striata*. These species have also been grown in other parts of the world, and their use appears to be extending (Cheeke, 1988, Cheeke, 1998).

2.2 Geographical Distribution

The Crotalaria species are in the main annuals, however many are perennials. While the plant life is basically upright, some are semi-erect, others pretty prostrate. There is outstanding variation in plant height, from less than 1 foot to 15 feet, depending on the species. They are generally monofoliolate or trifoliolate, now and again having greater than three leaf-lets. The branching varies with the species. Some have an upright central stem with little or no branching, whilst others are very profusely and finely branched. The species that have been used agriculturally are

large, upright, and diffusely branched, with the ex- ception of *Crotalarla juncea*, which is sparingly branched. *Crotaluria spectabilis* with plant life and pods, displaying regular habit of boom some species, such *as Crotalaria retusa* and *Crotalaria lanceolata* E. Mey., mature a large extent of seed early, inside one hundred to one hundred forty days from the planting date. Many others are too late to mature seed. *Crotalaria striata* and *Crotalaria spectabilis* Roth 2 signify an intermediate kind as regards maturing seed; requiring a hundred twenty five to a hundred seventy five days earlier than many pods are mature. Most species proceed to set pods and mature seed all summer season and fall. (Mckee & Enlow, 1931)

2.3 Parts Used for Medicinal Purpose

Roots, seeds, pods, flower and leaves.

2.4 Taxonomical Classification

Rank	**Scientific Name and Common Name**
Kingdom	Plantae – Plants
Subkingdom	Tracheobionta – Vascular plants
Superdivision	Spermatophyta – Seed plants
Division	Magnoliophyta – Flowering plants
Class	Magnoliopsida – Dicotyledons
Subclass	Rosidae
Order	Fabales
Family	Fabaceae/Leguminosae – Pea family
Genus	*Crotalaria* L. – rattlebox
Species	*Crotalaria longirostrata* Hook. & Arn. – longbeak rattlebox

2.5 Common Names

- **castanet-plant** (Source: Dict Rehm) - English
- **long-beak rattlepod** (Source: State Noxweed Seed) - English
- **chipilín** (Source: Dict Econ Pl) - Spanish
- **chipilín de comer** (Source: Dict Rehm) - Spanish

2.6 Plant Description

Herbs and shrubs, annuals and perennials.

Leaves: Alternate, simple, 1-foliolate or palmately compound with 3–7 leaflets; leaflets often with translucent glands; stipulate; stipple sabsent (Riet-Correa and Méndez, 2007).

Flowers: Usually in terminal racemes, sometimes leaf opposed or rarely axillary; bracteate. Calyx 5-toothed, ± equal, sometimes 2-lipped with upper 2 teeth ± united and lower 3 teeth ± united. Corolla venation sometimes dark; standard ± circular or ovate, sometimes pubescent outside; wings shorter than standard, with a patch of ruffles in rows; keel curved to 90?, ciliate, sometimes incurved, beak tip sometimes twisting spirally. Stamen monadelphous, sheath split on upper side; anthers alternately long and basifixed and short and dorsifixed. Ovary: 2-ovuled; style incurved or bent, longitudinal line of hairs on inside; stigma terminal(Riet-Correa and Méndez, 2007).

Pods: Pods are inflated, dehiscence sometimes incomplete; seeds ± reniform, with or without an aril, usually smooth, funicles slender (Riet-Correa and Méndez, 2007).

Chapter-3

Crotalaria juncea

3.1 Introduction

Crotalaria juncea is an erect, laxly branched annual plant growing 1 - 3 metres tall with a sturdy and deep tap-root system. The plant has been cultivated considering the fact those prehistoric times, mainly in India, for its fibre. It is one of the earliest of the fairly named fibres of India, being cited in early Sanskrit beneath the title of 'sana'. It is extensively grown in many areas of the tropics and subtropics, along with Africa, Asia and Australasia, as an inexperienced manure crop and for its fiber. It has come to be adapted in places (Dinakaran, Godala & Dharani, 2011; Malashetty, Sharanabasappa, 2004; Chouhan & Singh, 2010; Malashetty, & Patil 2004; Adams & Gianturco, 1956).

Figure 7: Crotalaria juncea (Malashetty, & Patil, 2004)

3.2 Phytochemistry

Table 1 shows some of the important phytochemicals isolated from the plant. Javed, Saleem, Yamin and Chaudri (1999) analyzed seed lipids and proteins of *Crotalaria juncea* for fatty acids

Table 1: Phytochemical constituents isolated from different parts of Crotalaria juncea

Plant part used	Phytochemicals isolated	References
Leaves	Riddelline, seneciphylline, senecionine, trichodesmine, chodesmine alkaloids, galactose-specific lectin and cardiogenic 3-O- [β]-d-xylopyranoside.	Dinakaran, Godala & harani , 2011; Malashetty, Sharanabasappa Patil, 2004; Chouhan & Singh, 2010; Malashetty & Patil, 2004; Adams & Gianturco, 1956
Seeds	Toxic dehydropyrrolizidine alkaloids (DHPAs) (isohemijunceinestrichodesmine and junceine Carbohydrates protein Toxic amino acids a-amino-b-oxylaminopropionic acid, a-aminogoxylaminobutyric acid and/or a,g-diaminobutyric acid. Another compound reported to be in sunn hemp seeds is cardenolidecardiogenin 3-O-betaD-xylopyranoside	Al-Snafi, 2015; Javed & Chaudri, 1999; Chouhan& Singh, 2011; Pilbeam and Bell. 1979; Yadav and Thakur, 1994
Plant fibre	Moisture, cellulose,hemi-celluloses,lignin,pectin	Maroyi,2011; CSIR (Council of Scientific and Industrial Research),1948-1976

Stem	Cellulose ,pentosan ,urinic anhydrite	Maroyi 2011; CSIR (Council of Scientific and Industrial Research), 1948-1976
Dried stalks of the plant	Moisture, ether extract, albuminoids, carbohydrate(35.8%), woody fibreand soluble mineral matter.	Maroyi 2011; CSIR (Council of Scientific and Industrial Research), 1948-1976

and amino acids respectively. Gas chromatographic analysis of the oil gave palmitic acid (16.01-18.09%), stearic acid (7.29-10.15%), oleic acid (6.69-14.41%), linoleic acid (54.44-62.36%), linolenic acid (0.7-7.86%), myristic acid (0.197%), arachidic acid (1.199%) and behenic acid (1.369%). Pasha (1996) in their acidic and alkaline hydrolysis technique, the defatted seed cake used to be hydrolysed and observed that it contained all the integral amino acids barring methionine and six non-essential amino acids. The percentage composition of amino acids (g/100g): critical amino acids (isoleucine 1.17, leucine 2.10, lysine 1.67, phenylalanine 0.92, threonine 0.88, tryptophan 0.53, tyrosine 0.78 and valine 0.96); and nonessential amino acids (alanine 2.12, arginine 2.72, glutamic acid 9.45, glycine 1.53 and proline 1.10). In some other find out about from Prasad (2013) uncommon amino acid, 2-amino-5-hydroxyhexanoic acid used to be also isolated from the seeds of *Crotalaria juncea*.

Seeds of *Crotalaria juncea* were reported to contain 0.074% of toxic dehydropyrrolizidine alkaloids (DHPAs) (isohemijunceines, trichodesmine, and junceine). *Crotalaria juncea* seeds were observed to contain carbohydrates, protein, oil, moisture and ash. Seed lipids and proteins of *Crotalaria juncea* were investigated for unsaturated fats and amino acids

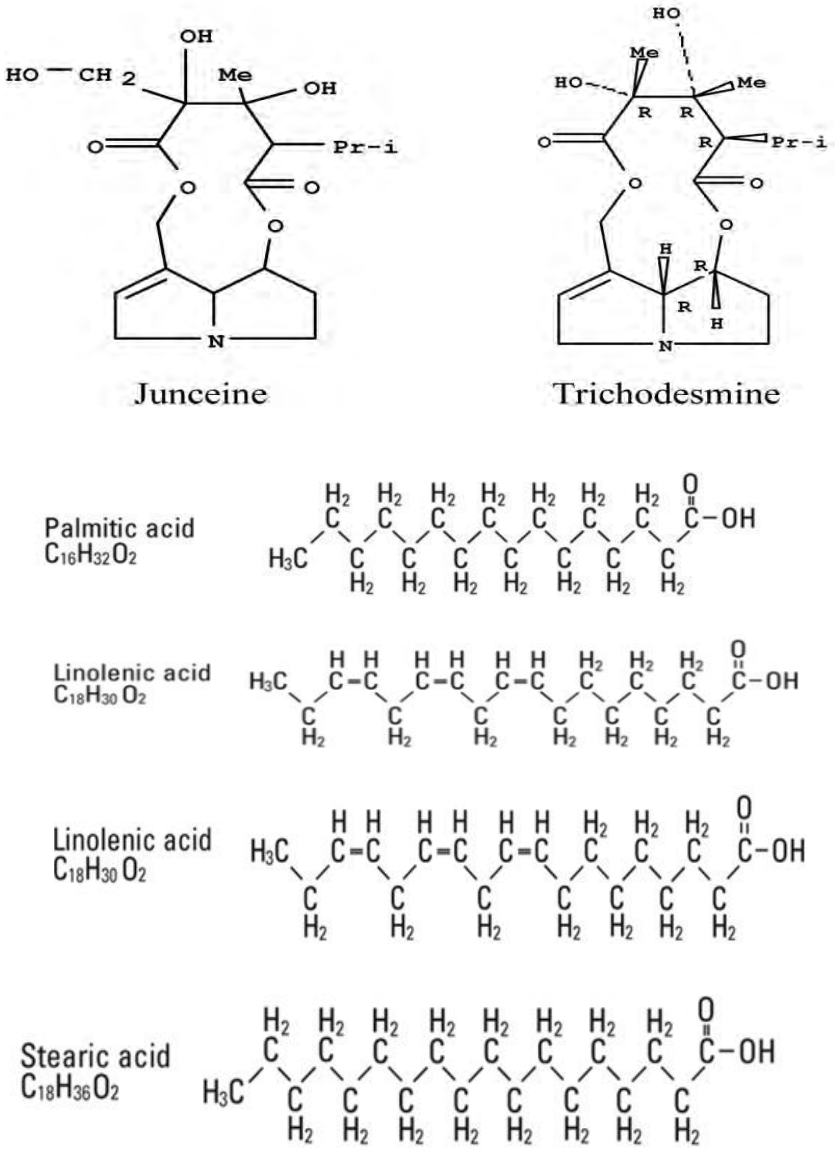


Figure 8: Structures of selected phytochemicals from Crotalaria juncea (Adams & Gianturco, 1956)

arrangement. Gas chromatographic investigation of the oil revealed palmitic acid (16.01-18.09%), stearic acid (7.29-10.15%), oleic acid (6.69-14.41%), linoleic acid (54.44-62.36%), linolenic acid (0.7-7.86%), myristic acid (0.197%), arachidic acid (1.199%) and behenic acid (1.369%) (Al-Snafi, Sh& Ah, 2015: Javed, et al., 1999, Chouhan, et al., 2011). The plant fibre contained 10% moisture, 67.8% cellulose, 16.6% hemi-celluloses, 3.5% lignin, 0.3% pectin, 1.4% water solubles and 0.4% fat and wax. The stems contained: cellulose 78.3%; pentosan

3.6%; urinicanhydrite 1.7%; acetyl content 1.5% and lignin 4.0%. Minor constituents included: fat and wax 0.5%; nitrogenous matter 1.4% and ash 0.3%. Monosaccharide constituents of the plant included: glucose 80.3%;xylose 5.2%; mannose 11.7%; galactose 2.1%; arabinose 1.7% and rhamnose 0.4%. Dried stalks of the plant for cattle feed, contained 14.4% moisture, 1.1% ether extract, 11.3% albuminoids, 35.8% carbohydrate, 27.4% woody fiber, and 6.4% soluble mineral matter. Seeds contained 8.6% moisture, 34.6% crude protein, 4.3% fat, 41.1% starch, 8.1% fibre, and 3.3% ash. Seeds were reported to contain trypsin inhibitors, and were said to be poisonous to cattle. Seeds oil contained 46.8% linoleic acid, 4.6% linolenic acid, and 28.3% oleic acid, and 20.3% saturated acids. The seeds also contained the toxic pyrrolizidine alkaloids trichodesmine, juncein, senecionine and seneciphylline and 25.6% of the polysaccharide galactomannan.

3.3 Pharmacological Activity

3.3.1 Hypolipidemic activity: The uncommon amino acid, 2-amino-5-hydroxyhexanoic acid remoted from the seeds of *Crotalaria juncea*, confirmed dose structured lipid reducing endeavor in the in vivo experiments and additionally confirmed precisely in vitro antioxidant activity. The cyclized compound, 3-amino-6-methyltetrahydro-2H-pyran-2-one showed better lipid reducing and antioxidant profile than the parent compound. Anti-obesity impact of *Crotalaria juncea* leaves extract was documented in excessive fats brought about weight problems in rats (Shailja & Trivedi, 1982).

3.3.2 Effects on reproductive systems: The alcohol extract was located to be the most advantageous in causing anti-implantation and pregnancy interruption activities. These negative

results on fertility were reversible upon removal of the extract treatments. The alcohol extract was once found to possess estrogenic activity (Pessoa et al., 2013).

3.3.3 Antioxidant activity: Antioxidant endeavor of *Crotalaria juncea* extracts have been studied in goat liver lipid peroxidation, linoleic acid emulsion, α-amylase and lipase inhibitory activity. All the extracts had proven antioxidant property, α-amylase, and lipase inhibitory properties. Aqueous extract was once observed to show most antioxidant undertaking on goat liver (Pessoa et al., 2013).

3.3.4 Antibacterial &Antifungal activity: The ethanol extract of flora phase (CJFEE) and seeds part (CJSEE) were evaluated for the antibacterial undertaking by way of the agar disc diffusion method towards *E. coli, E. faecalis, K. pneumonia, P. aeruginosa, S. flexneri, S. aureus, S. dysenteriaeand V. cholera*. Results revealed that CJSEE possesses widespread antibacterial exercise in opposition to the *E. coli, K. pneumonia, P. aeruginosa, S. aureus and V. chlorae*. However, the ethanol extract of seeds phase had higher antibacterial than ethanol extract of flower components of *Crotalaria juncea* (Pessoa et al., 2013).

The antibacterial endeavor of crude extracts organized in sodium phosphate buffer in opposition to Xanthomonas pressure was once studied. There has been found a particularly robust recreation of *Crotalaria juncea* extracted in sodium phosphate buffer towards plant bacterial pathogen, *Xanthomonas axanopodis* pv, punicae. Moderate antifungal exercise has been said in the methylene chloride and methanol extract of aerial components of *Crotalaria juncea* of Indonesian beginning (Webber, 2011).

3.3.5 Anti-diarrhoeal effects: The anti-diarrhoeal consequences of methanolic extract of leaves of *Crotalaria juncea* (MECJ) was studied towards castor oil-induced diarrhea model and small gut transit model in rats; its antioxidant activity was once located to be attention based and

CJSPE has displayed dose dependant, sizeable inhibition of no manufacturing in the remoted rat peritoneal macrophages (Shailja & Trivedi, 1982).

3.3.6 Anti-Inflammatory effect: Anti-inflammatory effect of the *Crotalaria juncea* seed oil (CJSPE) was once assessed through its impact on NO radical production in remoted macrophages from rat peritoneal (in vitro method); and carragennan-induced paw edema rat mannequin and cotton pellet-induced granuloma formation in rat model (in vivo method). The authors concluded that CJE extensively inhibited adjuvant brought on arthritis and has an extensive anti-inflammatory effect ($p<0.001$). It has anti-ulcerogenic property in contrast to indomethacin, which may also be due to appetite suppressant endeavor (Shailja & Trivedi, 1982).

3.3.7 Hepatoprotective activity: According to the results, it used to be proved that the Crotalariajuncea seed extract (CJSE) possessed hepatoprotective potency in a dose structured manner by way of reducing the elevated stages of marker enzymes and via growing the reduced antioxidant enzyme activity (Webber, 2011).

3.3.8 Other activities: Recently, transgenic plant life expressing immunogenic proteins of foot-and-mouth disease virus (FMDV) have been used as oral or parenteral vaccines against foot-and-mouth disorder (FMD). They showcase benefits like price effectiveness, absence of processing, thermostability, and effortless oral application. FMDV VP1 protein of single serotype has been basically used as an immunogen. A bivalent vaccine with tandem-linked VP1 proteins of two serotypes, A and O, current in transgenic forage crop *Crotalaria juncea* (Webber, 2011).

3.4 Contraindication and toxicity

Acute toxicity of ethanolic extract of the leaves of *Crotalaria juncea* was once carried out in rats, However, as an end result of sunn hemp seeds contents of several pyrrolizidine alkaloids, it was

poisonous to animals and birds when ingested in ample amount (100). Seeds of *Crotalaria juncea* contained 0.074% of poisonous dehydropyrrolizidine alkaloids (DHPAs) (isohemijunceines 0.05%, trichodesmine 0.016%, and junceine 0.008% (Al-Snafi, 2016).

Chapter- 4

Crotalaria pallida

4.1 Introduction

Crotalaria pallida is an erect, well-branched, every so often strong perennial herb with stems that become extra or less woody. It can develop up to 2 meters tall. The plant has a pretty long history of cultivation as a green manure and ground cover crop, although it is much less grown at current due to its susceptibility to pests and illnesses in Asia. It is still often cultivated in southeastern USA (Wei et al., 2012).

Figure 9: Crotalaria pallida (Wei et al., 2012)

4.2 Phytochemistry

Hu (2007) in their phytochemical find out about of the seeds of *Crotalaria pallida* led to the isolation of two uncommon homoisoflavonoids (Cropalliflavone A Cropalliflavone), every other flavonoid Cropalliflavone C , Usaramine-N-oxide, Cropallin A, Cropallin B alongside with sixteen recognized compounds,the sixteen known compounds were identified as six flavonoids, diosmetin (Jia et al., 2003), luteolin (Liang et al., 2011), acacetin-8-C-neohesperidoside (Larionova et al., 2010), obovatachalone (Yin et al., 2006), 5,30,40-trihydroxy-200,200-

dimethylpyrano isoflavone (Wei et al., 2012) and alpinumisoflavone (Han et al., 2005); one alkaloid, usaramine (Bourauel, 1998); one sesquiterpenoid, (-)-methyl dihydrophaseate (Li et al., 2012); six phenylpropanoids, ferulic acid two (Zheng et al., 2004), p-hydroxyl ethyl cinnamate (Li et al.,2008), ethyl caffeate (Tu et al., 1999), p-hydroxycinnamic acid methyl ester (Chang and Gong, 2005), 4,40-bis(1-propenoic acid methyl ester)-30-methoxydiphenyl ether (Li et al., 2007) and ethyl (E)-3-(4-(4-((E)-3- ethoxy-3-oxoprop-1-en-1-yl)-2-methoxyphenoxy)phenyl) acrylate (Noshita et al., 2015); one lignin, ethyl (E)-3-[(2R,3R)-2,3-dihydro-2-(4-hydroxy-3 methoxyphenyl)-7-methoxy-3-ethoxycarbonyl-1-benzofuran-5yl] propenoate (Constantin et al., 2012); and one phenolic acid, sonchifolinin B (Zhang et al., 2008), by using comparing their spectroscopic data with these pronounced in the literature. Hu et al., 2017 extracted powdered seeds of *Crotalaria pallida* (21.0 kg) with 75% ethanol (3 -70 L, 7 days each) at room temperature. Panda, Das, & Das(2015)in their article stated that the two preliminary phytochemical screening showed that the exclusive solvent extracts of *Crotalaria pallida*, showed the presence of alkaloids, flavonoids, terpenoids, saponins, phenols, steroids and tannins

Table 2: Phytochemicals isolated from different parts of Crotalaria pallida

Plant part used	Phytochemicals isolated	References
Seed	Flavonoids (cropalliflavones A-C), Alkaloids (usaramine-N-oxide and cropallins A-B)	Hu, Chou, & Zhang, 2017
Leaf	Linolenic acid, palmitic acid, linoleic acid(omega-6 fatty acid)	Ukil, Laskar, & Roy, 2016
Barks	5,7,40-trihydroxy-20-methoxyisoflavone	Ko, et al., 2004

in all the solvent extract & carbohydrates absent in all the extract. The ethanol extract yielded strongly, all the phytochemicals followed by means of petroleum ether, n-butanol and ethyl acetate. The n-butanol extract additionally yielded all the phytochemicals at poor presence. Among Cropalliflavones A-C, B was reported to show moderate cytotoxicity against the MCF-7 cell line and C showed moderate anti-inflammatory activity (Hu, Chou, & Zhang, 2017). Methoxyisoflavone has anti-cancer properties. Treatment of MCF-7 human breast carcinoma cells with this compoundresulted inthe accumulation of CYP1A1 mRNA and elevation in CYP1A1-specific 7-ethoxyresorufin O-deethylase (EROD) activity. Their role as an anti-diabetic agent and in lipid regulation was also suggested (Puli, Lai, & Bhushan, 2006: Berghe, et al., 2006: Han, Kim, & Jeong, 2006).

4.3 Pharmacological activity

Hu, Chou, & Zhang (2017) mentioned in their article *Crotalaria pallida* Ait (Leguminosae) has been used as people remedy in southwest and east China. *Crotalaria pallida* is additionally regarded as ‗Zhu-Shi-Dou'', its roots are used to treat scrofula, mastitis and dysentery; its stems and leaves are used to deal with diarrhoea; and its seeds are used to deal with neurasthenia, dizziness, leucorrhoea and tumours (Lian, 1986; The National Assembly of Chinese Herbal Medicine Editorial Committee, 1996). Modern pharmacological research has demonstrated that this species displays a variety of organic activities, which include anti-inflammatory, antimicrobial, estrogenic and mutagenic activities (Ko et al., 2004; Pelegrini et al., 2009; Weng et al.,2003; Arzt and Mount, 1999; Lin et al., 2006; Boldrin et al., 2013).

4.3.1. Anti-inflammatory effect: Ho (2017) in their article the anti-inflammatory activity of the compounds had decided in accordance to a previous technique with minor changes (Weng et al., 2003) using aminoguanidine hydrochloride (Yuke Chemical, China) as the high-quality control.

Briefly, RAW 264.7 cells(Cell Bank of Shanghai Institutes for Biological Sciences, Chinese Academy of Sciences, China) had been plated in 96-well plate at2 _ 105 cells per well. After incubation overnight, the cells had been treated and motivated with 1 mg/mL of LPS (L2654, Sigma) for 24 h.Then, production of NO used to be decided primarily based on the Griess reaction. Compared with aminoguanidine hydrochloride, solely Cropalliflavone C had average anti-inflammatory activity, with an IC50 value of 16.07 mM. Cropalliflavone A, Cropalliflavone B, Cropallin A, Cropallin B, diosmetin had susceptible effects.

4.3.2 Cytotoxicity: Cytotoxicity was once evaluated through Ho (2017) in two human cancer cell lines along with one human colorectal carcinoma and another human breast adenocarcinoma, MCF-7, which have been got from the Cell Bank of Shanghai Institutes for Biological Sciences. Cytotoxicity was evaluated with the aid of the MTT assay (Zhou et al., 2013) with slight modifications; adriamycin (Pfizer, Italy) was used as a positive control. Briefly, CaCo2 and MCF-7 cells had been seeded into 96-well plates at 5104 cells/well and incubated for 24 h. Then, the cells have been handled with the tested compounds at various concentrations and mobile viability was obtained by scanning with a microplate reader at 570 nm. Cropalliflavone B had average cytotoxicity. Cropalliflavone A, Cropalliflavone C, Usaramine-N-oxide, Cropallin B exhibited moderate or no cytotoxicity against both the MCF-7 and CaCo2 phone lines.

4.3.3 Anti-diabetic activity: Panda, Das, & Tripathy (2015) in their experiment with alloxan caused diabetic rats found among the specific extracts of *Crotalaria pallida*, considerable anti-diabetic pastime was once noticed in animal corporations dealt with with ethanol extract of leaves, it had exhibited distinctly significant anti-diabetic activity These consequences are same with the general drug (Glibenclamide). The recreation showed through this extract is of great importance and justified its use in the diabetic control in the folklore medicines. The antidiabetic

endeavor of the extracts is in the order of ethanol> nbutanol> petroleum ether> ethyl acetate (Panda, Das, & Tripathy, 2015).

4.4 Toxicity

Additionally, Panda (2015) revealed in their acute toxicity study that no mortality was found in any solvent extract at any dose in Swiss albino mice, which confirmed that *Crotalaria pallida* leave extract would be non-toxic in the living body (Panda, Das, & Tripathy, 2015).

Chapter- 5

Crotalaria retusa

5.1 Introduction

Crotalaria retusa is an erect, annual plant or short-lived perennial with more or much less woody stems. It can grow from 60 - 120cm tall. The plant is harvested from the wild for neighborhood use as a food, medication and source of materials. It is once in a while cultivated for the fibre it provides, as a medicinal plant, and is additionally grown as a green manure crop. is now and again grown only as an ornamental, though it is additionally on occasion considered to be a weed (Schild et al., 2007).

Figure 10: Crotalaria retusa (Schild et al., 2007)

5.2 Phytochemistry

Crotalaria retusa, generally referred to as the devil bean or rattle box, is one of the severa weeds in the Fabaceae family. It is a legume that has the capability of amassing monocrotaline, an important toxicant with a huge diploma of toxicity in animals (World Health Organization,

1988). This compound has been advised to have a viable for killing tumors due to the fact that it is successful of killing lung cells (Schoental and Head, 1955). Very little is then again recognized of its ant proliferative endeavor on cancerous cells (Anim, et al., 2016).

Table 3: Phytochemicals isolated from Crotalaria retusa

Plant part used	Phytochemicals isolated	References
Seed Flour	Main Minerals- Magnesium, Calcium, phosphorus, Sodium, potassium, Lead, Nickel, Copper, Arsenic	Aremu, Bamidele, & Amokaha, 2012
Seed oil	Main Fatty acids- Linoleic acid, Oleic acid, Stearic acid, Palmitoleic acid, Arachidic acid, Palmitic acid	Aremu, Bamidele, & Amokaha, 2012
Pod	General glycoside,Saponins, Tanins	Larbie et al., 2016
Flower	Flavonoids, Sterols	Larbie et al., 2016
Stem	Saponins, Tanins, Alkaloids	Larbie et al., 2016

The seeds of *Crotalaria retusa* have been shown to be high in magnesium content and contained harmful metals such as nickel, arsenic and selenium. Results of fatty acid composition on the seed oils revealed appreciable quantity of polyunsaturated fatty acids particularly linoleic acid. The acid & iodine values showed that the seed oils can be categorized as nondrying oils and that the oils may not be suitable as edible oil and soap production. however can be useful for the production of paint & shampoo (Aremu, Bamidele, & Amokaha, 2012).

Tannins were reported to show inhibition of carcinogenesis, host-mediated antitumor activity, antiviral activity, and inhibition of active oxygen, such as inhibition of lipid peroxidation and lipoxygenase, xanthine oxidase, and monoamine oxidase (Okuda, Yoshida& Hatano, 1992).

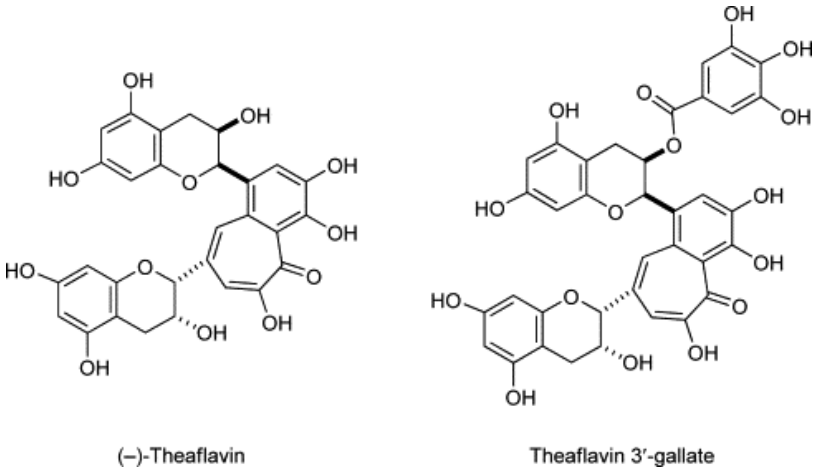


Figure 11: Structure of Tanins (Okuda, Yoshida, & Hatano, 1992)

The presence of general glycosides, anthracene glycosides, saponins, tannins, alkaloids, flavonoids, sterols and triterpenoids was analyzed using standard methods (Trease and Evans, 1989; Sofowora, 1993; Harborne, 1998). Total phenolic content (TPC) was determined using the Folin–Ciocalteau assay with slight modification (Marinova et al., 2005).

5.3 Pharmacological Activity

5.3.1 Antioxidant activity: The antioxidant activity of *Crotalaria retusa* leaf, pod, seed, flower and stem extracts was determined using the free radical scavenging activity by DPPH method with some modification (Blois, 1958).

5.3.2 Anti-proliferative activity: The MTT cell viability assay confirmed that solely the stem of this plant had anti-proliferative activity towards all the three most cancers cells (Jurkat, MCF 7 and PC 3). Jurkat was once most sensitive to all the *Crotalaria retusa* extracts used in this research compared to the different cells. The stem of *Crotalaria retusa*, is wonderful in inhibiting the increase of Jurkat, MCF 7 and PC 3 cancer cells. However, its toxicity towards regular cell (WRL 68) renders it a less suited chemotherapeutic choice (Anim et al., 2016).The seed comprises hepatotoxic alkaloid, monocrotaline, which requires bioactivation to grow to be toxic to hepatocytes (John et al., 2005). Thus, the flower (other than the seed) of *Crotalaria*

retusa used to be the most hepatotoxic phase of this plant (toxic to WRL 68 cells), eventhough the seed has the highest degrees of monocrotaline. These findings endorse that indeed, monocrotaline, even though hepatotoxic would require bioactivation (John et al., 2005), consequently its decreased toxicity in vitro (Anim et al., 2016). The flower ought to possibly contain sure compounds that would no longer require bioactivation consequently due to it‘s found toxicity in vitro. Data from this study suggests *Crotalaria retusa* leaf is a good source of phenolic compounds with good antioxidant properties (Anim et al., 2016).

5.4 Toxicity

The seed of *Crotalaria retusa* has been accounted for by Maia et al. (2013), to have elevated quantities of the hepatotoxic alkaloid, monocrotaline, which expects bioactivation to cause toxic endeavor to hepatocytes (John et al., 2005). Along these lines, the flower (other than the seed) of *Crotalaria retusa* used to be the most hepatotoxic piece of this plant (harmful to WRL 68 cells), even although the seed has the biggest amounts of monocrotaline. These discoveries endorse that undoubtedly, monocrotaline, however hepatotoxic would require bioactivation (John et al., 2005). The flower may want to incorporate positive aggravates that would no longer require bioactivation subsequently; it‘s discovered toxic endeavor in vitro. Every one of the concentrates examined was once cytotoxic towards the normal human liver phone (WRL 68), alongside these strains exhibiting a really terrible selectivity. This proposes some stage of poisonous satisfactory when any piece of this plant is ingested to alleviate a malady condition. In any case, further in vivo studies will be required to verify this (John et al., 2005).

Chapter- 6

Crotalaria Verrucosa

6.1 Introduction

Crotalaria verrucosa is an erect or spreading, much-branched, annual, sub-woody plant growing 50 - 100cm tall. The plant is collected from the wild for local use as a medicine. It is sometimes grown as a green manure and is a likely decorative (Cheeke, 1988).

Figure 12: Crotalaria verrucosa (Cheeke, 1988)

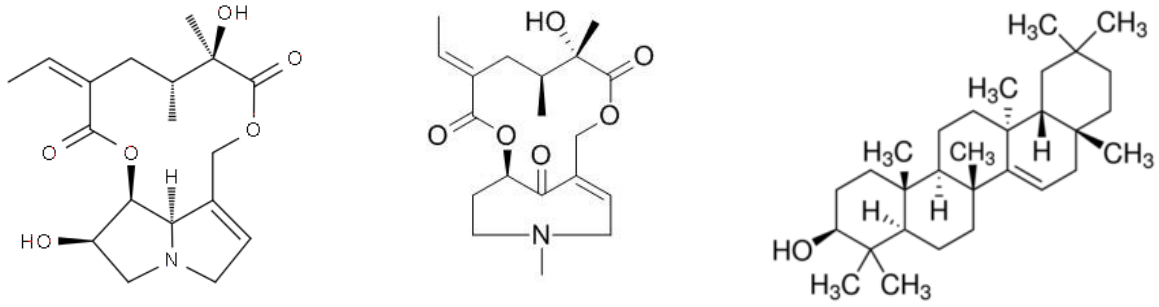
6.2 Phytochemistry

Table 4: Phytochemicals isolated from Crotalaria verrucosa

Plant parts used	Phytochemicals isolated	References
Seeds and Stems	β-sitosterol	Riazunnisa, 2015
Seeds	Crotalaburnine (also known as Anacrotine)	Roeder & Wiedenfield, 2013
Seeds	Crotaverrine acetate	Roeder & Wiedenfield, 2013

	(Oacetylcrotaverrine or Ligularidine)	
Seeds	Crotaverrine (Ocrotaverrine)	Roeder & Wiedenfield, 2013
Seeds	Isosenkirkine	Lekharani et al.,2013
Seeds	Isosenkirkine Acetate	Lekharani et al.,2013
Stem	Tri-terpenoid [Taraxerol (Alnulin)]	Yadava & Mattews,1993
Leaves	(Necic lactone)2-methyl-3-(2-oxo-[5H]-5-hydroxymethyl-5-methylfuran-3-yl)-propanoic acid	Suri & Dhar, 1989
Leaves	Tropane alkaloids (Not found)	Yadava & Mathews, 1993
Stem	Unsaturated fatty acid(Not found)	Yadava & Mathews, 1993

Crotalaburnine is known to have anti-inflammatory activity. Tropane alkaloids are commonly used as anticolic and spasmolytic drugs (scopolamine) in both digestive and urinary tract spastic conditions (Indian Journal of Pharmacy,1972).



Crotalaburnine Crotaverrine Alnulin

Figure 13: Selected components isolated from Crotalaria Verrucosa (Chaturvedula & Prakash, 2012)

6.3 Pharmacological Activity

6.3.1 Antipyretic activity: The study conducted via Nawrin (2015) chiefly induces pyrexia in Wistar rats through subcutaneous injection of brewer‘s yeast (20% w/v in distilled water at 10mL/kg b.w.). After a length of 19hrs, the initial rectal temperature was recorded and the *Crotalaria verrucosa* extracts of different concentrations (100, 250 and 500 mg/kg b.w.) have been orally administered to distinct rats, the results of which have been comparable to administration of well-known drug, Paracetamol 150mg/kg. The discount in temperature used to be recorded at 1hr, 2hr and 3hrs following the treatment. It was found that the sample dose of 500mg/kg b.w. produced a huge discount in temperature (from 40.33°C to 37.48°C) related to that of Paracetamol 150mg/kg (from 40.42°C to 37.51°C). And it was sufficiently concluded that the 500mg/kg b.w. possesses strong antipyretic endeavor increased than 250mg/kg

(temperature reduction from 40.67°C to 38.55°C) whilst 100mg/kg b.w. does no longer limit hyperthermia extensively (from 40.27°C to 39.63°C) (Nawrin et al., 2015).

6.3.3 Thrombolytic activity: From the study carried out by Nawrin et al. (2015), it was once successively concluded that the leaf extract of *Crotalaria verrucosa* failed to produce a strong clot lysis activity in comparison to the wellknown drug, Streptokinase. The percentage of thrombolytic exercise of *Crotalaria verrucosa* leaf extract towards HRBC clot denaturation was once found to be 26.81% in contrast to that of Streptokinase (80.65%). In this study, 100uL of *Crotalaria verrucosa* extract was taken for every alpine tube containing thrombus to which the 500uL of blood withdrawn from healthful volunteers was introduced and weighed. Similar was carried out for the general drug, Streptokinase. The tubes have been then incubated at 37°C for 90min after which the supernatant was removed from the tubes, which was then reweighed to look at clot disruption and the p.c thrombolytic activity was once then calculated (Nawrin et al.,2015).

6.3.4 Anti-diabetic activity: The anti-diabetic endeavor of *Crotalaria verrucosa* has been investigated by Nawrin et al. (2015) by means of artificially developing type-II diabetes on Wistar rats through intra peritoneal injection of alloxan monohydrate. At the 72nd hour, the blood glucose degree was once tested to be above 140mg/dL, thus, confirming diabetic condition. Thereafter, three extraordinary doses of *Crotalaria verrucosa* have been orally administered to the Wistar rats: 100mg/kg, 250mg/kg, 500mg/kg b.w., the outcomes of which have been compared with that of Standard drug, Glibenclamide 2.5mg/kg b.w. during a time interval of 0, 7, 14 and 21 days the use of commercially available glucose kits. The blood glucose stage of the Wistar rat precipitated with *Crotalaria verrucosa* extract of 500mg/kg b.w. on Day-0 and Day-21 was located to be 284.54mg/dL and 190.33mg/kg b.w. respectively,

whereas that of Glibenclamide showed a tremendous decrease in blood glucose stage from 281.49mg/dL to 177.12mg/dL. The author thus, concludes that the ethanolic extract of *Crotalaria verrucosa* possesses full-size anti-diabetic activity, much less than that of Glibenclamide (2.5mg/kg) (Nawrin et al.,2015).

6.3.5 CNS depressant: The CNS depressant endeavor of *Crotalaria verrucosa* was once observed on Swiss albino mice via ―Hole cross test" and ―Open field test". The test described through Khatoon et al. (2014) was once followed for the ―Hole go test" and the technique described by way of Al-Mahmud, Bachar, Qais, & Shams-Ud-Doha, (2013) was once observed for ―Open field test" with selective modifications. For both the tests, Diazepam 1mg/kg b.w. used to be chosen as the reference standard which used to be orally administered to the animals 20min before the beginning of experiment. The discount in ―Whole cross activity" reflected the CNS depressant recreation of the sample on the Swiss albino mice, whereas for the ―Open area test", the limit in the variety of squares crossed by way of the animal in an open subject in 20min is an indication of CNS depressant activity. The result of the test carried out through Nawrin et al. (2015), sufficiently concluded that the maximum diminishes in motor characteristic was exhibited through the Crotalaria verrucosa extract of 500mg/kg b.w. which was once slightly much less than that of Diazepam (1mg/kg b.w.) (Al-Mahmud & Shams-Ud-Doha, 2013).

6.3.6 Antibacterial activity: In a study carried out with the aid of Riazunnisa, Prasad, Sudha, and Khadri (2015), the antibacterial recreation was examined for n-butanol extracts of *Crotalaria verrucosa* (100ug/mL) via measuring the diameter (mm) of the area of inhibition using the Agar well diffusion technique towards the bacterial strains namely, *Bacillus subtilis* (G +ve), *Klebsiella pneumonia* (G –ve), *Escherichia coli* (G –ve), *Proteus vulgaris* (G –ve) and *Pseudomonas aeruginosa* (G +ve). In this study, Gentamycin was used as the preferred drug. It

was located that the region of inhibition in *Crotalaria verrucosa* extract for B. *subtilis* and *K. pneumonia* used to be 15mm each, 13mm for E. coli, 14mm for P. vulgaris and 12mm for P. aeruginosa. On the other hand, for Gentamycin, the area of inhibition for the above strains have been 20mm, 16mm, 18mm, 15mm,and 20mm, respectively. Thus, the n-butanol extract of *Crotalaria verrucosa* possesses a ―broad spectrum" of antibacterial endeavor towards a panel of bacteria responsible for most of the common diseases (Riazunnisa, 2015).

6.3.7 Anti-fertility activity: The information got in the study conducted through Singh et al. (2011) indicated that 70% ethanolic, aqueous and 95% ethanolic extract of aerial part of *Crotalaria verrucosa* exhibited tremendous anti-implantation and early abortifacient recreation in dose structured manner in female wistar albino rats compared to 95% ethanolic extract. The 95% ethanolic, 70% ethanolic and aqueous extracts of *Crotalaria verrucosa* at a dose of 500 mg/kg b.w., 250 mg/kg b.w. were found to possess exceedingly significant estrogenic activity as indicated by using expand in uterine weight, vaginal cornification, anduterotropic responses. Other biochemical modifications such as the concentration of glucose, cholesterol and alkaline phosphatase was discovered to be greater in the dealt with group (*Crotalaria verrucosa*) in comparison to the control group and considerably less than wellknown group (Singh et al., 2011).

6.3.8 Wound-healing activity: The aqueous extract of *Crotalaria verrucosa* was discovered to possess substantial wound-healing doable on Wistar albino rats when it was once examined on three wound models along with incision, excision and dead area wounds. It was once discovered that co administration of *Crotalaria verrucosa* with dexamethasone notably expanded the breaking energy in incision-type of the model in evaluation with the dexamethasone handled group.

Table 5: Pharmacological activity of Crotalaria verrucosa

Pharmacological activity	Plant part	References
Antipyretic	Leaves	Nawrin *et al.* 2015
Thrombolytic	Leaves	Nawrin *et al.* 2015
Thrombolytic	Leaves	Nawrin *et al.* 2015
CNS depressant	Leaves	Nawrin *et al.* 2015
Antibacterial	Leaves	Riazunnisa, Prasad, Sudha, & Khadri 2015
Anti-fertility	Leaves	Singh et al. 2011
Wound-healing	Leaves	Kumari et al. 2010
Hepatoprotective activity	Leaves	Lekharani et al. 2013

As for the excision wound model, the share of wound contraction used to be significantly elevated by two doses of test extract (all barring twelfth and 16th day of drug treatment) and it additionally reversed dexamethasone suppressed wound contraction. Furthermore, it reduced the time required for epithelialization and reversed the epithelialization delaying impact of dexamethasone. This effectively represents the extensive wound-healing endeavor of *Crotalaria verrucosa.* It was evident by way of the reduce in the length of epithelialization, increase in price of wound contraction, pores and skin breaking energy and granulation tissue dry weight content material (Kumari et al., 2010).

6.3.9 Hepatoprotective activity: In a study investigated through Lekharani et al. (2013), *Crotalaria verrucosa* validated the hepatoprotective action against paracetamol-induced hepatotoxicity in Wistar rats. The study concludes that the remedy of ethanolic extract of

Crotalaria verrucosa motives massive protection against each paracetamol caused liver injury and protects in opposition to any amplify in serum enzyme levels and bilirubin in a dose-responsive manner. Other parameters such as LP (Lipid peroxidation), SOD (Superoxide dismutase), CAT (Catalase), GSH (Glutathione) and glycogen contents had been additionally measured from the liver. Furthermore, upon performing the histopathological studies, it was found that the Wistar rats handled with ethanolic extract of *Crotalaria verrucosa* showed absence of centrilobular necrosis and absence of vacuolization of cytoplasm of the hepatic cells, as a result proving the protective motion in opposition to hepatic injury by *Crotalaria verrucosa* (Lekharani et al.,2013).

Chapter-7

Crotalaria madurensis

7.1 Introduction

Crotalaria madurensis is an endemic species to Eastern Ghats, India, used for unusual illnesses by using adivasi tribes in the area. It grows every so often alongside the hill slopes of Nallamalais, Kurnool district of Andhra Pradesh and it is endemic to Eastern Ghats (Venkata Raju & Pullaiah 1995). The ethno-medico-botanical research of plant revealed that the plantis used through the Chenchu and Lambada tribe for the therapy of scabies. Fresh leaves beaten and paste applied externally and seeds had been cooked and given in curry alongside with the meals (Bhakshu, 2002).

Figure 14: Crotalaria madurensis

7.2 Phytochemistry

Anthocyanin isolates and anthocyanin-rich combinations of bioflavonoids may additionally provide safety from DNA cleavage, estrogenic activity (altering improvement of hormone-dependent disorder symptoms), enzyme inhibition, boosting manufacturing of cytokines (thus

regulating immune responses), anti-inflammatory activity, lipid peroxidation, decreasing capillary permeability and fragility, and membrane strengthening (Lila, 2004).

Table 6: Chemical constituents of Crotalaria madurensis

Part of the plants	Chemical constituents	References
Leaves	Anthocyanins, Antracene glycosides, Flavonoids, Catecholics compounds	Bhakshu, 2008
Flowers	Myo-inositol, Sophradiol 3-O-ß-D-4C1-glucouronopyranoside, Quercetrin	Hala, Mohamed, Magada, Batran, & Omayma, 2008
Stems	Flavonoids, crotmadineandcrotmarine	Hala et al., 1984

Flavonoids possess many biochemical properties, but the best described property of nearly each group of flavonoids is their potential to act as antioxidants. Several flavonoids such as catechin, apigenin, quercetin, naringenin, rutin, and venoruton are mentioned for their hapatoprotective activities (Kumar & Pandey, 2013).

7.3 Pharmacological Activity

7.3.1 Anti-microbial Activity: This plant was reported to have antimicrobial activities against *M. luteus, S. aureus, P. aeruginosa, E. coli, K. pneumoniae, S. aureus, B. subtilis* (Bhakshu, 2008). It was also reported to have anti-fungal activities (Bhakuni & Chaturvedi, 1984).

7.3.2 Anti-oxidant activity: Antioxidant activity or free-radical scavenging activity was observed of this plant (Hala et al., 2008).

Chapter-8

Crotalaria brevidens

8.1 Introduction

Chweya (1985) recognized *Crotalaria brevidens* as one of various indigenous leafy greens used in Kenya which (based on their P-carotene, vitamin C, mineral and protein content) ought to be developed as valuable cultivated or semi-cultivated crops. Young leafy shoots of *Crotalaria brevidens* var. intermedia are cultivated as vegetables through the Luo and neighboring ethnic classes of Kenya, Tanzania and Uganda (Johns and Kokwaro 1991; Tallantire and Goode 1975).

Figure 15: Crotalaria brevidens (Abukutsa-Onyango, 2004)

8.2 Phytochemistry

Plants containing pyrrolizidine alkaloids have been of medicinal interest since very early times and recently of renewed interest due to their varied and remarkable tumor inhibitory activity and toxic effects. The active component has been identified as indicine-N-oxide. Antitumour activitiesare also reported with monocrotaline,which is said to be more destructive to malignant cells than normal ones (Zalkow et al., 1979).

Table 7: Phytochemicals isolated from Crotalaria brevidens

Part of the plant	Constituent	References
Leaf	Vitamin C, Carotenoid, pyrrolizidine alkaloids	Uiso & Johns,1996
Flower	pyrrolizidine alkaloids	Uiso & Johns,1996
Seeds	pyrrolizidine alkaloids	Uiso & Johns,1996

8.3 Environmental impact

8.3.1 Soil improver and green manure: Slenderleaf (*Crotalaria brevidens*) is an N-fixing legume: it improves the N status of the soil and can be intercropped with finger millet crops, providing valuable N return to the next-year finger millet crop (Chweya, 1997). Slenderleaf does properly on slopes and has been used in soil erosion manage (Duke, 1981). In Brazil, slenderleaf has been used in coffee plantations as a green manure and cover crop. It avoided soil erosion by using including moisture and reducing soil temperature. Slenderleaf also decreased weed boom (Muzilli et al., 1992).

8.3.2 Striga hermonthica controller: Slenderleaf (*Crotalaria brevidens*) is reported to promote the germination of striga, a parasitic plant that is a major problem for maize and millet growers. In the presence of Crotalaria, striga germinates and later dies due to the lack of a suitable host plant (Abukutsa-Onyango, 2004).

8.4. Toxicity

Seeds of *Crotalaria brevidens* comprise toxic pyrrolizidine alkaloids, specifically integerrimine and usaramine (Smith et al.,1981; WHO,1988).Pyrrolizidine alkaloids have been found to be toxic for all animal species (Schoental et al., 1963; WHO 1988).

Chapter-9

Crotalaria ferruginea

9.1 Introduction

Crotalaria ferruginea is an erect to ascending, much-branched annual to short-lived perennial with stems that can convert fairly woody; it can propagateto 20 - 60cm tall, sometimes to 150cm. The plant is occasionally collected from the wild for home grown therapeutic usage. It has at times been used as greencompost (n.d.).

Figure 16: Crotalaria ferruginea (Li et al., 2008)

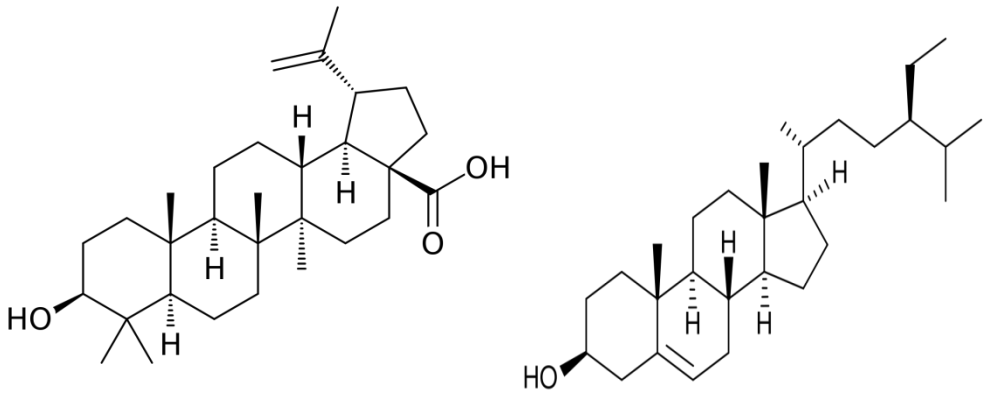
9.2 Geographical Location

East Asia - southwest China, India, Nepal, Bhutan, Bangladesh, Myanmar, Thailand (Li et al., 2008).

9.3 Phytochemistry

Twelve compounds were reported to be found from ethyl acetate extract of the whole plant and their structures were observed as β-sitosterol (I), alpinumisoflavone (II), genistein (III), dotetracontanoic acid (IV), dotriacontanoic acid (V), 1-hentriacontanol (VI), (2S, 3S, 4R, 12E,

2′R)-2-(2′-hydroxyl-docosanoylamino) eicosane-1, 3, 4-trihydroxy-12-ene (VII), daucosterol (VIII), betulinic acid (IX), 3′, 5-dihydroxy-4′-methoxy-2″, 2″-dimethylpyrano-(5″, 6″, 6, 7)-isoflavone (X), 12-oleanene-3β, 22β, 24-triol (soyasapogenol B, XI) and laburnetin [4′, 5, 7-trihydroxy-6-(2-hydroxy-3-methyl-3-butenyl) isoflavone, XII](Li et al., 2008).



β-sitosterol Betulinic acid

Figure 17: Selected isolated compounds from Crotalaria ferruginea (Li et al., 2008)

9.4 Pharmacological Activity

9.4.1 Anti-inflammatory: *Crotalaria ferruginea* showed inhibitory actions against phosphodiesterase-4 (PDE4), a healing target of asthma, with IC50 values ranging from 2.57 to 8.94 μM showing its possession of anti-inflammatory activity. Its constituent β-sitosterol was reported to have anti-inflammatory action. It was reported that the In vivo effect of β-sitosterol in a model of delayed-type hypersensitivity (DTH). They revealed that this compound can modulate cell-mediated edema but it was not effective on the arachidonate pathway of intact cells and did not inhibit the leukocyte infiltration measured as myeloperoxidase activity in biopsies. They emphasized that its response to oxazolone might be due to a different pathway

independent of interleukin-4. Moreover, β-sitosterol was not able to inhibit the cyclooxigenase (COX) pathway responsible for prostaglandin E2 (PGE2) synthesis (Saeidnia et al., 2014)

9.4.2. Anti-cancer effect: Experimental inhibition of colon and breast cancer development by β-sitosterol, which is a major constituent of this plant was observed. It was stated that this compound can affect different levels of tumor development, such as their inhibitory effects on creation, promotion and induction of cancerous cells, as well as inhibition of tumor (Saeidnia et al., 2014).

Chapter-10

Crotalaria spectabilis

10.1 Introduction

Crotalaria spectabilis is an erect, much-branched annual to perennial plant with stems that can grow to be greater or less woody and persist; it can develop 60 - 150cm tall. The plant is harvested from the wild for nearby use as a food and medicine. It is often grown as a soil improver and stabilizer, having the introduced advantage of being in a position to minimize soil nematode populations. It is additionally frequently grown as an ornamental, valued especially for its long flowering season (Ninkaew & Chantaranothai, 2017).

Figure 18: Crotalaria spectabilis (Ninkaew & Chantaranothai, 2017)

10.2 Geographical Location

East Asia - Pakistan, India, Nepal, Bangladesh, Myanmar, Thailand, Malaysia. Naturalized throughout the Tropics (Ninkaew & Chantaranothai,2017).

10.3 Phytochemistry

Table 8: Phytoconstituents isolated from Crotalaria spectabilis

Part of the plant	Constituents	Reference
Leaves	Saponins, tannins, flavonoids, monocrotaline	Tinker & Lauter, 1956
Seeds	Monocrotaline	Neal, Rusoff, & Ahmann, 1935.
Stem	Serine and cyteine proteases	Pacheco & Silva-Lopez, 2012
Roots	Serine and cysteine proteases	Pacheco & Silva-Lopez, 2012
Flowers	Serine and cysteine proteases	Pacheco & Silva-Lopez, 2012

Monocrotaline is a pyrrolizidine alkaloid having many properties such as blood pressure lowering but also toxic to animals. Serine and cysteine protease is proteolytic that break down proteins (Pacheco & Silva-Lopez, 2012).

10.4 Pharmacological Activity

10.4.1 Proteolytic Activity: Proteolytic occasions manage gene expression that is accountable for cell growth, differentiation, division or reproduction, as well as senescence, meiosis, gametophyte survival, epidermal cell fate, stomata development, chloroplast biogenesis, elimination of damaged or improperly folded proteins, processing and focused on of proteins, zymogens and peptide hormones via digestion of signal peptides, take part in programmed cell

death, and nearby and systemic defense responses (Kurepa et al., 2009). *Crotalaria spectabilis* is stated to have proteolytic endeavor and was once found to have protease enzymes such as Serine and cysteine proteases (Pacheco & Silva-Lopez, 2012).(Pacheco & Silva-Lopez, 2012).

10.4.2 Hypertensive Activity: *Crotalaria spectabilis* was once suggested to reason pulmonary hypertension and arterial adjustments in rats. After therapy of rat with this plant, right ventricular hypertrophy was once found with anextend in pulmonary arterial medial muscle, a decreased quantity of small arteries and ―ghost" arteries (Hislop & Reid, 1974).

Chapter-11

Crotalaria sessiliflora

11.1 Introduction

Crotalaria sessiliflora is an erect, annual to short-lived perennial plant. It can develop 30 - 100cm tall with stems frequently branching from the lower parts. The plant is harvested from the wild for neighborhood use as a food and medicine (n.d.).

Figure 19: Crotalaria sessiliflora (Yoo & Kim, 2004)

11.2 Geographical Location:

E. Asia - China, Japan, India, Nepal, Bhutan, Bangladesh, Myanmar, Thailand, Cambodia, Laos, Vietnam, Malaysia, Indonesia, Philippines, New Guinea (Yoo & Kim, 2004).

11.3 Phytochemistry

Integerrimine, monocrotaline and tri-chodesmine are pyrrolizidine alkaloids.

Table 9: Phytoconstituents isolated from Crotalaria sessiliflora

Part of the plant	Constituents	References
Whole plant	Flavonoids (2′,4′,5,7-tetrahydroxyisoflavone, 2′,4′,7-trihydroxyisoflavone, 4′,7-dihydroxyflavone, isovitexin), hydroquinone	Yoo & Kim, 2004
Seeds	Integerrimine, monocrotaline and tri-chodesmine	Röder, Liang, & Kabus, 1992

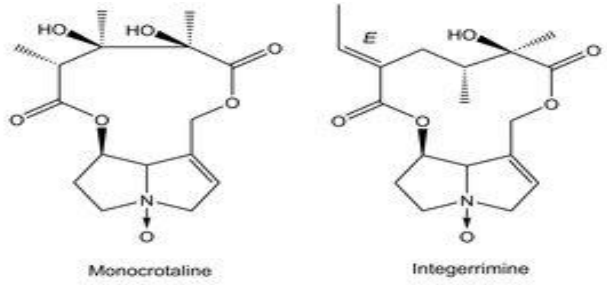


Figure 20: Selected alkaloids isolated from Crotalaria sessiliflora (Röder & Kabus, 1992)

11.4 Pharmacological Activity

11.4.1 Anti-oxidant Activity: Antioxidants such as phenolic compounds play a necessary function in the non-enzymatic mechanism and have been suggested to have organic activities such as anticancer, anti-inflammation and prevention of coronary heart disease. *Crotalaria sessiliflora* was once reported to have anti-oxidant compounds such as hydroquinone, vitexin, orientin and isoorientin (Munim, Negishi, & Ozawa, 2003).

11.4.2 Anti-tumor activity: *Crotalaria sessiliflora* was reported to have pyrrolizidine alkaloids that have anti-tumor properties such as monocrotaline trans-trans platynecic acid (trans, 2 S, 3 R) and retronecine and they showed tumor inhibitory activity against Walker carcinoma 256 in rats (Liang, 1980).

11.4.3 Hypotensive effects: This plant was reported to have vasodilatory and hypotensive effects on rats. Presence of vitexin and orientin was suggested to be responsible for this effect (Koh, et al., 2007).

11.5 Toxicity

No specific mention of toxicity has been seen for this species (Cowan, Allen, & Allen, 1982).

Chapter-12

Crotalaria burhia

12.1 Introduction

Crotalaria burhia (Fabaceae) is an undershrub, fibrous plant; found all over the desert extensively growing on sand dunes, theplant is commonly known as khip. Its leaves and branches are used as a cooling medicine. Fresh plant juice is applied on eczema. *Crotalaria burhia* is also very useful in gout, hydrophobia and swellings (Talaviya & Suman, 2014).

Figure 21: Crotalaria burhia (Talaviya & Suman, 2014)

12.2 Geographical Location

It is common in the dry parts of West Pakistan, India (Punjab, Rajasthan and Gujarat) and Afghanistan (Talaviya, Vyas, Sharma, Indoria, & Suman, 2014).

12.3 Phytochemistry

Croburhine is a novel pyrrolizidine alkaloid from *Crotalaria burhia*.

Table 10: Phytoconstituents isolated from Crotalaria burhia

Part of the plant	Constituents	Reference
Leaves	Alkaloids like crotalarine, monocrotaline, croburhine, crosemperine, glycosides, tannins, protein, amino acid, flavanoids, steroids, triterpenoids, mucilage and gum	Saboon et al., 2015
Roots	alkaloids, flavonoid, phenol, polyphenol, tannins, steroids, triterpenoids and anthraquinones	Saboon et al., 2015

12.4 Pharmacological Activity

12.4.1 Antioxidant activity: The root of *Crotalaria burhia* was subjected for antioxidant assay in different concentrations (1-1 280 µg/mL) and different systems i.e 2,2‘-diphenyl-1-picrylhydrazyl assay, superoxide radical assay andlipid peroxidation assay. Methanolic extract of concentration 1280 µg/mL showed significant scavenging activity and the maximum percentage inhibition was observed in superoxide anion (96.66%) which is followed by 2,2‘-diphenyl-1-picrylhydrazyl (94.85%) and lipid peroxidation (89.68%) assay (Alang et al., 2010).

12.4.2 Antimicrobial activity: Antibacterial activity of *Crotalaria burhia* (whole plant) was investigated in four extracts of methanol, chloroform, petroleum-ether and water against

Staphylococcus aureus by using cup plate agar diffusion method. Antibacterial screening showed that methanol extract has good antibacterial activity in the concentration of 150 µg/mL whereas the other extracts were found inactive (Soni, 2014). For the same activity, ether and alcoholic leaf extracts of *Crotalaria burhia* were tested against bacterial pathogens i.e. *Staphylococcus aureus* (Gram-positive), *Escherichia coli* (Gram-negative) and a fungal pathogen *Candida albicans*. Bothextracts showed positive reactions against all test organisms (Kapoor & Pandita, 2013). The root of plant also exhibited certain medicinal properties, so it was screened for antimicrobial activity against different strains of bacteria and fungi. For this purpose, four different extracts of plant which were aqueous, petroleum-ether, chloroform and methanol extract were used. Tests were carried out by using agar disc diffusion method. All extracts showed growth inhibition of Gram-positive and Gram-negative bacteria but Gram-positive bacteria appeared to be more susceptible than the Gram-negative bacteria. The same extract also showed significant antifungal activity (Talaviya & Suman, 2014).

12.4.3 Anti-inflammatory activity: The anti-inflammatory activities of four fractions of ethanolic extract of *Crotalaria burhia* root in Wistar albino rats were tested. The animals were divided into different groups in which two were taken as control groups, and two groups were treated with anti-inflammatory drugs while the other groups were treated with four fractions of hexane, chloroform, ethyl acetate and water with oral administration. The result shows that ethyl acetate was found more effective than hexane and chloroform but water had shown negligible anti-inflammatory activity (Talaviya & Suman, 2014).In another investigation, methanolic extract of the whole plant is assessed for anti-inflammatory activity and showed significant result in test organism (Kataria, 2012).

12.4.4 Antinociceptive activities: Methanolic extract of the whole plant of *Crotalaria burhia* was tested against the inflammation-induced pain in mice and the extract at concentrations of 100, 200 and 400 mg/kg showed significant antinociceptive activity in test organism (Talaviya & Suman, 2014).

Chapter-13

Others

13.1 *Crotalaria longirostrata*

This is a perennial herb which grows up to five feet. Its flower is of yellow color and flowering time is usually late summer or early fall. Commonly used as culinary herb and as a vegetable. Commonly known as Chiplin, Chepil. Available mostly in Central America north to Mexico. Chipilin was considered to be high in calcium, iron, thiamine, riboflavin, niacin and ascorbic acid (Morton, 1994). The seeds of this plant have toxic alkaloid but it is not monocrotaline which is found in the seeds of 20% of the 600 species included in the genus Crotalaria.

Figure 22: Crotalaria longirostrata (n.d.)

13.2 *Crotalaria assamica*

It is a newly found species. Stems and branches warty, glabrous; peduncles Crotalaria 5 cm long; calyx 6 – 7 mm long, glabrous with conspicuous reticulate venation; pods narrowly ellipsoid. It was reported to have hepatotoxic activity. Similar to the other family of Crolataria family, this plant also contains pyrrolizidine alkaloids (Krishnaraj, Mohanan&Antony, 2011).

Figure 23: Crotalaria assamica (Krishnaraj, Mohanan&Antony, 2011)

13.3 *Crotalaria agatiflora*

Evergreen shrub or small tree up to 1-10 m tall; generally glabrous, younger shoots softly hairy. Leaves greyish-green, 3-foliolate; leaflets on a brief stalk (petiole), petiole mostly longer than leaflets, glabrous to denseley hairy. Flowers lemon-yellow or greenish-yellow, with a projecting greenish or crimson beak; calyx regularly tinged purple; in many-flowered racemes to 400 mm long. Flowers bloom from spring to autumn. Fruits greenish-purple pods, inflated, to a hundred mm long, seeds unfastened in dry pod. Native to Tropical East Africa and North-East Africa (Tanzania and Kenya). In South Africa it is existing in Gauteng, North West, Limpopo, Mpumalanga, and KwaZulu-Natal province. It is invasive also in Australia (New South Whales) and in Hawaii. Crotalaria species have been broadly used in Chinese standard medication to deal with a number of kinds of internal cancers. *Crotalaria agatiflora* is used as a medicinal plant in quite a few African nations for the cure of bacterial and viral infections as well as for cancer (Roux, Hussein, & Lall, 2011).

Figure 24: Crotalaria agatiflora (Roux, Hussein, & Lall, 2011)

13.4 *Crotalaria cunninghamii*

Crotalaria cunninghamii is a shrub developing 1 - 2 meters tall. The plant is harvested from the wild for nearby use as a remedy and source of fiber. The fiber is of excessive high-quality and has viable for industrial production. The plant is also grown as a decorative in gardens, valued in particular for its large, colored flowers. There are no predominant threats regarded to this species, however, the region the place this species occurs is threatened with the aid of habitat degradation. The plant is categorized as 'Least Concern' in the IUCN Red List of Threatened Species (2013). It is located in Australia - Western Australia, Northern Territory, South Australia, Queensland, New South Wales, Victoria. The sap from the leaves is used traditionally to deal with swellings on the body and as eyewash to treat eye infections. The stems are a source of fiber. This was used traditionally by the Aboriginal Australians for cords and for making sandals to protect them from the hot wilderness sand. The fiber is comparable in standard to that obtained from *Crotalaria juncea*, which is a valuable, high quality, robust fiber that is grown on an industrial foundation and used to make wire and cord; canvas and fishing nets; and paper and pulp (Cowan, & Allen, 1982).

Figure 25: Crotalaria cunninghamii (Cowan, & Allen, 1982)

13.5 *Crotalaria medicagenia*

Crotalaria mediagenic is an erect and branched annual herb, develop in farms and loans and extensively distributed in the Thar Desert. It has trifoliate leaves with raceme inflorescence (5-15 yellow flowers) and used as favorable camel feed in north western India. It is native to the Indian Thar desert. Also discovered in E. Asia - southern China, Afghanistan, Indian subcontinent, Myanmar, Thailand, Laos, Vietnam, Indonesia, Philippines, New Guinea, Australia (Sankhla, Meghwal, Tak, Tak, & Gehlot, 2015). The plant is bitter and expectorant. It is used to assist expel bile and phlegm. The juice of the leaves is said to decrease salivation. It is used both internally and externally in the therapy of scabies and impetigo. A paste of the leaf is taken with milk to deal with white discharge (Dymock, Warden & Hooper, 1890). *Crotalaria medicaginea* is distinctly palatable to horses and has been linked to a range of chronic diseases in horses. *Crotalaria medicaginea* has been linked with hepatic lesions and photosensitization in the Northern Territory and with lesions of liver, lung, and urinary bladder in northwestern Australia (Fletcher & De Voss, 2011).

Figure 26: Crotalaria medicagenia (Fletcher & De Voss, 2011)

13.6 *Crotalaria podocarpa*

Erect annual up to 70 cm tall with spreading lower branches. Most parts with spreading hairs. Leaves 3-foliolate; leaflets variable however frequently linear, on long-lanceolate or obovate elliptic, 1.5-7 cm long. Flowers clear yellow, sometimes slightly reddish tinged; wings slightly shorter than keel;keel angled in lower 1/2 with a straight beak, hairless however often bushy on the beak. Pod 2-3 cm long, quite greatly cylindrical and inflated when young, contracted into the 2.5-5 mm long stipe, hairless. The aerial components of *Crotalaria podocarpa* are recognized in homeopathy for their antirheumatic, antiphlogistic and expectorant activities (Wanjala et al., 1999).

13.7 *Crotalaria zanzibarica*

Crotalaria zanzibarica is a perennial leguminous shrub native to Africa. This plant, which is usually disbursed along roadsides, riverbanks, and in abandoned fields, typically establishes symbiosis with rhizobia forming root nodules (Huang, Liu, Chen, & Kao, 2016). Leaves are 3-foliolate, stipules absent. Flowers are in an elongated raceme, trendy petal yellow with purplish streaks, mainly closer to the base. Pod is 3-4.5 cm long, black, pendent at maturity, seeds are orange to reddish-brown; 50-70 per pod (Huang, Liu, Chen, & Kao, 2016).

13.8 *Crotalaria aegyptiaca*

Crotalaria aegyptiaca (Benth), a low shrub that reaches about 60 cm high, is frequently discovered in the sandy soils of wasteland wadis. *Crotalaria aegyptiaca* is primarily distributed in the Middle East, inclusive of Egypt and the Arabian Peninsula. Additionally, it spreads in the course of all areas in Oman. *Crotalaria aegyptiaca* containing pyrrolizidine alkaloids (PAs) is used in ordinary remedy and as an antitumor. Sheep and goats do not graze *Crotalaria aegyptiaca* because of the Pas‘ toxicity, but is grazed with the aid of camels and gazelles (Al-Subhi, Hogenhout, Al-Yahyai, & Al-Sadi, 2017).

13.9 *Crotalaria albida*

Crotalaria albida is an annual to short-lived perennial, erect to ascending plant developing 10 - 150cm tall. The plant is generally branched alongside the stem, but on occasion solely forms branches at the base of the stem. The plant is harvested from the wild for neighborhood medicinal use. A common and considerable species, it is classified as 'Least Concern' in the IUCN Red List of Threatened Species (2013). Commonly discovered in E. Asia - China, Pakistan, India, Sri Lanka, Nepal, Bhutan, Bangladesh, Myanmar, Thailand, Cambodia, Laos, Vietnam, Malaysia, Indonesia, Philippines. The juice of the root is used in the remedy of indigestion. The juice of the plant is used in the cure of bed wetting. A paste of the plant is applied topically as a treatment for warts, in particular those on the sole of the toes (Kilham & Manandhar, 2003).

13.10 *Crotalaria laburnifolia*

Crotalaria laburnifolia is a very variable, evergreen shrub growing from 60 - 200cm tall. The plant is harvested from the wild for nearby medicinal use. It is sometimes grown in gardens as a medicinal plant, has been used as a green manure and is sometimes planted as an ornamenta. An

infusion of the entire plant is used as a gargle to deal with sore throats and mouth inflammations. Medicines organized from the seed have a blood-purifying effect and are used to treat sore throats, skin ailments and as an emmenagogue. Pyrolizidine alkaloids such as anacrotine and madurensine have been extracted from the seeds in South Africa, the former being antispasmodic and maybe hepatotoxic. Crotalaria seed additionally includes flavanone glycosides (Harborne, 1993).

13.11 *Crotalaria incana*

Crotalaria incana varies from an erect annual to a somewhat woody perennial plant. It often grows from 25 - 130cm tall, notably to 350cm, generally with spreading branches. The plant is occasionally harvested from the wild for nearby use as a medicine. It has proven promise as an inexperienced manure crop in coffee. The plant carries toxins, which include pyrrolizidine alkaloids. Cattle keep away from ingesting it. Flowers and unripe fruits are used as abortifacient in Paraguay, the place the pods are considered as a magic treatment for treating mute and stuttering children. The plant is broadly used in folk medication in Colombia to remedy gonorrhea, for baths and poultices, and as a disinfectant for wounds and sores (Gómez-Sosa, 2000).

There are other plants such as *Crotalaria aridicola, Crotalaria axillaris, Crotalaria candicans, Crotalaria crassipes, Crotalaria crispata, Crotalaria dura, Crotalaria fulva, Crotalaria globifer, Crotalaria goreensis, Crotalaria grahamiana, Crotalaria grantiana,Crotalaria intermedia, Crotalaria laburnifolia, Crotalaria madurensis, Crotalaria mitchelii,Crotalaria mucronata, Crotalaria nana, Crotalaria novae-hollandiae,Crotalaria semperflorus, Crotalaria stricta, Crotalaria trifoliastrum* etc. that belongs to crotalaria family. But, there wasn‘t much studies found about them (Aronson, 2014).

Chapter-14

Conclusion

Plants have a vital job in the treatment of distinctive maladies in especially imperative association of drug. There are several plants on the earth which lies unexplored in the field of prescription. One such Species is Crotalaria L. is a wealthy wellspring of alkaloids, specifically pyrrolizidone alkaloids and poisonous amino acids in seeds. It has a promising spot in the Ayurveda for its abortificient, emetic, purgative, uncleanliness and blood maladies. The class *Crotalaria L*. species (family Fabaceae) is considered as the largest variety, with around 600 species appropriated all via the tropics and subtropic areas of the world, which can be utilized as opposing to nematodes in maintainable harvest era frameworks. The Genus Crotalaria is pantropical and the maximum species diversity occurs in Africa and Madagascar (ca. 540 species) with further expansions into South America (64 species), and North America (34 species). The most frequent species are *Crotalaria sagittalis, Crotalaria rotundifolia* and *Crotalaria spectabilis.* The less frequent species are *Crotalaria purshii, Crotalaria lanceolata, Crotalaria pallida, and Crotalaria ochroleuca. Crotalaria L.,* species have been accounted for to comprise alkaloids, saponins and flavonoids as compound markers with integral N-oxides of the genera Leguminaceae. They additionally have two antileukemic, antitumor, antispasmodic, antineoplastic, cardiodepressent, hypotensive properties. The leaves are the excellent remedy for ptyalism, looseness of the bowels, scabies and impetigo. However, Crotalaria produces toxic pyrrolizidine alkaloids (PAs), which are responsible for the occasional intoxication of grazing livestock (hepatic veno-occlusive disease). *Crotalaria retusa* seeds are some of the most toxic of Crotalaria species. However, these pyrrolizidine alkaloids are responsible for the anti-mutagenic activity of the plants of this Family. There is a big extent of potential among Crotalaria L. genus

so there is a need to be done a wide range of animal model experiments to explore the therapeutics for different indication.

Chapter-15

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