2. REVIEW OF LITERATURE

2.1 Taxonomic position of *Murraya koenigii* Spreng.

Murraya koenigii Spreng belongs to family Rutaceae (citrus family). It is a small tree up to six meters in height and 15-40 centimeters in diameter. A number of genotypes were identified from different states of India (Kirthikar and Basu, 1935; Adesina, 1988: Verghese, 1989: Paul *et al.*, 2007).

2.1.1 Distribution

Murraya koenigii is distributed from south and East Asia to Australia (Reisch *et al.*, 1994). It grows wild and is found almost throughout India up to heights of 1500 to 1655 m. It abundantly occurs in outer Himalayas, Assam, Chittagong, upper and lower Burma, Andaman Islands, Maharatra, Andhra Pradesh and in the forests of Western Ghats in Karnataka *Murraya koenigii* is being cultivated in commercial scale in some districts of Andhra Pradesh, Karnataka and Tamilnadu. Its leaves are extensively used for culinary purpose. It's an important export commodity from India (Verghese, 1989, Ranade *et al*., 2006).

2.2 Vernacular name/s of *Murraya koenigii* Spreng in various languages

2.2.1 Indian languages

Botanical	-	*Murraya koenigii*
Synonyms	-	*Bergia koenigii, Chalcas koenigii*
Bengali	-	Barsunga
Gujarathi	-	Mitho Limdo
Hindi	-	Meetha neem, Kari patta, Kathnim, Bursunga
Kannada	-	Karibevu
Malayalam	-	Kariveppilei, Kareapela
Marathi	-	Karipat, Karhi patta, Karhinimb, Jhirang

Oriya	-	Bansago
Sanskrit	-	Girinimba, Suravi
Tamil	-	Karivempu, Karuveppilei, Karivepila
Telugu	-	Karepaku, Karuvepaku

2.2.2 Foreign languages

Burmese	-	Pindosine, Pyim daw thein
Danish	-	Karrry bald
Dutch	-	Kerriebladeren
English	-	Curry leaves
French	-	Feuilles de cari, Feuilles de cury, Caloupilé (Réunion), Carripoulé (Ile Maurice)
German	-	Curryblätter
Hungarian	-	Curry levelek
Icelandic	-	Karrilauf
Indonesian	-	Daun kari
Italian	-	Fogli de Cari
Laotian	-	Khi be
Malay	-	Daun kai pla, Karupillam
Norwegian	-	Kariblader
Singhalese	-	karapincha
Spanish	-	Hoja
Swahili	-	Bizari, Mchuzi
Tagalog	-	Bignay
Thai	-	Bai karee

2.3 Pharmacological properties

Murraya koenigii has been mentioned in the traditional medicinal system Ayurveda (Sathyavati *et al*., 1987). Bark, root, leaves, fruits and fruit pulp of *Murraya koenigii* are widely used in the treatment of diabetes, obesity, vomiting, constipation, indigestion, diarrhoea, dysentery, piles, nausea, to relieve kidney pain etc. A few

reports are available on the scientific probing to validate the pharmacological properties of *Murraya koenigii*. Some constituents of *Murraya koenigii* are reported to have anti fungal activity (Das *et al*., 1965). Anti-spasmodic and anti-amoebic activity reported by Bhakuni *et al*. (1969) and Kong *et al*. (1986). Ramsewak, *et al*. (1999) and Rahman and Gray, 2005 reported antimicrobial activity. Antitrichomonal activity was reported by Adebajo *et al*. (2006.) The apoptotic activity of mahanini, pyrayafoline-D and murrafoline-I, corbozole alkaloids from *Murraya koenigii* in human myeloid cancer cell line HL-60 have been reported (Roy *et al*., 2004; Ito *et al*., 2006). The positive ionotropic effect of *Murraya koenigii* extracts reported by Narayana and Sastry, (1975) and Shah and Juvekar, (2006).

Since ancient times, plants have been an exemplary source of drugs/medicines. Ayurveda and other Indian literature mention the use of plants in treatment of various ailments. India has about 45,000 plant species and among them, several thousands have been claimed to possess medicinal properties. Researches conducted in last few decades on plants mentioned in ancient literature or used traditionally for diabetes have shown experimental or clinical anti-diabetic activity.

2.3.1 Antidiabetic activity

Narayana and Sastry (1975) reported the hypoglycemic activity of *Murraya koenigii*. The aqueous extract of the leaves of *Murraya koenigii* after oral as well as intravenous administration to normal and alloxan diabetic dogs produced the hypoglycemia.

Santhakumari *et al*. (1987) reported the hypoglycemic activity of crushed leaves of *Murraya koenigii* in rabbits, human volunteers and alloxan induced diabetic rats. Iyer and Mani (1990) reported that curry leaves powder supplementation (12g

providing 2.5 g fibre) to 30 non-insulin dependent diabetes mellitus patients for a period of 1 month resulted in the transient reduction in fasting and post-prandial blood sugar levels.

Khan *et al.,* 1995 reported the hypoglycemic activity of *Murraya koenigii* and attributed to increased glycogenesis and decresed glycogenolysis and gluconeogenesis. Methanol extract of *Murraya koenigii* leaves are reported to produce hypoglycemia in human volunteers and alloxan induced rats and rabbits (Bhat, 1995: Rupashree, 1999)

Yadav *et al,* (2002) reported that feeding of diet containing various doses of curry leaf powder (5, 10 and 15%) to normal rats for 7 days as well as to mild and moderate diabetic rats for 5 weeks showed varying hypoglycemic and anti-hyperglycemic effect. Bawden *et al.,* (2002) reported the alpha amylase inhibitory activity of cold hexane extract of *Murraya koenigii.*

Yadav *et al.,* (2004) reported that the *Murraya koenigii* supplemented diet could reduce the development of insulin resistance and diabetes. Vinuthan *et al.,*(2005) reported antidiabetic activity of methanol extract of *Murraya koenigii.* Kesari *et al.,* (2005) reported the hypoglycemic effect of aqueous extract of *Murraya koenigii.* Recently Xie et al (2006) reported the hypoglycemic and hypolipidemic activity of *Murraya koenigii* in ob/ob mice. Arulselvan *et al.,* (2006) and Narendhirakannan *et al.,* (2006) reported the antidiabetic affect of ethanol extract of *Murraya koenigii* in STZ induced diabetic rats.

2.3.2 Hypolipidemic effect

Khan et al. (1996) reported that *Murraya koenigii* leaf powder and *Brassica juncea* seeds decreased the levels of cholesterol and phospholipids in the dimethyl hydrazine (DMH) induced colon carcinogenesis experimental animals. Bile acids and

neutral sterols in liver and feces, showed a sharp increase in the groups given *Murraya koenigii* leaf powder and *Brassica juncea* seeds when compared with the control.

Rats supplementation with the addition of 10% curry leaf or 10% mustard seeds, at a level of 10% body weight for a period of 90 days resulted in a reduction in total serum cholesterol and LDL + VLDL, an increase in the HDL, lower release of lipoproteins into the circulation and an increase in the LCAT (lecithin cholesterol acyl transferase) activity (Khan, 1996).

Murraya koenigii supplementation to atherogenic diet was found to decrease plasma triglyceride, plasma phospholipid in male albino rats (Khan *et al*., 1998). Xie et al (2006) reported the hypoglycemic and hypolipidemic activity of *Murraya koenigii* in ob/ob mice.

When the earlier work was reviewed, it was clear that the majority of the work pertains to the whole leaves or leaf powder of *Murraya koenigii*. Very few studies were conducted to find out the antidiabetic or antioxidant or hypolipidemic activity of different extracts of the *Murraya koenigii* leaves. The studies in this direction would aid in the discovery of bioactive compound present in *Murraya koenigii*.

2.3.3 Antioxidant activity

In rats fed with *Murraya koenigii* leaf powder and *Brassica juncea* seeds, there was a decrease in the concentration of malondialdehyde, while hydroperoxides and conjugated dienes were increased in liver and heart. There was increased activity of Superoxide dismutase and catalase in liver and heart of administered groups. Glutathione levels in liver, heart and kidney were lowered in rats administered these

spices. Glutathione reductase, glutathione peroxidase and glutathione S-transferase activity showed a sharp increase in the administered group (Khan 1996).

Addition of *Murraya koenigii* leaf powder in the high fat diet resulted in reduction of lipid peroxidation (thiobarbituric acid reactive substances) level to a beneficial extent. Histological studies also indicated the modulation of hepatic functions to near normal level (Khan et al., 1997).

Carbazole alkaloids isolated from *Murraya koenigii* are recognized as sources of natural antioxidants and thus play an important role in the chemoprevention of diseases resulting from lipid peroxidation (Nakathani, 2000).

Oral feeding of 15% of powdered leaves of *Murraya koenigii* and 10% powder of seeds of *Brassica juncea* for a period of 60 days to streptozotocin diabetic rats showed the nephro protective effect. There was improvement in Serum glucose levels, body weight, urine volume, serum creatinine, and urinary albumin (UAE) levels. *Murraya koenigii* can be best utilized by promoting as preferable food adjuvant for diabetic patients (Grover et al., 2003).

Baliga et al. (2003) reported the dose-dependent nitric oxide (NO) scavenging activity of aqueous leaf extract of *Murraya koenigii*. This study suggests that *Murraya koenigii* might be a potent and novel therapeutic agent for scavenging of NO and the regulation of pathological conditions caused by excessive generation of NO and its oxidation product, peroxynitrite.

It was suggested that an aryl hydroxyl substituent on the carbazole rings from *Murraya koenigii* plays a role in stabilizing the thermal oxidation and rate of reaction against DPPH radical (Tachibana, 2003). *Murraya koenigii* treatment exerts a therapeutic protective nature in diabetes by decreasing oxidative stress and pancreatic beta-cell damage (Arulselvan and Subramanian, 2007)

2.4 Phytochemistry of *Murraya koenigii*

The *Murraya koenigii* leaves possess 66.3% moisture; 6.1 % protein; 1.0% fat (ether extract); 16.0% carbohydrate; 64.0 % fibre; 4.2% mineral matter; 810.0 mg calcium; 600.0 mg phosphours; 3.1 mg Iron:12600 i.u. carotene (as vitamin A): 2.3 mg nicotinic acid and 4 mg/100 g vitamin C. The leaves are devoid of thiamine and riboflavin. The leaves are a fair sources of vitamin A, a rich source of calcium. Due to the presence of oxalic acid in high concentration (1.35% total oxalates; 1.15% soluble oxalates) the nutritional availability of calcium was affected. The free amino acids present in the leaves are aspargine, glycine, serine, aspartic acid, glutamic acid, threonine, alanine, proline, tyrosine, tryptophan, y – amino butyric acid, phenylalanine, leucine, isoleucine and traces of ornithine, lysine, arginine and histidine. The leaves also contain a crystalline glucoside, koenigin and a resin. The twigs and leaves contain 0.8% potash on dry mater basis (Radhakrishnan *et al*., 1955: Ananthasamy *et al*., 1996; Wang, 2003; Maheswari and Subramanian, 2003; Math and Balasubramaniam, 2005.).

From the root and stem bark of the curry leaf plant many carbzole alkaloids, viz., murrayanine, murrayastine, murrayacine and murrayazolinol have been isolated. On bacterial oxidation murrayanine gets converted to mukoeic acid (Bhattacharyya *et al.*, 1989). (Details presented in tabular form).

The essential oil (0.169%) obtained by steam-distillation of the leaves was analysed and sixty-two constituents were identified. The major constitutents were B-caryophyllene (7.3%) and terpinen-4-01 (6.1%). In a study oil of curry leaf was subjected to programmed screening which yielded 27 positively identified

components. The most important ones responsible for the intense characteristic aroma were, B-phellandrene, B-caryophyllene, B- gurjunene, B-elemene and b-thujene. An oleoresion was prepared from the leaves by using different solvent, that obtained by petroleum ether was found to be organoleptically the bets, yielding upto 6-15% from the mature leaves. Curry leaf extractives were also available in water/oil soluble and emulsified form (Kureel, 1970a; Gupta and Nigam, 1970; Kureel, 1970b; Verghese, 1989: Zhu and Ding, 1991).

The seeds contain a fatty oil. Total seed lipids extracted amounted to 4.4% of dry seed. This consisted of 85.4% netural lipids, 5.1% glycolipids and 9.5% phospholipids. The fatty acid compostion of the total lipids showed that oleic and lionielic acid were the predominant acids followed by palamitic acid (Hemavathy, 1991; Kureel, 1969; Adesina, 1988; Wassmuth, 1995; Chakrabarty, 1997; Adebajo and Reisch, 2000; Bringmann, 2001).

2.4.1 The methanol soluble phytochemical constituents of *Murraya koenigii* Spreng Leaf

Sl.No	Chemical Constituents	Quantity (per 100gm)	Activity
1.	Cadinene (Sesquiterpene)	5.2%	Hypoglycemic (Tommasi et al., 1991), Hypotriglyceridemic and fungitoxic (Rajendra and D'souza, 1998)
2.	Carotene	12600i.u.	Hypocholesterolemic and antioxidant (Fuhrman et al., 2000)
3.	β-cayophyllene	7.3%	Fungitoxic (Rajendra and D'souza, 1998)
4.	Dipentene	15.9%	Hypoglycemic (Tommasi et al., 1991) and Fungitoxic (Rajendra and D'souza, 1998)
5.	β-elemene	7.09%	Fungitoxic (Rajendra and D'souza, 1998)
6.	Fat	1%	Stored energy (Murray et al., 1996)
7.	β-gurjunene	NA	Fungitoxic (Rajendra and D'souza, 1998)
8.	Mahanimbime	NA	Antioxidant (Scavenges superoxide radicals) (Ramsewak et al., 1999)
9.	Mahanine	NA	Anti-inflammatory (Ramsewak et al., 1999)
10.	Murrayanol	NA	Anti-inflammatory (Ramsewak et al., 1999)
11.	Nicotinic Acid	2.3 mg	Enhances insulin secretion (Patole and Agte, 1998), decreases cholesterol, Triglyceride. LDL and VLDL (Satyanarayana, 1999)
12.	β-Phellandrene	6.5%	Fungitoxic (Rajendra and D'souza, 1998)
13.	Proline	NA	Glycogenic (West et al., 1967)
14.	Resin	NA	Slower glucose adsorption and reduces LDL-C (Anderson et al., 1991)
15.	Terpine	6.1%	Fungitoxic (Rajendra and D'souza, 1998)
16.	β-Thujene	NA	Fungitoxic (Rajendra and D'souza, 1998)

NA: *Information not available.*

2.4.2 The aqueous soluble phytochemical constituents of *Murraya koenigii* Spreng Leaf

Sl.No	Chemical Constituents	Quantity (per 100gm)	Activity
1.	Alanine	NA	Stimulate insulin secretion and glycogenic (Berne and Levy, 1988)
2.	Arginine	NA	Hypocholesterolemic, (Rajamohan and Kurup, 1997) and stimulate insulin secretion (Berne and Levy, 1988)
3.	Aspartic aid	NA	Glycogenic (West et al., 1967)
4.	Calcium	810mg	Stimulate insulin secretion and activates lipase (Satyanarayana, 1999)
5.	Carbohydrate	16.0%	Lowers cholesterol and stimulate insulin secretion (Murray et al., 1996)
6.	Glutamic acid	NA	Glycogenic (West et al., 1967)
7.	Glycine	NA	Glycogenic (West et al., 1967)
8.	Histidine	NA	Glycogenic (West et al., 1967)
9.	Iron	3.1%	Enhances insulin secretion (Patole and Agte, 1998) and Oxidative Phosphorylation (Satyanarayana, 1999)
10.	Isoleucine	NA	Glycogenic and Ketogenic (Satyanarayana, 1999)
11.	Leucine	NA	Stimulate insulin secretion and ketogenic (Berne and Levy, 1988)
12.	Lysine	NA	Hypercholesterolemic (Rajamohan and Kurup, 1997) and stimulate insulin secretion (Berne and Levy, 1988)
13.	Low Lysine: Arginine ratio	NA	Hypocholesterolemic (decreased HDL-C and LDL+VLDL fraction), hypotriglyceridemic (Rajamohan and Kurup, 1997)
14.	Nicotinic acid	2.3mg	Enhances insulin secretion (Patole and Agte, 1998), decreases cholesterol, triglyceride, LDL & VLDL (Satyanarayana, 1999)

NA: *Information not available.*

15.	Ornithine	NA	Glycogenic (West et al., 1967)
16.	Phenylalanine	NA	Glycogenic and Ketogenic (West et al., 1967)
17.	Phosphorous	600mg	Phospholipid formation (Satyanarayana, 1999)
18.	Proline	NA	Glycogenic (West et al., 1967)
19.	Protein	6.1%	Lowers cholesterol, triglyceride (Rajamohan and Kurup, 1997)
20.	Serine	NA	Glycogenic (West et al., 1967)
21.	Threonine	NA	Glycogenic (West et al., 1967)
22.	Tryptophan	NA	Hypocholesterolemic, hypotriglyceridemic and glycogenic (Rogers and Pesti, 1992)
23.	Tyrosine	NA	Glycogenic and ketogenic (West et al., 1967)
24.	Vitamin C	4mg	Antioxidant, enhances insulin and HDL-C, decreases cholesterol, triglyceride & LDL-C (Manjunatha et al., 2001)

2.4.3 The chemical constituents of *Murraya koenigii* spreng.

Sl. No.	Chemical constituents	Nature	Plant part (conc.)	Reference
1.	Cadinene (-)	Sesquiterpene	Essential oil (5.2%)	Nigam & Purohit, 1961
2.	Dipentene	Monoterpene	Essential oil (15.9%)	Nigam & Purohit, 1961
3.	Murrayanine	Carbazole alkaloid	Leaf	Chakraborty *et al.* 1965
4.	Cyclomahanimbine	Indole alkaloid	Leaf	Kureel *et al.* 1969
5.	Koenidine	Indole alkaloid	Leaf	Narasimhan *et al.* 1970
6.	Koenigine	Indole alkaloid	Leaf	Narasimhan *et al.* 1970
7.	Koenine	Indole alkaloid	Leaf	Narasimhan *et al.* 1970

8.	Mahanine	Indole alkaloid	Leaf	Narasimhan *et al.* 1970
9.	Murrayazoline	Carbozole alkaloid	Leaf	Chakraborty *et al.* 1973
10.	Koenimbine	Indole alkaloid	Leaf	Narasimhan *et al.* 1975
11.	Mahanimbine (+)	Indole alkaloid	Leaf	Narasimhan *et al.* 1975
12.	Isomahanimbine (+)	Indole alkaloid	Leaf	Narasimhan *et al.* 1975
13.	Mahanine (-)	Indole alkaloid	Leaf	Narasimhan *et al.* 1975
14.	Curryanigine	Indole alkaloid	Stembark	Narasimhan and Kelkar, 1976
15.	Curryanine	Indole alkaloid	Stembark	Narasimhan and Kelkar, 1976
16.	Mukonine	Carbazole alkaloid	Leaf	Roy *et al.*, 1982
17.	Mukolidine	Carbazole alkaloid	Leaf	Roy *et al.*, 1982
18.	Mukonol	Carbazole alkaloid	Leaf	Bhattacharyya & Chakraborty 1984
19.	2-methoxy-3-methyl carbazole	Carbazole alkaloid	Leaf	Bhattacharyya & Chowdhury s1985
20.	Murrayazolinol	Carbazole alkaloid	Leaf	Bhattacharyya *et al.*, 1989
21.	Bikoeniquinone	Indole alkaloid	Roots (0.001109%)	Ito *et al.*, 1993
22.	Formlycarbozole	Indole alkaloid	Roots (0.00072%)	Ito *et al.*, 1993
23.	Bis-3-hydroxy-3-methyl carbozole	Indole alkaloid	Roots (0.00136%)	Ito *et al.*, 1993
24.	Eustifoline-C	Indole alkaloid	Roots (0.0005%)	Ito *et al.*, 1993
25.	Girinimbine Girinimbine	Indole alkaloid Indole alkaloid	Roots (0.1622%) Stem (0.015%)	Ito *et al.*, 1993 Ito *et al.*, 1993

	Mahanimbine	Indole alkaloid	Root (0.0113%)	Ito *et al.*, 1993
26.	Mahanimbinol Mahanimbinol Mahanine Mahanine	Indole alkaloid Indole alkaloid Indole alkaloid Indole alkaloid	Roots (0.00863%) Stem (0.0425%) Roots (0.00113%) Stem (0.00116%)	Ito *et al.*, 1993 Ito *et al.*, 1993 Ito *et al.*, 1993 Ito *et al.*, 1993
27.	Bismahanine	Indole alkaloid	Stembrak (0.0208%)	Ito *et al.*, 1993
28.	Mukoenic acid	Indole alkaloid	Stembark (0.00081%)	Ito *et al.*, 1993
29.	Mukoenine A	Indole alkaloid	Stembark (0.0015%)	Bhattarcharyya *et al.* 1994
30.	1-hydroxy-3-methyl carbazole	Indole alkaloid	Stembark (0.0022%)	Bhattarcharyya *et al.* 1994
31.	2-methoxy-3-methyl	Indole alkaloid	Stembark (0.0022%)	Bhattarcharyya *et al.* 1994
32.	Heraclenin	Coumarin	Seed	Reisch *et al.* 1994b
33.	Heraclenin	Coumarin	Seed	Reisch *et al.* 1994b
34.	Imperatorin	Coumarin	Seed	Reisch *et al.* 1994b
35.	Girinimbilol	Indole alkaloid	Stembrak (0.15%)	Reisch *et al.* 1994a
36.	Mahanimbinol	Indole alkaloid	Stembark (0.29285%)	Reisch *et al.* 1994a

2.4.4 Compounds identified in the essential oil of *Murraya koenigii* leaves by GC- MS

Compound	Percentage
Terpenes	
Camphene	2.16
Dipentene	11.3
α-pinene	0.87
Sabinene	0.10
Sesquiterpense	
Aromadendrene	0.78
β-Bisabolene	2.3
cis-Caryophyllene	11.74
Dehydro aromadendrene	2.75
Trans-Caryophyllene	6.29
Iso Caryophyllene	6.72
β-Elemene	7.09
Junipene	4.90
Zingiberene	1.01
Alcohols	
β-Costol	0.9
α-Eduesmol	9.61
β-Eudesmol	2.61
Frnesol	1.56
Menthol	2.83
Spathulenol	0.88
Steary alcohol	1.01
α-Terpineol	1.04
Ketone	
Carvo menthone	2.3
Iso menthone	0.6

Aldehyde	
Citral	0.76
Stearaldehyde	1.53
Esters	
Butyl myristate	0.66
Linalyl acetate	0.93
Acids	
Palmitic acid	4.64
Stearicterrie acid	0.70