CHAPTER 9

INTRODUCTION
THE HISTORY OF MEDICINAL PLANTS

From earliest times mankind has used plants in an attempt to cure diseases and relieve physical suffering. Primitive peoples of all ages have had some knowledge of medicinal plants, derived as a result of trial and error. These primitive attempts at medicine were based on speculation and superstition. Most savage people have believed that disease was due to the presence of evil spirits in the body and could be driven out only by the use of the poisonous or disagreeable substances calculated to make the body an uninhabitable place in which to remain. The knowledge regarding the source and the use of the various products suitable for this purpose was usually restricted to the medicine of the tribe. As civilisation progressed the early physicians were guided substantially by these observations.

In all the early civilisations there was much interest in drugs plants. In China, as early as 5000 to 4000 B.C., many drugs were in use. There are Sanskrit writings in existence which tell the methods of gathering and preparing drugs. The Assyrians, Babylonians and ancient Hebrews were all familiar with their use. Some of the Egyptian papyri, written as 1600 B.C., record the names of many of the medicinal plants used by the physicians of that day, among them myrrh, cannabis, opium, aloes, hemlock, and cassia. The Greeks were familiar with many of the presentday drugs, as evidenced by the works of Aristotle, Hippocrates, and Theophrastus. Even in their highly developed civilisation, however, the supernatural element was still uppermost. Only a few men were considered able,
because of some special power, to distinguish between valuable and harmful plants. These rhizotomoi, or root diggers, were an important caste in ancient Greece. The Romans were less interested in healing plants. However, in 77 B.C. Dioscorides wrote his great treatise, "De Materia Medica", which dealt with the nature and properties of all the medicinal substances known at that time. For fifteen centuries this work was held in high esteem, and even today it is valued by the Moors and Turks. Pliny and Galen also wrote about drug plants.

After the Dark Ages were over, there came the period of herbalists and encyclopedists, and the monasteries of Northern Europe produced vast compendiums of true and false information regarding plants, stressing in particular the medicinal value and folklore. It was about this time that the curious "Doctrine of signatures" came into being. According to this superstitious doctrine all plants possessed some sign, given by the creator, which indicated the use for which they were intended. Thus a plant with heart shaped leaves should be used for heart ailments, the liverleaf with its three-loved leaves for liver troubles and so on. Many of the common names of our plants of today owe their origin to this curious belief. Such names as heartsease, Solomon's seal, dogfoot violet, and liverwort carry on the old superstition.

From this crude beginning study of drug plants has progressed. The growing systematisation of the study of plants from the eighteenth century for contribution to human health allowed the dawn in the later period of a distinct branch of learning as
'pharmacognosy'. Outstanding advances in the nineteenth century influenced pharmacognosy and science and were generally discovery of alkaloids as active principles of some plant drugs, isolated by Verosne, Sertiinner, Pelletier and Caventon between 1803 and 1820. Since then, pharmacognosy has been continually pursued for utilitarian ends.  

A fascinating area of research, which has not proved unrewarding, is the examination of plants used for medicinal, narcotic and other purposes by primitive tribes. As a result of modern isolation and pharmacognostical procedures, new drugs usually find their way into medicine as purified substances rather than in the form of other galenical preparations.

The biologically active compounds can be studied from two different aspects - one, phytochemical, involving the studies of the nature and chemistry of the compound and two, pharmacological, involving the studies of the effects produced by the compounds in the biological system. A thorough and exhaustive review on various screening procedures has been published by Fransworth.

India has an inexhaustible plethora of natural wealth, especially of indigenous drugs. Indian flora is highly cosmopolitan in nature too. Out of the total 11,000 species of plants growing here, more than 2,000 are said to possess medicinal properties and still play a vital role in catering for drugs needs of the major portions of the population, in the form of extracts, decoctions, infusions, dry powders, etc., in Unani and Ayurvedic systems of medicine.
Leguminoseae, the second largest family of flowering plants, contains about 600 genera and 12,000 species and includes more important medicinal plants than any other family. It is divided into three sub-families, the Papilionaceae, the Mimosideae and the Caesalpiniodeae containing 377, 40 and 133 genera, respectively. The constituents of the Leguminoseae plants are cyanogenetic glycosides, saponins, tannins, mucilage, anthocyanins and alkaloids.

The amino acids and the alkaloids of the sub-family Papilionaceae may be grouped in a general way on the basis of broad biosynthetic derivation of the total group by one of several metabolic excursions from intermediary metabolism of basic amino acids such as lysine, ornithine, arginine and others. The first group of substances includes alkaloids of lupinine, nescic acid and arabasine type and the biogenic amines such as trigonelline and piperidine groups. The second group of alkaloids present are tetrahydroarabasine type alkaloids such as ammodendrine and odenocarpine in several genera of Leguminoseae.

Sub-family Papilionaceae is an extremely important family as from its members are obtained nutritious materials, valuable medicines and virulent poisons. The members exhibit varied properties of the substances they possess. Some are amylaceous, other oleaginous, many yield resins, balsams and dyes, not a few are astringent, acrid and bitter, narcotic and poisonous, emetic and purging tonic and restorative.
The seeds are often antiperiodic and roots anthelmintic. 6

Mucuna is an important genera of the sub-family Papilionaceae which occurs in tropical and temperate regions. It is composed of about 120 species. Some of the important ones are: *Mucuna pruriens* Baker, *M. cochinchinerensis* Cheval., *M. decqeingians* Meritt., *M. monosperma* DC, *M. atropurea*, *M. bractealae* DC, *M. capitata*, *M. gigantea* DC, *M. hirsuta*, *M. macrocarpa*., *M. nigricarb* Stend., *M. utilis*, etc.

Seeds of *M. monosperma* DC are used in cough, asthma and infection of tongue. The seeds of *M. capitata* are considered to be tonic. Bark of *M. gigantea* DC (elephant cowitch) is used externally for rheumatic complaints and powdered seeds are used as purgative in Hawaii.
**Mucuna pruriens** Baker

*(Fabaceae; Papilionaceae)*

- *M. prurita* Hook; *Stizolobium pruriens* (Linn.) Medic.

**English**: Cowhage, Cowitch plant

**Hindi**: Kawaanch, Kawach

**Ayurvedic description**:

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**Actions/Uses**: Urichya, bhrimhanee, balya, vaajeekara, vaatahara (root—yonisankochaka)
Mucuna pruriens Baker is a herbaceous twinning annual, found all over India and in Andaman and Nicobar Islands. Leaves trifoliate; leaflets broadly ovate, elliptic or rhomboid ovate, unequal at base; flowers axillary, pendulous, racemos, purple; pods curved, 5 to 10 cm x 1.5 to 1.8 cm longitudinally ribbed, turgid, densely clothed with persistent pale brown or grey, irritant bristles; seeds black, 4 to 6 in pods, ovoid (12 mm long) with funicular hilum. Pods are covered with stiff hair which produce an intense irritation of the skin if unconsciously handled.

The plant is found in bushes, hedges, damp places, ravines and shrub jungles throughout the plains of India. It is reported to be the best of sal plantations in Bengal. It is useful as green manure and cover crops. It is also grown for its pods and young leaves which are used as vegetable and fodder.7

Properties and Uses Ascribed in Traditional Medicine:

Seeds, roots and legumes are used due to the presence of contents of resin, tannin and fat and traces of manganese. Seeds are astringent, anthelmintic and aphrodisiac. It is also used in leucorrhoea, profuse menstruation and paralysis. Seeds are prescribed in the form of powder in dose of 20 to 40 grains in leucorrhoea. Spermatorrhoea, etc. They are also said to absorb scorpion poison when applied to the part stung.
The roots are said to be used as a remedy for delirium associated with fever and also used as a diuretic, purgative and emmenagogue. A strong infusion of roots with honey is given in cholera; used in dropsy in the form of paste applied all over the body; also said to be useful in elephantiasis.

Fruits are said to be anthelmintic, whereas the hair covering, the seeds and pods are said to be vermifuge; leaves are applied to ulcers (Nadkarni, 1954; Chopra et al., 1954). The plant is used by some tribals (Santals) in sores, madness, cancer, ringworm, syphilis, cough, pleuritis, pain, dog-bite, snake-bite, scorpion sting and bone fracture (Jain & Tarafder, 1970). 8

Pharmacognostical Studies:

The seeds of Mucuna pruriens Baker non V. are black in colour with pale brown specks, reniform in shape, 9 to 12 mm long with funicular hilum and cellular pit growth round the hilum. The seeds coat is hard, thick and glossy. The embryo completely fills the seed and is made up of two large fleshy cotyledons. Transverse section of seed shows an outer testa with a palisade epidermis made up of rod shaped macrosclereids with thickened anticlinal walls. The hypodermis comprises bone shaped osteosclereids broad at the top and base and narrow in the middle. The furrow region at the hilum shows a double epidermis of macrosclereids, hypodermis of osteosclereids and a cortical region made up of thin walled cells with a group of trachied abutting at the end of the
raphe. The cotyledons contain abundant starch grains (simple) which are oval in shape with faintly marked concentric rings (Ghosh, 1983). 9

The seeds of *Mucuna utilis* are often sold in the market as *M. pruriens*, locally known as Alkushi. Pharmacognostic characteristics of the seeds of both the plants have been compared. The seeds of *M. utilis* are much larger (15 to 20 mm) in size than *M. pruriens* seeds (9 to 12 mm), with dull black colour and faint brown specks. Anatomically, the cell arrangements are the same in both species, though the vessels and trachieds show spiral thickening in *M. pruriens*. The osteocleroids and starch grains with transverse cleft at one end are much larger in *M. utilis*. The alcohol soluble content (3.5%), ether soluble extractives (4.5%), moisture content (12.5%), and protein contents (27.8%) are higher in *M. utilis*, whilst the ash value (3.4%) and the water soluble extractive (14.0%) were less than *M. pruriens*. The microchemical study revealed a higher concentration of tannin, anthraquinone, resin, fat, oil and saponin in *M. utilis* than *M. pruriens* (Ghosh, 1982). 10

Chemical Studies:

*M. pruriens* seeds have been reported to be a good source of 3,4-dihydroxyphenylalanine (L-dopa). Damodaran and Ramaswamy (1937) 11, have reported the isolation of L-dopa from the seeds in a yield of 1.5 per cent, *M. utilis*, a
cultivated species of *Mucuna* contained much less (0.24%) content of L-dopa (Ghosh, 1982). Mucuna pruriens, in addition, contained a number of amino acids. Their composition in the seeds (Pant et al., 1974; Niranjan and Katiyar, 1979) and pods (Thatnagar & Tewari, 1971) has been reported as histidine (2.6%), lysine (1.7%), methionine (0.3%), phenylalanine (1.3%), tyrosine (0.63%), valanine (2.6%), threonine (2.4%), tryptophan (1.8%), and total amino acid (19.43%). Distribution of nitrogen in the seed proteins was found as water soluble albumin, globulin and non-protein nitrogen (70.5%), albumin (5.6%), globulin A (66.9%), non-protein nitrogen (6.9%), globulin B (16.3%), glutelin (2.8%), and prolamin (traces).

The alcoholic extract of *M. pruriens* seeds gave four alkaloids. viz., mucurine and mucuradine (Mehta and Majumdar, 1944; Santra & Majumdar, 1953); purienine and purieninine (Majumdar and Zalani, 1953). The 80 per cent alcoholic extract of seeds showed the presence of five indolic compounds, two of which were identified as tryptamine and 5-hydroxytryptamine (Pant & Joshi, 1970).

Different parts of *M. pruriens* except trichomes of pods yield four indole-3-alkylamines, viz., *N*,*N*-dimethyltryptamine along with two unidentified 5-oxy-indole-3-alkylamines and a B-carboline. Choline was reported in all parts of the plant. The trichomes of the pods gave only 5-hydroxytryptamine (Ghosal and Singh, 1970; Ghosal et al., 1971), whereas the stem leaf showed the presence
of 6-methoxyharman (Ghosal, 1972).\textsuperscript{18}

\textit{M. pruriens} seed oil was found to contain stearic, palmitic, myristic, arachidic, oleic, linoleic acid and a sterol (Mehta and Majumdar, 1944).\textsuperscript{12} The seed oil had HBr reacting acids as 1.3 per cent of total fatty acids (Ahmad et al., 1978).\textsuperscript{19} The epoxy acids identified were cis-12,13-epoxyoctadec-trans-enoic acid and cis-12,13-epoxyoctadec-cis-9-enoic (vernolic) acid (Hasan et al., 1980).\textsuperscript{20}

**Pharmacological Studies:**

The claim of Ayurvedic physicians that \textit{M. pruriens} (Kapikachchu) is effective in the treatment of parkinsonism, has prompted many pharmacologists and clinicians to investigate its effect on the central nervous systems.

The powdered seed extract of \textit{M. pruriens} was devoid of anticholinergic activity. The extract showed hypotensive action in dogs and spasmodic action in guinea pig preparation, the effect being blocked by mepyramine maleate and not by atropine sulphate.

The extract had no effect on frog rectus, but revealed a histaminergic activity. The observation suggested that the seed powder may act by some mechanism other than through anticholinergic property in parkinsonism (Ramawamy et al., 1979).\textsuperscript{21}

Various fractions obtained from \textit{M. pruriens} seeds were evaluated against oxotremorine-induced tremors in mice and reserpine-induced rigidity, hypokinesia and catatonia in rats.
The results indicated that extracts had no anticholinergic activity but had a potent antiparkinsonian effect which was not however, entirely due to L-dopa. The L-dopa free fraction of the seed showed significant antiparkinsonian activity at a dose of 200 mg/kg i.p. (Nath et al., 1981). 22

*M. pruriens* seed diet produced hypoglycemic effects in normal rats (Pant et al., 1968). However, such diet had insignificant effect in alloxan-treated rats (Joshi & Pant, 1970). In another study, the seed extract (50% ethanolic) did not show any hypoglycemic activity in rats (Dhawan et al., 1977; Sharma et al., 1978). The extract was also found to be devoid of diuretic, anti-inflammatory, antipyretic, anticoagulant, respiratory, CVS or CNS effects. The LD₅₀ of the extract was 100 mg/kg i.p. in albino rats (Sharma et al., 1978). 23

*M. pruriens* seed diet showed a hypocholesteremic effect in rats (Pant et al., 1968). 24 In another study, the protein isolate of the seeds in the diet led to a reduction in the cholesterol content of the liver and blood in rats (Singh et al., 1976). 25

The seed extract of *M. pruriens* showed antifungal activity against *Helminthosporum sativum* (Bhatnagar et al., 1961). 26 The aqueous and alcoholic extracts of pods showed anthelmintic activity against *Taenia caviae* obtained from the dog intestine and *Paramphistomum cervi* from
The rumen of sheep (Reogi et al., 1964). The acetone extract of the roots was toxic to the insect Euproctis lunata, being 1.9 times as toxic as the extract of Jatropha curcas seeds (Srivastava et al., 1983).

Since M. pruriens is known to produce itching which is attributed to the trichomes present on the pods, various extracts (aqueous, acetone and petroleum ether extracts) of the trichomes were investigated for their histamine release property. The extract produced a dose-dependent hypotensive effect attributed to cholinergic action. Respiratory changes produced in the rat were comparable with those produced by histamine. The aqueous extract produced a dose-dependent contraction of guinea pig ileum, which was partially blocked by chlorpheniramine suggesting the presence of histamine, although none of the extracts had any effect on rabbit jejunum. Though the extracts did not produce any degranulation of the mast cells or any respiratory changes in the guinea pig, a histaminergic action could not be ruled out (Mogre et al., 1981).

Indolic bases derived from M. pruriens showed antispasmodic action on smooth muscle preparations against spasms induced by acetylcholine, histamine, serotonin and oxytocin. Neuromuscular blocking activity of d-tubocurarine type was observed by 5-methoxy-N,N-dimethyltryptamine and an unidentified 5-oxy-indole-3-alkylamine, whereas the
unidentified β-carboline only potentiated the acetylcholine response on frog rectus abdominis. The alkaloids in small doses increased the carotid blood pressure in dogs, followed by tachyphylaxis, hypotensive response and again tachyphylaxis by subsequent doses. In anaesthetised dogs, 5-methoxy-N,N-dimethyltryptamine and the unidentified 5-oxy-indole-3-alkylamines caused severe respiratory depression, bronchospasm and acute hypotension leading to death in higher concentration. These compounds also produced hyperactivity in albino rats (Ghosal et al., 1971; Ghosal & Singh, 1970).

The total alkaloids of M. pruriens seeds showed weak neuromuscular blocking effects on frog rectus abdominis (Bhattacharya & Sanyal, 1969).

The total indole alkylamines isolated from various parts of Mucuna pruriens comprising N,N-dimethyltryptamine, its N-b oxide, bufotenine, 5-methoxy-N,N-dimethyltryptamine, and two chemically unidentified 5-oxy-indole-3-alkylamines produced marked behavioural changes including excitation, tremors, piloerection, etc. They antagonised phenobarbitone-induced hypnosis, inhibited reserpine-induced ptosis, showed hypothermia and sedation, reduced chlorpromazine-induced catatonia and increased the amphetamine toxicity in aggregated rats (Bhattacharya et al., 1971a).

Marked behavioural effects produced by N,N-dimethyltryptamine,
5-methoxy-\( N, N \)-dimethyltryptamine and bufotenine in mice and rats were almost completely antagonised by pretreatment of the animals with chlorpromazine (Ghosal, 1972).\(^{18}\)

Bufotenine showed both in vitro and in vivo anticholinesterase activity similar to but 20 to 30 times weaker than that of physostigmine (Bhattacharya and Sanyal, 1971).\(^{32}\)

A quaternary base (plicate, m.p. 242-44°C), isolated from 11 species of Leguminosae including \( M. \) pruriens (roots) has been reported to be pharmacologically identical to choline (Bhattacharya et al., 1971b).\(^{33}\)

The alcoholic extract (50%) of \( M. \) imbricata DC (Dhawan et al., 1977) and \( M. \) monosperma DC ex Wight (Dhawan et al., 1980)\(^{34}\) were found to have no antibacterial, antifungal, hypoglycemic, CNS, anticancer or diuretic actions. The extracts had no effect on the isolated guinea pig ileum. \( M. \) imbricata extract produced CNS-depressant effect in mice and was devoid of antiinflammatory effect. The \( LD_{50} \) of the extract was 1000 mg/kg i.p. in mice. \( M. \) monosperma extract showed abortifacient and antiimplantation effect in rats and hamsters, respectively. It had no antiviral effect. The \( LD_{50} \) of the extract was 250 mg/kg i.p. in mice.

**Clinical Studies:**
In 15 psychiatric patients, \( M. \) pruriens (15 g of crude seed powder) was found to significantly inhibit the
prolactin response to chlorpromazine injection, as effectively as 0.5 g of L-dopa. No side effects were observed in these patients (Vaidya et al., 1978a). The effect of M. pruriens seed powder was also studied in two women with functional hyperprolactinemia in a dose of 15 g t.d.s. for 24 weeks in one patient and 10 weeks in another. Therapeutic responses were assessed by monitoring serum prolactin, grade of galactorrhea, clinical parameters of ovulation and resumption of menstrual cycles. M. pruriens (containing 0.75 to 1 g L-dopa in 15 g) as well as L-dopa were found ineffective in inhibiting prolactin secretion, restoring ovarian function and treating galactorrhea, in contrast to bromoergocryptine which restored ovarian function and was effective in treating galactorrhea (Vaidya et al., 1978b).

M. pruriens is an ingredient of several commercial preparations claimed to have beneficial effects in the management of various sexual disorders. One such preparation is Tentex forte which has other constituents like musk, saffron, yohimbine hydrochloride, nux vomica pulvis, makardhwaj, shilajeet, Withania somnifera, Sida cordifolia, Bombax malabaricum, Argyreia speciosa and swarnamakshik Usma as well as Mustong which contains M. pruriens, Glycerhiza glabra, Withania somnifera, Tribulus terrestris, Myristica fragrans and Tinospora cordifolia.

Some uncontrolled clinical studies have claimed to have
found these compound preparations to be effective in improving libido and performance in man.

Several (unconfirmed) reports are available in the market, claiming the efficacy of a commercial herbo-mineral geriatric tonic (Geriforte, manuf, Himalaya Drugs, Bombay), as a restorative in improving physical, physiological and mental states as well as various subjective and objective accompaniments of general debility in normal and aged subjects; patients with enlarged prostate subjected to surgery as well as post-surgical convalescence. The same preparation has been claimed to have anti-stress effect and effective in neurological disorders including toxic neuropathy. The preparation has also been purported to be useful singly or as an adjunct in senile muscular degeneration, primary open-angle glaucoma, senile osteoporosis, degenerative arthritis and postoperative bed rest, early healing of fractures, diabetic neuropathy, menopause syndrome and hyperlipidemia, etc. This compound is claimed to have shown antiviral effect too against vaccinia virus, a beneficial effect in minimising the atheromatous changes due to hyperlipidemia.
Research Envisaged

Keeping in view the therapeutic activity concerning the role of *Mucuna pruriens* Baker seeds as aphrodisiac and in disorders of sex physiology such as azoospermia and oligozoospermia, for which it is prescribed in the indigenous system of medicine, it was proposed to carry out phytochemical and pharmacological investigations of the plant seeds in the following lines:

A. Phytochemical Studies:

These studies involved extraction, isolation and characterization of the pharmacologically active seed constituents, both alkaloidal and non-alkaloidal in character.

i. Extraction of alkaloids using petroleum ether, ethanol and chloroform in a Soxhlet extractor packed with the coarsely powdered seeds.

ii. Isolation of the alkaloids using column chromatography, and their separation and purification.

iii. Extraction of non-alkaloidal constituents from the seeds powder and its lipid fraction to obtain polar lipids.

B. Pharmacological Studies:

These studies involved their individual as well as collective (as the seed powder) role in male fertility. The parameters to be studied for an elaborative fertility assessment in male albino rats, were as follows:
i. Chromosomal Studies:

Study of effects of the seed powder, and its individual constituents, separately (upon determination of their \( \text{ALD}_{50} \) in rats), on the chromosomes of germinal cells to test occurrence of any mutagenicity, the absence of which would indicate safety of the test samples in the treated subjects.

ii. Studies on Castrated and Chemically Hypophysectomised Rats:

The two conditions for creating artificially induced subfertility to note effects with clarity for any change in fertility upon administration of the samples.

Castrated rats: Observation of weight changes in the reproductive organs of immature castrated rats to note if the samples elicited any androgenic response which reduce postcastrate degenerative changes in the reproductive organs.

Chemically Hypophysectomised rats:

Observation of fertility changes in adult male rats chemically hypophysectomised or 'functionally sterilised' by microdoses of estradol propionate and in adult male rats (untreated by estradol propionate) considering following parameters for fertility assessment:

1. Changes in weights of reproductive organs.
2. Histological examination of testes and epididymis.
3. Sperm count assessment through the examination of epididymal tissue squashes.
4. 'Sperm motility' assessment through the examination of tissue squashes.

5. Estimation of fructose content in the coagulating gland.


Overall assessment of fertility through collective study of these parameters to establish the role of *Mucuna pruriens* Baker seeds in male reproductive physiology and explore their potential as a pro-fertility drug.
REFERENCES: INTRODUCTION & LITERATURE SURVEY


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