INTRODUCTION
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The genus *Crotalaria* belongs to the Natural Order *Leguminosae* and comprises over 300 species out of which about 45 grow in India. Extensive work has been done on some foreign species of *Crotalaria*, but unfortunately the Indian members of the genus *Crotalaria* have completely escaped the attention of Indian workers. The alkaloids isolated from various species of *Crotalaria* belong to a group called 'Senecio Alkaloids' because they were first detected in the genus *Senecio*. The more appropriate name of 'Senecio Alkaloids' is 'Pyrrolizidine Alkaloids'. Many of the pyrrolizidine alkaloids have been shown to possess certain desirable physiological properties. Platiphylline produces an atropine-like effect, the p-aminobenzoate and the aminoquinoline derivatives of trachelanthamidine show local anaesthetic and antimalarial properties respectively. Recently one of the pyrrolizidine alkaloids has been actually used in Russia as muscle relaxant as a substitute for curare. In my own work I have observed that monocrotaline, isolated from seeds of *C. sericea*, possesses powerful hypotensive and oxytocic property. More recently it has been discovered that monocrotaline isolated from *C. spectabilis* (*C. sericea*) possesses tumour-inhibitory activity. Thus, this genus offers promising possibilities to discover more therapeutically active compounds. This was one of the reasons to undertake a detailed phytochemical investigation on some Indian species of this genus.
Schoental in 1961 reported that herbal remedies including plants containing pyrrolizidine alkaloids are used in rural areas of tropical and sub-tropical countries for the treatment of many common diseases like cold, fever, rheumatic pains, stomach disorders of children and similar diseases. On the other hand, prolonged use of pyrrolizidine alkaloids have been proved experimentally to produce hepatotoxic action in several species of animals. The Liver Diseases Sub-committee of the Indian Council of Medical Research, while discussing the infantile cirrhosis of the liver in India in 1955, reported high occurrence of liver disorders and liver tumours especially among young children. This may be due to the use of herbal drugs containing pyrrolizidine alkaloids. Thus, indiscriminate use of indigenous plants containing pyrrolizidine alkaloids is a potential danger to the public health of India. Poisoning cases in human beings by accident have also occurred (Henry) through the presence of Senecio seeds in food grains where the latter have been grown as crops in fields infested by plants containing pyrrolizidine alkaloids. Keeping in view national health, the plants containing pyrrolizidine alkaloids were examined for their chemical nature.

Recently, some foreign species of Crotalaria have evoked a world wide interest in the scientific field as they have been found to be toxic to livestock. A large number of animals are reported to die annually by consuming these plants mainly on account of liver cirrhosis. Although some Indian
Crotalarias have been reported toxic to animals yet nothing much is known about the specific alkaloids which are believed to produce slow cumulative toxicity to animals. In order to preserve cattle wealth of India, it was considered worthwhile to undertake detailed chemical investigations on this genus.

More recently it has been observed by Clark that heliotrine, a pyrrolizidine alkaloid causes powerful mutagenic activity in *Drosophila*. He has shown that the mutagenic activity of heliotrine is due to blocking effect of alkaloid on maturation of immature germ cells, so that as soon as the available spermatozoa and spermatids have been utilized, the males are no longer capable of breeding, although they may remain alive and active as long as three weeks after treatment. It has also been further reported that hydrolytic products of heliotrine do not show any mutagenic activity, suggesting that strong mutagenic activity of heliotrine is probably a property possessed by the molecule as a whole. Thus, a number of pyrrolizidine alkaloids from various plants of *Crotalaria* may assume practical importance if they show mutagenic activity following ingestion by agricultural livestock.

Several Indian species of *Crotalaria* have been used in indigenous system of medicine since very early times. Externally many species have been used for sore throat, scabies and impetigo. Internally some species have been
Fig. I  The Plant of C. aerica Retz.
Fig. 2 The Plant of *C. medicaginea* Lam.
Fig. 4 The plant of *C. grahamiana* W. & A.
Fig. 5 The Plant of *C. ferruginea* Grah.
used in derangement of stomach and infant diarrhoea. They have also been used as purgative, emmenagogue and for purification of blood. The diverse therapeutic use of these plants in Indian system of medicine has led to ambiguity. In view of liver damaging and toxic properties of some of the pyrrolizidine alkaloids, it would be worthwhile to determine if the species used in Indian medicine possess such undesirable actions.

Morphology

1. Crotalaria sericea Retz.

The plant (Fig.1) *C. sericea* Retz. (family Leguminosae) has a fairly wide distribution in India. The common names of the plant are:

<table>
<thead>
<tr>
<th>Language</th>
<th>Common Name</th>
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<tr>
<td>Bengal</td>
<td>Jhanjhania, Pipulijhunjhun, Atarsi Sans</td>
</tr>
<tr>
<td>Hindi</td>
<td>Jhunjhunia</td>
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<tr>
<td>Sanskrit</td>
<td>Ghantarava</td>
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<td>Vern.</td>
<td>Jhumjhum</td>
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It is a short undershrub varying from 2½ feet to 6 feet in height. The **branches** are stout, striate and subglabrous. The **stem** is robust and grooved. **Leaves** are simple, nearly sessile, variable in breadth, oblong lanceolate, acute or subacute, mucronate, glabrous above, finely silky beneath and have a narrow base. The **stipules** are small, leafy and persistent. **Flowers** are ½ to 1" long, in elongate terminal 20-50 flowered racemes. **Pedicels** are
longer than the calyx with one large foliaceous ovate bract at the base of each pedicel and a pair of minute subacute bracts on each pedicel below the middle. Calyx is pubescent, almost glabrous from outside. Tube is campanulate nearly half as long as the teeth, upper teeth are large triangular, acute and slightly broad at the base, the lower teeth are smaller and less deeply cut than the upper and are linear-lanceolate. Corolla is yellow, nearly twice as long as the calyx. Pods are glabrous, oblong, nearly 1½ to 2 inch long. The fruit is an inflated pod. Seeds are many and usually from 15 to 30 in each pod. Seed colour is black with a distinct steel blue tinge.

2. *Crotalaria medicaginea* Lam.

The plant (Fig. 2) *C. medicaginea* Lam. is found throughout India and is popularly known in Punjab as Gulabi. The other common names of plant are:

- Gujarati: Ranmethi
- Hindi: Gulabi
- Marathi: Jenjaru
- Porebunder: Adabaumethi

The plant is a perennial herb with a woody rootstock, much branched and has height 2-3 feet. The stem is almost cylindrical and the branches are numerous. Leaves are 3-foliolate, petiole being 3-5 mm. long. Leaflets are 6-10 x 3-4 mm., oblanceolate, apiculate, glabrous from above
and more or less silky beneath with very short distinct petioles. The **stipules** are persistent. **Flowers** are in terminal and leaf-opposed, 2-6 flowered racemes. The **peduncles** are longer than the leaves. The **bracts** are minute, linear-subulate. **Calyx** is 2.5 mm. long, silky outside with appressed hair. Calyx teeth are triangular, acute, arising from the campanulate tube. **Corolla** is yellow, twice as long as the calyx, standard being silky on the back. **Pods** are obliquely subglobose, about 3 mm. long and contain 2 seeds, which are buff coloured.

3. *Crotalaria striata* DC.

The plant (Fig.3) *C. striata* DC. (Syn. *C. mucronata* Desv.) is popularly known as Sen in Hindi and Jhunjhunia in Assami.

The plant is an erect branching shrub with robust thinly silky branches reaching a height of about 7 feet. The **stem** is cylindrical and woody at the base. **Leaves** are 3-foliolate with a petiole, 3-9 cm. long. **Leaflets** are 5-10 cm. long, membranous, elliptic or ovate-acute in shape with mucronate apex. **Flowers** 40-60, are present in stiff terminal raceme, 12-25 cm. long. The individual flowers are small in size, about 1.5 cm. long, but have distinct curved keel-petal, floral parts are yellow striped with red or purplish lines. **Calyx** is hairy and forms broad tube like structure, teeth being lanceolate. **Corolla** is
yellow nearly twice as long as the calyx. **Pods** are deflexed (bent down) with short stalk, 3-5 cm. long, 1.0 cm. broad, cylindrical but slightly curved. The **pods** are slightly hairy when young but become glabrous on maturity. **Seeds** are small, reddish brown in colour and are 35-40 in number in each pod.

4. *Crotalaria grahamiana* W. & A.

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The plant (Fig. 4) *C. grahamiana* W. & A. is quite distinct from other species because it is easily identifiable by its showy flowers and 5-7 foliolate leaves. The plant, 5-7 feet is an erect branching shrub with deep root system. **Stem** is woody at the base and branching above. **Leaves** are 5-7 foliolate, palmate in appearance. The petiole is long stout and covered with silky hair. **Leaflets** are obovate, upper surface glabrous, lower densely covered with appressed silky hair giving a silvery-grey sheen to the leaf surface, margin entire, apex projecting to a small distinct point. The **stipules** are slender, lanceolate and reflexed. The **flowers** are in closely packed terminal racemes. The individual flowers are about 2 cm. long. The petals are bright yellow. The standard petal has few black streaks on the lower surface but not on the upper surface. **Pods** while fresh are green with a bluish sheen on upper part, turning brown on maturity, inflated, 5-7 cm. long and 1-2 cm. broad,
cylindrical, obtuse and hooked at the apex, glabrous. Each pod contains about 16 seeds which are flattened, almost black in colour.

5. *Crotalaria ferruginea* Grah.

The plant (Fig.5) is a perennial herb with erect branches. The plant is fairly stout with deep root system about 2-4 feet in height. The stem and branches are very much hairy, almost cylindrical in shape. Leaves are simple, sessile 6-7 cm. long, 1.5-2.0 cm. broad, broadly lanceolate, apex somewhat rounded, margin entire and whole lamina is covered with long hair, 0.2-0.3 cm. The stipules are 0.8-1.0 cm. long, hairy, leafy, deltoid and persistent. Flowers, 3-5 in terminal raceme, are yellow in colour, about 1-1.5 cm. long. The pedicel is long and hairy. Calyx is broadly lanceolate and much hairy. Corolla is yellow, standard being 1.5 cm. long and 1.0 cm. broad. Pods are inflated oblong with hard mucronate apex. Each pod contains small shining violet seeds varying from 60 to 90 in number.
Distribution and Habitat

*C. sericea* Ratz. is found in tropical regions throughout India from plains to 4000 feet, in Kumaon and valleys below Simla. In Assam it grows in grass-lands in swampy localities in Goalpara, possibly throughout lower Assam. Stewart says it is cultivated in Panjab as a garden flower. Wild growth of this plant in abundance has been observed in Chandigarh.

*C. medicaginea* Lam. grows in wild state throughout India from Himalayas to Ceylon and Burma. This plant also grows in abundance in Chandigarh. Flowers appear in August-September while fruits are available in November-December.

*C. striata* DC. is also available throughout India from Himalayas to Ceylon and Malaysia. Wild growth of this plant has been observed on Shillong-Nangpou Road in Assam. It is also cultivated in Darjeeling and Cinchona estate.

*C. grahamiana* W. & A. grows wild in South India on the hills of Travancore. This plant has also been cultivated in Ootacamund as a garden plant.

*C. ferruginea* Grah. grows from Nepal to Assam ascending up to 5,000-6,000 feet. It is common throughout India. This plant has sparse distribution in Chandigarh.
Commercial Value

*C. sericea* is used in United States as green manure but seldom as a direct forage, since the seeds and hay are reported to be unpalatable or even at times toxic to livestock. It is cultivated in Panjab as a garden flower but apparently never cultivated as an agricultural product although its fibre is sometimes prepared by maceration in water and used for making cordage. Recently, in the year 1958 Indian Council of Agricultural Research, New Delhi has published a research bulletin on 'Adhesives from protein of *C. juncea*'. The seeds have been shown to contain proteins and possibilities of extraction and use of protein for adhesive work have been described. But the fact is that it is not the protein that gives adhesiveness or is a commercial source for adhesives, rather it is the gum, present in endosperm of the seed which gives adhesiveness. In the present investigation seeds of *C. sericea* have been found to contain approx. 25% of endosperm which contains nothing but gum. This gum can also be put to similar uses as the gum from *C. juncea* used in various industries.

*G. medicaginea* is considered to be a good camel fodder. The seeds may be used as cattle feed after cooking with common salt. *C. ferruginea* was tried as green manure crop in Java but was found susceptible to insect damage.
C. striata has been used in U.S.A. as green manure. It is used in India as green manure and shade plant in tea, rubber and coconut plantations. Seeds are sometimes used as substitute for coffee. C. grahamiana contains gum in endosperm of seeds. This gum can be used as source of adhesives. This plant is also cultivated as garden plant and green manure.

**Toxicology**

Plants containing pyrrolizidine alkaloids are poisonous to livestock. Megalocytosis of the liver cells, a characteristic effect of pyrrolizidine alkaloids has been observed. Haemorrhages in the abdominal organs (especially of the liver), fatty changes in the liver leading to cirrhosis and prolongation of prothrombin time have been reported. Detailed pharmacological and toxicological properties of the pyrrolizidine alkaloids, have been reviewed in literature.

Previously known toxic species of Crotalaria include C. sagittalis, C. juncea, C. burkeana, C. dura and C. globifera. Leaves of C. mucronata (C. striata) contain alkaloids which are poisonous to goats. The toxic nature of the Senecio species to cattle is still a matter of considerable interest. Hepatotoxic activity of semisynthetic analogues of pyrrolizidine alkaloids has been discussed by Schoental and Mattocks. In another paper Schoental reported hepatotoxic action of pyrrolizidine (Senecio) alkaloids in relation to
their structure. Much work on the biological effect of pyrrolizidine bases has been done by Chen, Harris and co-workers. New interest in pyrrolizidine alkaloids was created due to the finding that they produced primary liver tumours in rats. It was early shown that these alkaloids produced cirrhosis in the liver of cattle. When the spring rains are delayed the cattle then graze on the more succulent Senecio plants in the absence of the young grasses. Therefore, considerable losses of livestock have been reported annually in South Africa.

Bull in 1956 reported the toxic nature of Haliotropium europaeum. Slow and long administration of these alkaloids causes severe liver damage and liver tumours. Usually the alkaloids show their effect soon after administration but pyrrolizidine alkaloids act insidiously and appropriate dosage may allow the animal to survive for many months in apparent good health before it ultimately succumbs to liver damage with megalocytosis of the liver cells, a characteristic effect of pyrrolizidine alkaloids. Hydrolytic products of these alkaloids are found to be nontoxic and produce no liver damage but this has not been proved conclusively. In some cases the toxicity is in some way associated with the unsaturated basic esters. Usually the pyrrolizidine bases occur in ester form but recently nonester pyrrolizidine alkaloids have also been reported. Such an example is found in C. anagyroides, C. trifoliastum and C. aridicola. It has
been observed that nonester pyrrolizidine bases are nontoxic to animals and do not produce liver cirrhosis.

The plants containing pyrrolizidine alkaloids responsible for certain diseases have been called in common terminology, 'poisonous ragwort' (England) and the diseases have been variously termed 'horse staggers' and 'Molteno disease' (South Africa), 'Walking disease' (Nebraska, U.S.A.), 'Pictouc' (Canada), 'Siras kaya' (Norway) and 'Winton disease' (New Zealand).

Some of the toxic effects produced by some of the foreign species of Crotalaria are given below:

Crotalaria:

C. burkeana is reported to be the cause of the laminitic form of Crotalism in cattle. This condition is an acute inflammatory process in the horn forming membrane of the hoofs. The animals suffer great pain and can move about only with great difficulty. Later the pain decreases but they walk still stiffly. The hoofs grow out and may reach enormous length and thus impede locomotion, but the disease is not directly fatal.

Missouri-bottom disease:

C. sagittalis or rattle box of the Eastern and Central United States is reported to be the cause of a disease 'Missouri-bottom disease' so called on account
of its prevalence along the Missouri river bed. This disease effects horses and in most cases is very slow in its progress. It almost uniformly proves fatal after a number of weeks or months. There is a general decline of bodily vigour throughout this period, marked emaciation and consequent weakness. In a number of cases marked coma or stupor has been observed. The animal often falls asleep while eating. A large number of horses are reported to die annually by consuming this plant.

Nothing much is known about the toxic properties of various species of Crotalaria found in India and no specific alkaloid has been isolated from any member of the genus. Plants of C. sericea (C. spectabilis) are reported to be poisonous to livestock. The plants are toxic to cattle under field and experimental conditions and fatal to chickens under experimental conditions. Seeds of C. striata are considered to contain poisonous alkaloids but washed and cooked seeds are non-toxic.

Therapeutic Uses and Pharmacology

In pharmacological behaviour most of the pyrrolizidine alkaloids are poisonous to livestock but more recently it has been observed that some of the pyrrolizidine bases have certain desirable physiological properties. Chen, Harris and Rose have noted that platyphylline which seems to be less prone to cause liver cirrhosis than its allies,
has an atropine-like action on the eye and the intestine. Goldenhershel has made a detailed study of this alkaloid as a possible substitute for atropine and concludes that at least as an antispasmodic, in diseases of abdominal organs, it has advantages over atropine. Similarly p-aminobenzoate derivative of trachelanthamidine has been shown to be as potent a local anaesthetic as cocaine hydrochloride. Aminoquinoline derivative of trachelanthamidine shows antimalarial properties. More recently one of the pyrrolizidine alkaloids from Senecio plant has been used in Russia as muscle relaxant and as a substitute for curare. In my own work the alkaloid monocrotaline isolated from C. sericea has been shown to possess powerful oxytocic property. It has also a prolonged and pronounced hypotensive effect and it does not show any toxicity in rats and pigeons in the doses in which it is effective pharmacologically. In a very recent communication monocrotaline, an active principle of C. spectabilis, has been shown to possess anti-cancer property.

Several other therapeutic uses from the different species of Crotalaria have been reported. Whole plant of C. sericea is used in scabies and impetigo. The roots of C. albida are considered to be purgative. Leaves and branches of C. burhia are used as cooling medicine. Seeds of C. juncea are used to purify blood. It is also used in
impetigo, psoriasis and as emmenagogue. Infusion of
whole plant of *C. laburnifolia* is used as gargle for
sore throat and inflammation of mouth. Seeds of
*C. mucronata* (*C. striata*) are sometimes used as substitute
for coffee. Roots of *C. prostrata* are used in derangement
of the stomach and infantile diarrhoea. Whole plant of
*C. retusa* is used in scabies and impetigo. Roots of
*C. trifoliatrum* are purgative. Juice of leaves of
*C. verrucosa* is used in scabies and impetigo both internally
and externally. It is considered to be efficacious in
diminishing salivation.

**Review of Literature**

Extensive work has been done on pyrrolizidine
alkaloids present in foreign Crotalarias. The pioneer
workers in the field of pyrrolizidine alkaloids are
G.P. Menshikov (Russia), G. Barger (Edinburgh) and R.H.F.
Manske (Canada). Significant contribution to the
chemistry of pyrrolizidine alkaloids has also been made
by C.C.J. Culvenor (Australia), R. Adams (U.S.A) and F.L.
Warren (S. Africa). Recently, some work on pyrrolizidine
alkaloids has also been carried out by T.R. Seshadri (India).
The work on pyrrolizidine alkaloid in detail is reviewed
by Manske. The research work which is carried out in the
preceding 15 years, some of which, not included by
Manske, is recorded here.
Series of papers have appeared on pyrrolizidine alkaloids by F.L. Warren, most of which elucidate the structure of alkaloids. Rosmarinine has been isolated from S. hygrophilus and its structure is assigned. Structure of retrorsine and isatidine and their necic acids has been given in a series of papers. General structure of necic acids has also been discussed and synthesis of few necic acids has been reported. The absolute configuration of heliotridane and the necine bases has been deduced. The occurrence and preparation of the N-oxides of pyrrolizidine bases has been described and improved method of isolation of alkaloids has been developed. General structure of Senecio alkaloids, structure of senecic acid and isatinecine have been established. An account of preliminary study of the IR absorption spectra of the Senecio alkaloids is given. The U,V extinction curves of some of 'necic' acids and Senecio alkaloids are recorded and their significance in structure of the alkaloid is indicated.

Considerable work on isolation and structure of pyrrolizidine bases has been done by Roger Adams and his co-workers. Monocrotaline has been isolated from C. retusa and its structure fully established. Structure of dicrotaline and trichodesmine are also reported. The composition of hieracifolline and jacobine has been given...
and different compounds were separated from them by partition chromatography. Ridelline, Seneciphylline and Senecionine have been isolated and identified from *C. juncea*. Structure of juncine, a new alkaloid from *C. juncea* has been established.

More recently work on pyrrolizidine alkaloids has been carried out in Australia by Dr. C. C. J. Culvenor and his co-workers. Heliotrine and lasiocarpine have been isolated from *Heliotropium europaeum*. A method of assay, based on partition chromatography has been developed and applied in estimation of many alkaloids. Hepatotoxic properties of *Heliotropium lasiocarpum* has been reported by Russian workers. The alkaloid heliotrine has been shown to possess mutagenic activity in *Drosophila*. The structure of heliotrine and lasiocarpine has been confirmed. Many alkaloids have been isolated from *S. jacobea*, and jacobine has been identified as seneciphylline. The alkaloids of *Erectites quadridentata* have been isolated and their occurrence mainly in the form of N-oxides has been proved. Three new alkaloids, retusine, retusamine and an incompletely characterized base m.p. 130-132° have been isolated from *C. retusa* in addition to monocrotaline. Possible structure of retusine has also been given. Two new alkaloids, echiumine and echimidine have been isolated from *Echium plantagounseum*.
Absolutely no work has been done on pyrrolizidine alkaloids present in Indian Crotalarias. Seeds of *C. sericea* (*C. spectabilis*) have been shown to contain alkaloid monocrotaline 3.2% by Roger Adams. Culvenor and Smith isolated spectabiline in addition to monocrotaline from Australian grown seeds of *C. spectabilis*. Seeds of *C. medicaginea* have been reported to contain, fat 6.76%, protein 23.31%, and carbohydrate 42.04%. Petroleum ether extractive of *C. medicaginea* has been worked and shown to contain hydrocarbon, phytosterol and some fatty acids by Mehta and Rana but isolation of alkaloid from other extractives have not been reported. In the present investigation alkaloids from *C. medicaginea* have been confirmed to be of similar nature as reported from *C. trifoliatrum*. *C. striata* gives senecionine in addition to 1-methylenepyrrrolizidine reported to occur in *C. anagyroides* and *C. damarensis*. The work on *C. ferruginea* and *C. grahamiana* has not been reported previously.

**Pyrrolizidine Alkaloids**

**Occurrence:**

Pyrrolizidine alkaloids are found within the families, *Leguminosae*, *Compositae*, and *Boraginaceae*. The alkaloids found in each family are closely related.
to each other and for the sake of brevity this group of alkaloids was at first named 'Senecio alkaloids' because they were first detected in Senecio. But the more appropriate and recent word for this group of alkaloid is 'pyrrolizidine alkaloids', since a basic moiety is always a methylypyrrolizidine. These alkaloids have special significance that they produce liver cirrhosis in cattle.

Within the family Leguminosae and Compositae, the genus Crotalaria and Senecio contain pyrrolizidine alkaloids. Senecio is the largest genus and comprises over one thousand species and most of these contain alkaloids. Brechtites, the closely related or perhaps synonymous genus also consists of species rich in alkaloids.

The genera, Heliotropium, Trachelanthus and Trichodesma belonging to the family Boraginaceae also contain pyrrolizidine alkaloids which are very similar to those extracted from Senecio or Crotalaria plants.

In frequent cases, the same alkaloid has been isolated from different species within the same genus. For example monocrotaline has been obtained from both C. spectabilis (C. sericea) and C. retusa. The alkaloid retrorsine has been extracted from as many as eight different species of Senecio. The pyrrolizidine alkaloids thus constitute a series of compounds, identical members of which are found in different genera within both the same and different botanical families. Those plants which serve as common source of different pyrrolizidine alkaloids are listed by Manske.
Chemical Constitution:

All the pyrrolizidine alkaloids contain only one nitrogen atom. But there are differences in the carbon content. Majority of alkaloids are those which contain eighteen carbon atoms. The hydrogen and oxygen contents of the alkaloids, considered as a series, are subject to wide variation.

In chemical constitution most of pyrrolizidine alkaloids are alkalamine esters of a C₈ hydroxy amine and a C₉₀ acid as for example retrorsine. This pattern was so regular that Manske proposed the name 'necine' for the basic portion and 'necic acid' for the acid part of alkaloid.

Hydrolysis of pyrrolizidine alkaloids is usually brought about by barium hydroxide, but acid hydrolysis is also carried out in some cases. The hydrolytic products are named as 'necine' (basic portion) and 'necic acid' (acid portion). The necic acids have been obtained in greater variety than have the necines. One individual necine may constitute the basic moiety of many different alkaloids, but there are only three necic acids which have been shown to constitute the acid moiety of more than one pyrrolizidine alkaloids. Platynecic acid (also called senecic acid lactone) has been obtained by alkaline hydrolysis of the alkaloids platyphylline and senecionine;
jaconecic acid, by hydrolysis of jacobine (from Senecio jacobea) and otosenine (from S. othonnae) and trachelanthic acid by hydrolysis of trachelanthine and trachelanthamine. The important necic acids and necines are listed in detail by Manske.

The pyrrolizidine alkaloids fall into three main categories.

1. Monoesters of the necine with monocarboxylic necic acid i.e. Heliotrine, Retrorsine, Helleurine etc.
2. Diesters of the necine with two different monocarboxylic necic acids, i.e. Lasiocarpine, Echiumine etc.
3. Cyclic diesters of the necine with dicarboxylic necic acid, i.e. Monocrotaline, Dicrotaline, Senecionine etc.

Third category represents a highly interesting group of compounds of wide natural occurrence, containing ring of medium size, the two ester groupings are part of 11 or 12 carbon members.

Very recently it has been observed that pyrrolizidine alkaloids also occur in the form of nonester pyrrolizidine alkaloids. They have usually 9 carbon atoms and have low molecular weight. They are usually liquids and have simple chemical structure. They are also found to be nontoxic to animals and do not cause liver cirrhosis to live-stock.
as is usually observed in ester type of pyrrolizidine alkaloids. So far five nonester pyrrolizidine alkaloids have been reported from the genus *Crotalaria*. They are:

1. 1-methylenepyrrolizidine (*C. anagvroides* and *C. damarensis*)
2. Methyl ether of retronecine (*C. trifoliastum*)
3. Methyl ether of supinidine (*C. trifoliastum*)
4. 7β-hydroxy-1-methylene-8β-pyrrolizidine (*C. goreensi s*)
5. 7β-hydroxy-1-methylene-8α-pyrrolizidine (*C. goreensi s*)

In the present investigation, discovery of base B from *C. medicaginea* increases the number of previously known nonester pyrrolizidine alkaloids to six.

**Pyrrolizidine Alkaloids as N-oxides**

Most of the pyrrolizidine alkaloids have been shown to occur in N-oxide or amine oxide form. They are formed by oxidation of the corresponding tertiary amine and the nitrogen of the parent alkaloid is attached to oxygen by a co-ordinate link to form N-oxide or amine oxides. They are, therefore, much weaker bases than the corresponding tertiary amine. The N-oxides are detected by following methods:

1. They give red colour with acetic anhydride.
2. They give heavy white precipitate with silicotungstic reagent.
iii) Rf value of N-oxides are altered, very slightly if at all when butanol-ammonia is substituted for butanol-acetic acid whereas the tertiary amine alkaloids have much higher Rf value in the basic solvent.

N-oxides of alkaloids are insoluble in chloroform hence isolation does not occur by general isolation procedure. The problem of the separation of the naturally occurring amines from amine oxides has been attacked by different ways.

1. In the first instance of isolation it was found that both trachelanthamine and its N-oxide could be extracted from an aqueous solution by dichloroethane.

2. Sequences of organic extractants such as ether followed by chloroform and chloroform followed by butanol take advantage of lower solubility of the N-oxide in the first solvent.

3. Extraction at increasing pH levels has also been employed.

4. Zinc dust and sulphuric acid is used to break the N-oxide into amine when it is extracted by chloroform.

As an extreme illustration, Senecio coronatus which previously yielded only traces of alkaloid soluble in chloroform gave increased yields of alkaloids when the
base was reduced with Zn/H$_2$SO$_4$ prior to isolation and commensurate to the toxic nature of plant.

A study of major alkaloids of *Senecio paucicalyculatus* Platt, by Pretorius indicated that the content of retrorsine increases whereas that of retrorsine N-oxide decreases with the age of plant. Similarly seneciphylline and platyphylline and their respective N-oxides, greatly predominate during the vegetative period, reach a maximum just before flowering and are substantially minor to the corresponding amine in the resting state.