CHAPTER II

HISTORICAL

The Occurrence of Alkaloids in Cassia spp.

There are about 500-600 species of *Cassia*, at least 18 species were reported to contain alkaloid which most of them are unknown alkaloids(21). The occurrence of alkaloids in this genus are shown in Table 1.

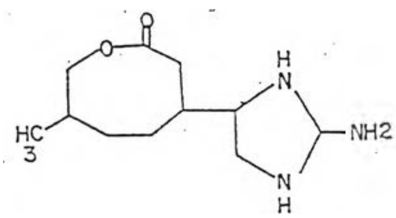
Table 1. The Occurrence of Alkaloids in Cassia spp.

Botanical Source	Alkaloid	Plant Part*	Ref.
Cassia absus Linn.	Chaksine	Sd	22,23
	Isochaksine	Sd	22
C. alata Linn.	Unknown	Lf	21
C. auriculata Linn	Pyrrolizidine alkaloids	Bk, Fl, Sd	24
C. bacillaris Linn.	Unknown	Lf, St	21
C. bicapsularis Lin	Unknown	Fr, Lf	21
C. brasiliensis Nierdl	Unknown	Fr, Lf	21
C. carnaval Speg.	Carnavaline	Lf	25
	Cassine	Lf	25
	Prosopinone	Lf	26
C. emarginata Linn.	Unknown	Lf	21
C. excelsa Shard.	Casselsine	Bk, Lf	27
	Cassilysine	Bk, Lf	28,29
	Cassilysidine	Bk	28,29

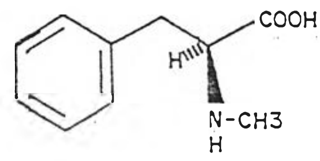
Botanical Source	Alkaloid	Plant Part*	Ref.
	Cassine	Lf, Tw	27
C. floribunda Cav. (*C. leavigata* Willd.)	N^1,N^8-dibenzoyl-spermidine	Fl	30
C. jahnii Britton.et Rose	Carnavaline	Lf	31
	Cassine	Lf	31
C. marylandica Linn	N-methyl-β-phenyl-alanine alkaloid	Lf	32
C. occidentalis Linn.	N-methyl morphine alkaloid	Sd	33
C. palellaria DC.	Unknown	Lf	21
C. siamea Lamk.	Cassiadinine	Fl	34
	Siamimine A	Lf	35
	Siamimine B	Lf	35
	Siamimine C	Lf	35
	Siamine	Lf , Sd	36,37
C. sophera Linn. (*C. torosa* Cav.)	Unknown	Lf	21
C. spectabilis DC.	Cassine	Lf, Sd,St	16,18
	Cassinicine	Lf, St	15
	Iso-6-carnavaline	Sd	17
	Iso-6-cassine	Lf	16,18
	Spectaline	Lf	16
	Spectalinine	Sd	17
	Unknown	Fl	21
C. tomentella Domin	Unknown	Fl	21

(* Bk = bark, Fl = flowers, Fr = fruit, Lf = leaf, Pd = Pods, Rt = roct, Sd = seed, St = Stem, Tw = twig).

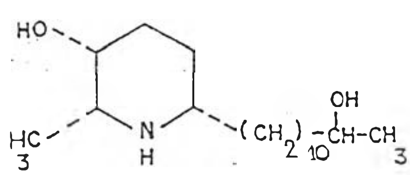
Figure 2 . Structures of Occurrent Alkaloids in *Cassia* spp.



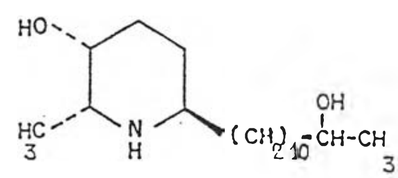
(1) Chaksine



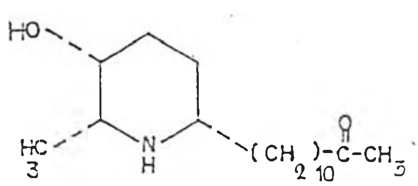
(2) N-Methyl-β-phenyl-alanine



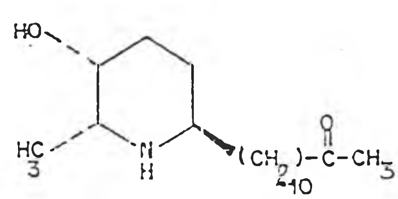
(3) Carnavaline



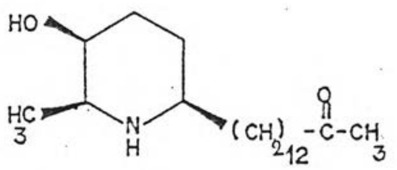
(4) Iso-6-carnavaline



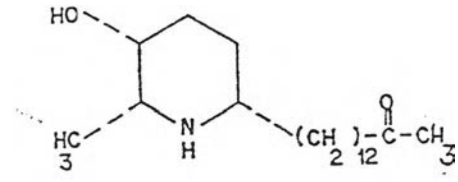
(5) Cassine



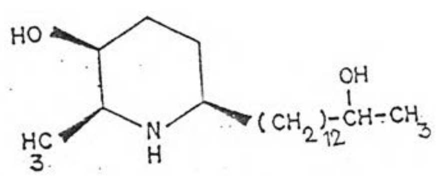
(6) Iso-6-Cassine



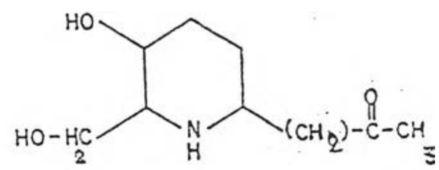
(7) Spectaline



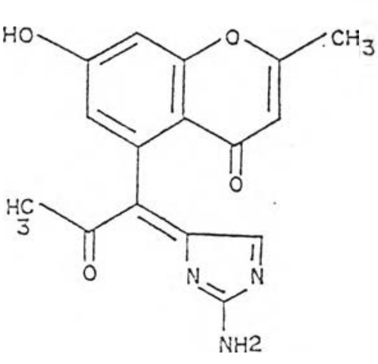
(8) Cassinicine



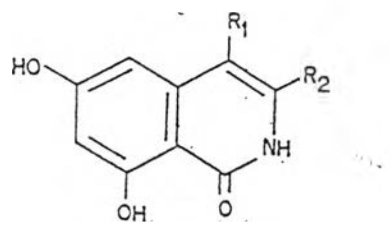
(9) Spectalinine



(10) Prosopinone



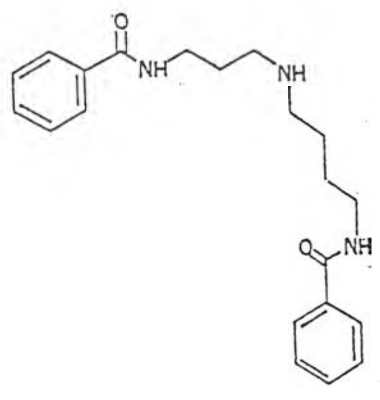
(11) Cassiadinine



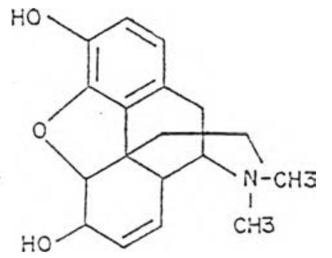
(12) Siamine, $R_1 = H$, $R_2 = CH_3$

(13) Siamimine A, $R_1 = R_2 = CH_3$

(14) Siamimine B, $R_1 = R_2 = H$



(15) N^1, N^8-Dibenzoyl Spermidine

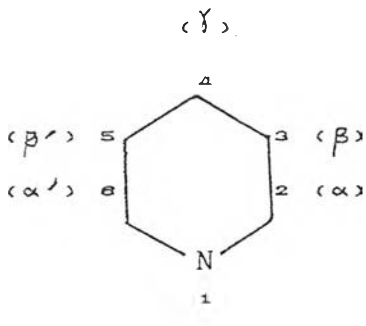


(17) N-Methyl-morphine

There have been various groups of alkaloid that presented in *Cassia* spp., cassine and related compounds can be classified into 2,6-disubstituted piperidin-3-ols groups (39), cassiadinine is a new chromone alkaloid from *Cassia siamea*(34) while siamine, siamimine A, B and C are owing to isoquinolone alkaloid group(35). Moreover there have been reported of spermidine alkaloid, pyrrolizidine alkaloid, pseudo-alkaloid such as N-methyl-β-phenylalanine and N-methyl-morphine alkaloid containing in this genus.

<u>Piperidine Alkaloids</u>

Piperidine alkaloids are nitrogenous natural products which have piperidine ring (<u>18</u>) as the distinguishing skeletal features.



(<u>18</u>) piperidine ring

The numbering in the piperidine system is same as that in pyridine type(38). The chemistry of piperidine is primary due to a secondary amine, whilst the basicity is dependent on the availability of the lone pair of electrons on nitrogen. Since the six-membered ring in piperidine is saturated, it exist all the possibilities of optical and geometrical isomers that are found in the cyclohexane series. The piperidine ring is not completely symmetrical, thus the position of the groups on the ring is also important in determining the number of such isomers (38).

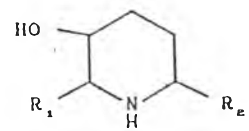
Classification of Piperidine Alkaloids

According to George M. Strunz and John A. Findlay (39), piperidine alkaloids can be classified limiting the class to alkaloids containing a piperidine type nitrogen heterocyclic that is not fused to a carbocyclic system. The conjugated piperidine amide alkaloids from *Piper* spp., the piperidine metacyclophane alkaloids from Lythraceae, the Nuphar alkaloids, the Solanum steroid alkaloids, and the sesquiterpene nicotinic acid ester from Celastraceae could be omitted here.

Therefore piperidine alkaloids can be classified into 10 groups :

1. 2,6-Disubstituted Piperidin-3-ols.

A series of piperdin-3-ols (19), most bearing C_1 and n-C_2 side chains at position 2 and 6 respectively, have been isolated from *Cassia* and *Prosopis* species, tropical Leguminosae. These alkaloids differ in the stereochemistry and oxygenation patterns of their side chain(39) (Table 2 , page 12).

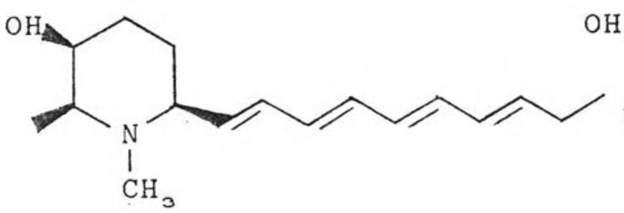


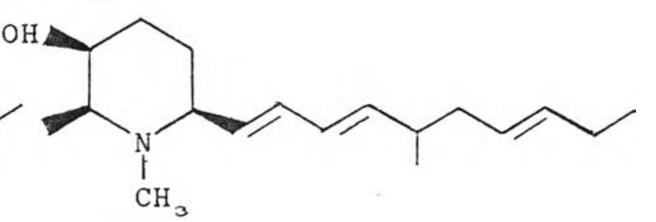
(<u>19</u>) piperidin-3-ols

Table 2. 2,6-Disubstituted Piperidin-3-ols from *Cassia* and *Prosopis* spp.

Source	Name	C-3-OH configuration	C-2 substituent	C-6 substituent
Cassia excelsa	Cassine	α	α-CH_3	α-$(CH_2)_{10}COCH_3$
C. spectabilis	Iso-6-cassine	α	α-CH_3	β-$(CH_2)_{10}COCH_3$
Prosopis spp.	N-Methylcassine	α	α-CH_3	α-$(CH_2)_{10}COCH_3$
C. carnaval	Carnavaline	α	α-CH_3	α-$(CH_2)_{10}CHOHCH_3$
C. spectabilis	Iso-6-carnavaline	α	α-CH_3	β-$(CH_2)_{10}CHOHCH_3$
Prosopis africana	Prosopine	β	α-CH_2OH	β-$(CH_2)_{10}CHOHCH_3$
P. africana	Prosopinine	β	α-CH_2OH	β-$(CH_2)_9COCH_2CH_3$
P. africana	Isoprosopinine A	β	α-CH_2OH	β-$(CH_2)_6CO(CH_2)_4CH_3$
P. africana	Isoprosopinine B	β	α-CH_2OH	β-$(CH_2)_7CO(CH_2)_3CH_3$
P. africana	(<u>+</u>)-Prosophylline	β	α-CH_2OH	α-$(CH_2)_9COCH_2CH_3$
P. africana	Prosafrine	α	α-CH_3	α-$(CH_2)_9CHOHCH_2CH_3$
P. africana	Prosafrinine	α	α-CH_3	α-$(CH_2)_9COCH_2CH_3$
C. carnaval	Prosopinone	?	CH_2OH	$(CH_2)_{10}COCH_3$
P. juliflora	Julifloridine	?	CH_3	$(CH_2)_{11}CH_2OH$
P. spicigera	Spicigerine	α	α-CH_3	α-$(CH_2)_{11}COOH$
C. spectabilis	Spectaline	β	β-CH_3	β-$(CH_2)_{12}COCH_3$
C. spectabilis	Spectalinine	β	β-CH_3	β-$(CH_2)_{12}CHOHCH_3$
C. carnaval	Alkaloid D	?	CH_3	$(CH_2)_3CHOH(CH_2)_{10}CHOHCH_3$

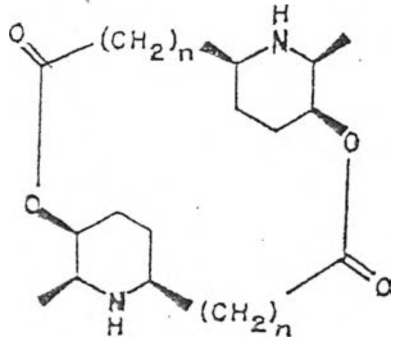
Cryptophorine(20) and cryptophorinine(21) were isolated from foliages of *Bathiorhamnus cryptophorus* (H. Perrier) R. Capuron (Rhamnaceae)(40).





(20) Cryptophorine (21) Cryptophorinine

Azimine (22) and carpaine (23) are macrocyclic dimeric bislactones elaborated, respectively, by *Azima tetracantha* L. and *Carica papaya* L.(41).



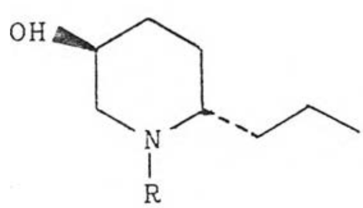
(22) n = 5 Azimine

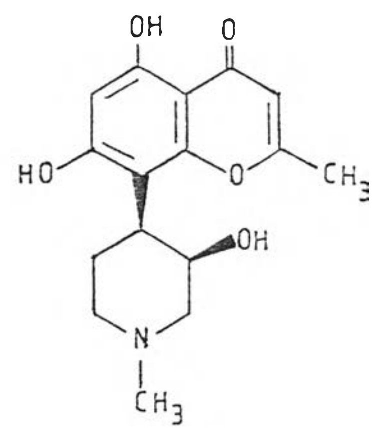
(23) n = 7 Carpaine

2. Other Piperidin-3-ols.

Pseudoconhydrine(24) one of the minor alkaloidal constituents of poison hemlock *Conium maculatum* L. (Umbelliferae)(42).

N-Methyl-pseudoconhydrine(25), a new natural product has been isolated as a major alkaloid from *C. maculatum* L. growing at high altitude in South Africa (43). The major alkaloid from the foliage and stem of *Amoora rohituka* (Meliaceae) is rohitukine (26)(44).

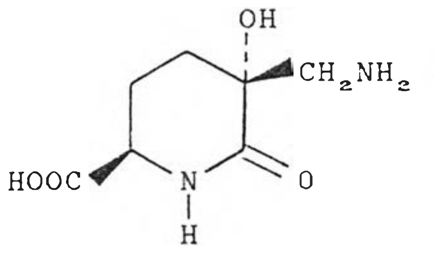




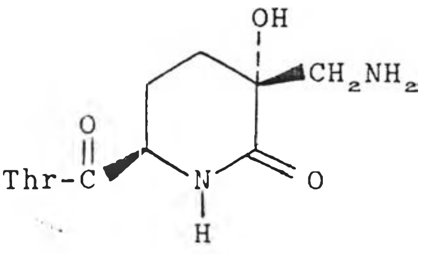
(24) R=H Pseudoconhydrine

(25) R=CH_3 N-Methyl-pseudo-conhydrine (26) Rohitukine

Tabtoxin-δ-lactam (27) is a piperidonamino acid produced by various *Pseudomonas* species, and is also a product of hydrolysis of tabtoxin. Tabtoxin readily undergoes isomerization to the more stable nontoxic δ-lactam isotabtoxin (28)(39).



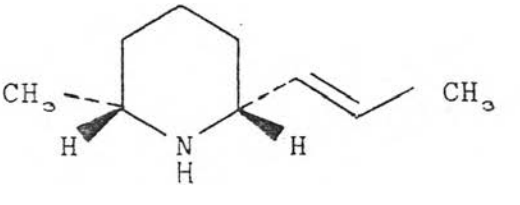
(27) Tabtoxin-δ-lactam



(28) δ-Lactam isotabtoxin

3. Pinus Alkaloids

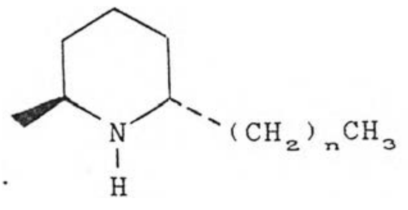
Alkaloids are not major metabolites of Pinus species; indeed, reports of their isolation from this genus have been rare. A base that has been obtained from various species of Pinus is (-)-pinidine (29)(45).

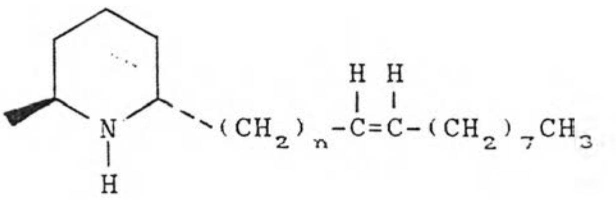


(29) Pinidine

4. Other 2,6-Disubstituted Piperidines.

The red form of the fire ant, *Solenopsis saevissima*, owes its trivial name to the potency of its venom , which exhibits hemolytic, insecticidal, and antibiotic activity. The venom was found to be composed of five constituent, designated solenopsin (30 - 34), and seem to be the only known non proteinaceous venom delivered by bite or sting (46).

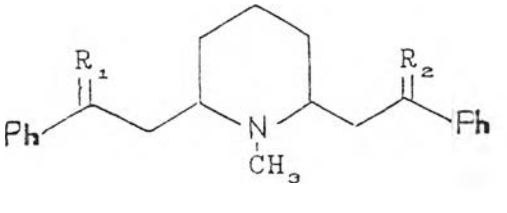




(<u>30</u>) Solenopsin A, n = 10 (<u>33</u>) Dehydrosolenopsin B, n = 3
(<u>31</u>) Solenopsin B, n = 12 (<u>34</u>) Dehydrosolenopsin C, n = 5
(<u>32</u>) Solenopsin C, n = 14

Another report was found that solenopsin derivatives were included side chains which n = 6, 8, and n = 7 of dehydrosolenopsin (47).

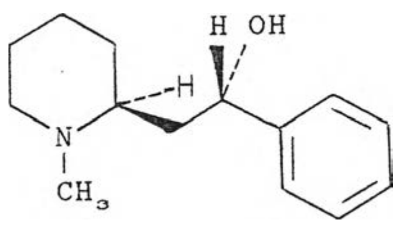
Alkaloids from both *Lobelia* and *Sedum* species might also be included in this section under the heading 2,6-disubstituted piperidines. Isolation of lobeline (<u>35</u>) from four Apalachian lobelias and indian lobelia has been reported(48). Lobelanine (<u>36</u>) and Lobelanidine (<u>37</u>) were also detected in the North American species (49).



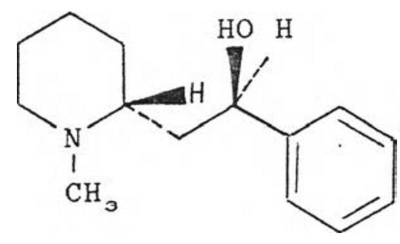
(<u>35</u>)	R_1 = H, OH, R_2 = O	Lobeline
(<u>36</u>)	R_1 = R_2 = O	Lobelanine
(<u>37</u>)	R_1 = R_2 = H, OH	Lobelanidine

5. <u>Sedum Alkaloids</u>.

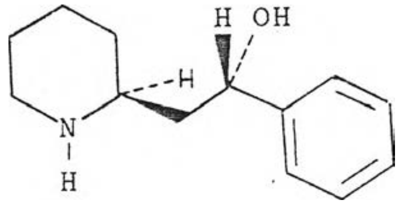
The presently known of Sedum alkaloids are shown below (50).



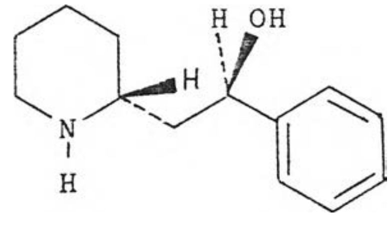
(<u>38</u>) Sedamine



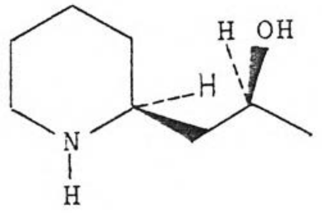
(<u>39</u>) Allosedamine



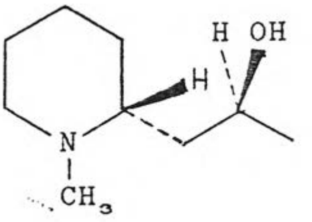
(<u>40</u>) Norsedamine



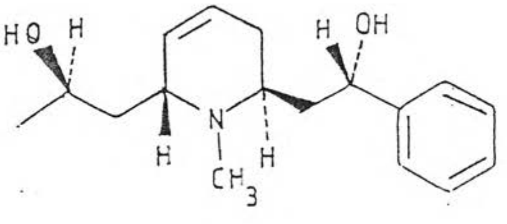
(<u>41</u>) Norallosedamine



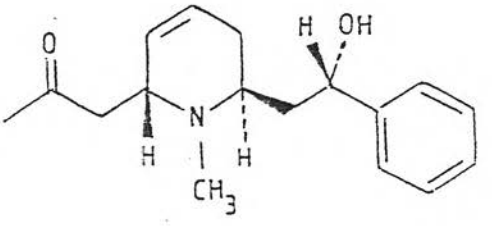
(42) Sedridine



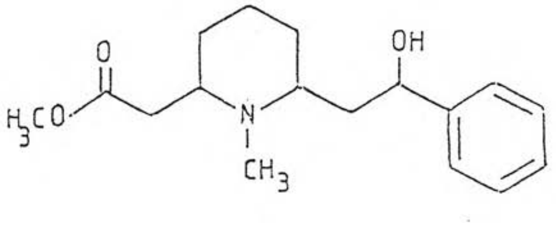
(43) N-Methylallosedridine



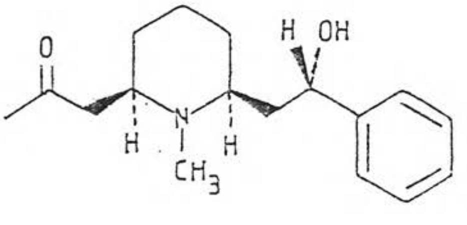
(44) Sedinine



(45) Sedracrine



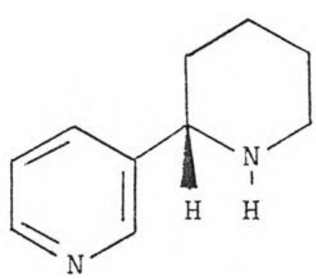
(46) Sederine



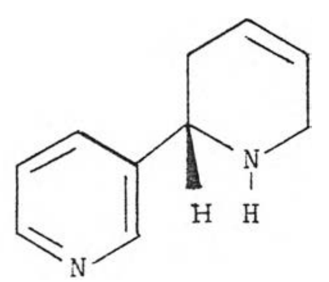
(47) Sedinone

6. Tobacco Alkaloids.

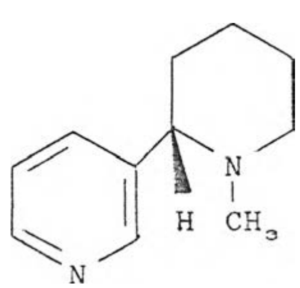
Tobacco continues to be a popular drug, although its use has abused somewhat in recent year as a consequence of the demonstrated adverse effects of smoking on health, Tobacco, which anabasine (48); first isolated from *Anabasis aphylla* is the major alkaloid of *Nicotiana glauca*, and a minor constituent of *N. tabacum*. (-)-Anatabine(49), a minor co-metabolite in several *Nicotiana* species, is Δ^4-dehydroanabasine. Anabasamine (51) was isolated from *Anabasis aphylla*.



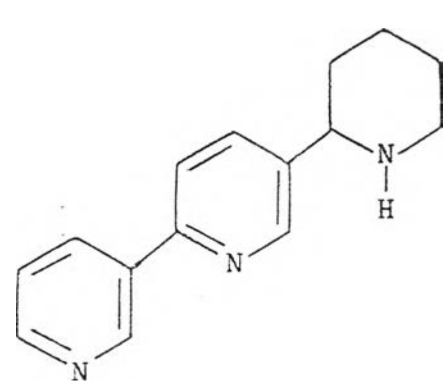
(48) Anabasine



(49) (-)-Anatabine

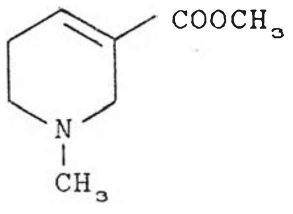


(50) 1-Methylanabasine

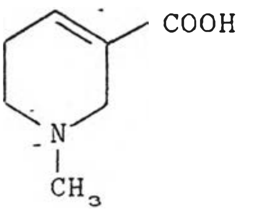


(51) Anabasamine

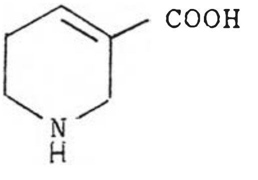
Arecoline (52) is a constituent of the fruit of the palm *Areca catechu* L.(Palmae), along with arecaidine (53), guvacine (54) and other compounds. The pronounced cholinergic activity of arecoline is responsible for some of effect associated with chewing of betel nut. Anthelmintic activity of arecoline has been reported (51).



(52) Arecoline

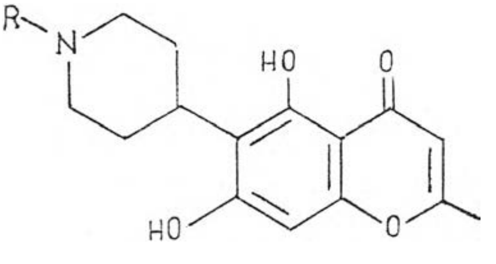


(53) Arecaidine



(54) Guvacine

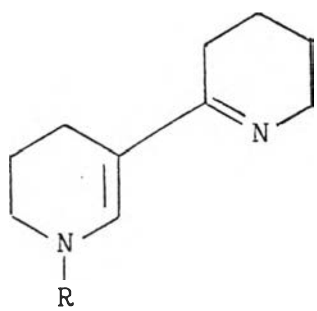
The new piperidine alkaloids from root bark of *Schumanniophyton problematicum* (Rubiaceae) are structure (55) and (56) (52).

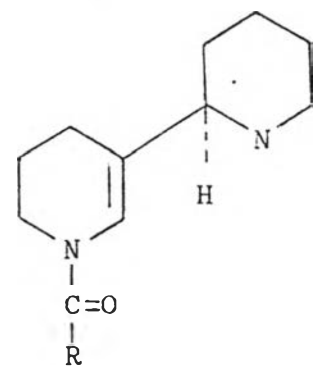


(55) R = H

(56) R = CH_3

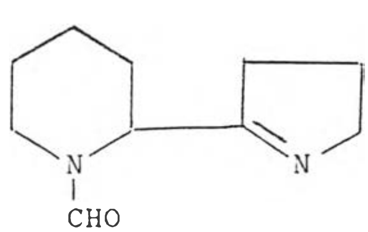
The major alkaloids found in extracts of *Lupinus formosus* Greene were hirtrine (57) and (+)-ammodendrine (58), N-acetylhirtrine (59) and (+)-N'-methylammodendrine (60)(39).





(57) R = H	Hirtrine	(58) R = H	(+)-Ammodendrine
(59) R = $COCH_3$	N-Acetyl hirtine	(60) R = CH_3	(+)-N-Methylammo-dendrine

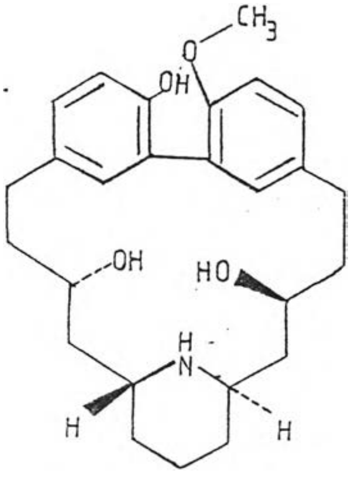
Smipine(61) is a novel alkaloid which has N-formyl group and a five-membered nitrogen heterocycle containing one degree of unsaturation (53).



(61) Smipine

7. Piperidine Metacyclophane Alkaloids.

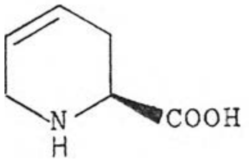
The piperidine metacyclophane alkaloids are subgroup of the Lythraceae alkaloids, lythranidine(62) is a representative of this class (54).



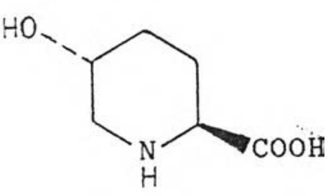
(62) Lythranidine

8. Pipecolic Acid Derivatives.

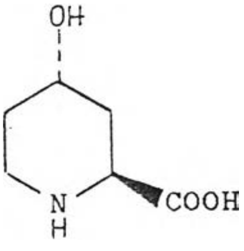
Pipecolic acid (63) is a piperidine alkaloid that has been found from various sources. The hydroxypipecolic acid (64 - 68) have been noted in various species of Brachystegioidae. An N-methyl-4-hydroxypipecolic acid isolate from *Millelia ovalifolia* seed, has been assigned structure (69). *trans*-4- Acetylamino -L- pipecolic acid (70) has been isolated from the leaves of *Calliandra haematocephala*, an N-methyl-4,5- dihydroxypipecolic acid (71)has been obtained from the indian tree *Pongamia glabra* and the N-methylpipecolic acid betaine homarine (72) has been isolated from marine sources.



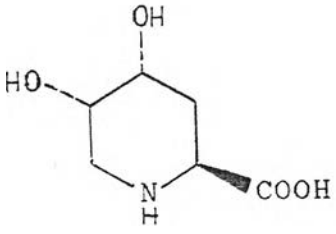
(63)



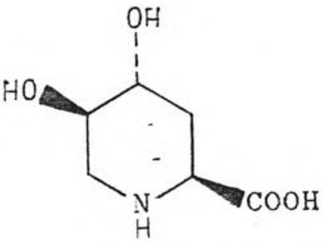
(64)



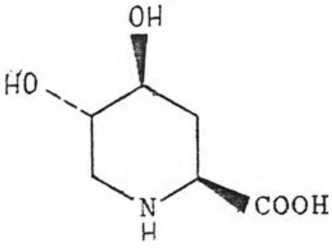
(65)



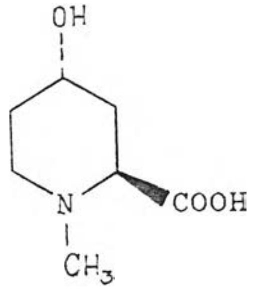
(66)



(67)



(68)



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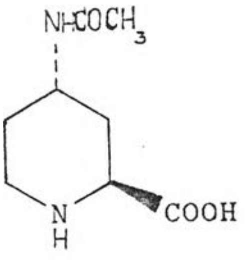
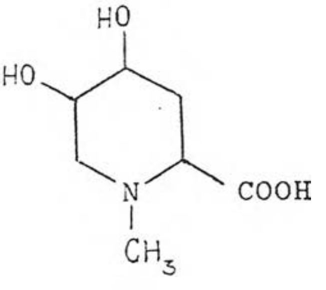
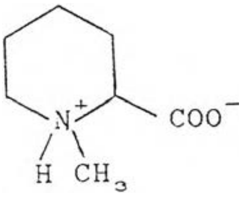


(70)



(71)

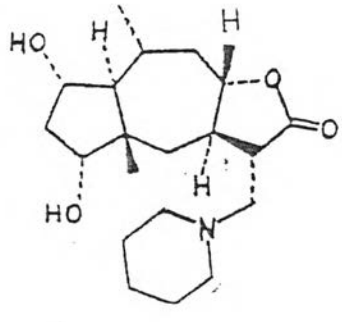


(72) Homarine

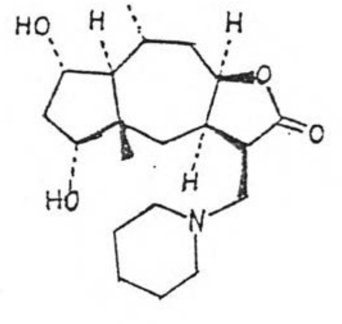
9. Terpenoid Alkaloids.

Gaillardia pulchella is the source of some novel sesquiterpenoid alkaloids possessing antiinflammatory activity. Following extensive chemical and spectroscopic studies Yanagita, *et. al* have established structures of pulchellidine (73) and neopulchellidine (74) (58,59).

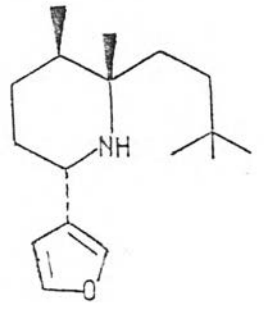
Nuphar alkaloids are included several substituted piperidines such as nupharamine (75), 3-epinupharamine, anhydronupharamine(76), nuphamine(77) and 3-epinuphamine (78)(60).



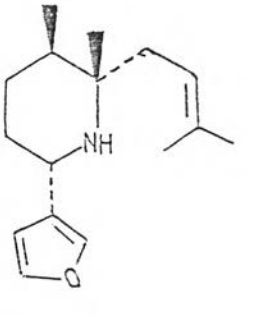
(73) Pulchellidine



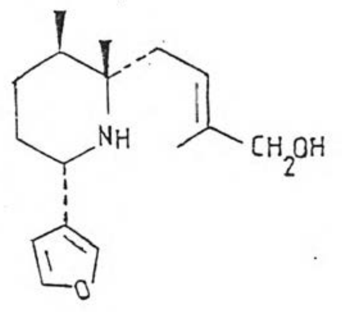
(74) Neopulchellidine



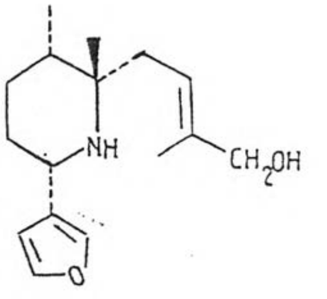
(75) Nupharamine



(76) 3-Epinupharamine, anhydronupharamine



(77) Nuphamine

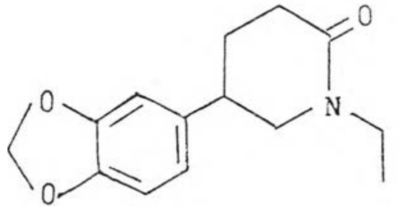


(78) 3-Epinuphamine

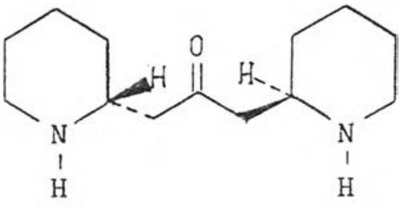
10. Miscellaneous

10.1 Piperidine from Higher Plants

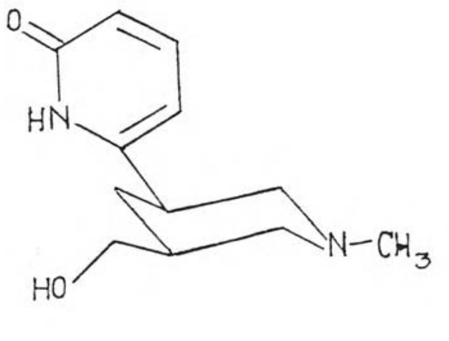
Structures of piperidine alkaloids in this groups are campedine (79) from *Campanula medium* (61), anaferine(80) from *Withania somnifera*(62), and kuraramine (81) along with isokuraramine(82) from *Sophora flavescens* (63).



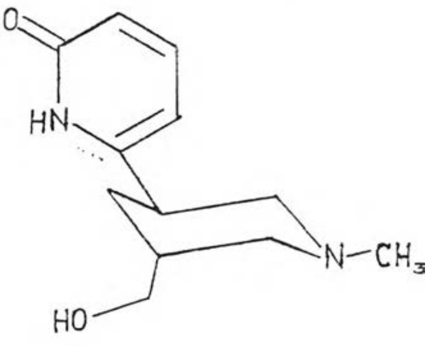
(79) Campedine



(80) Anaferine

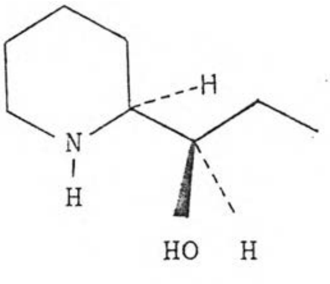


(81) Kuraramine

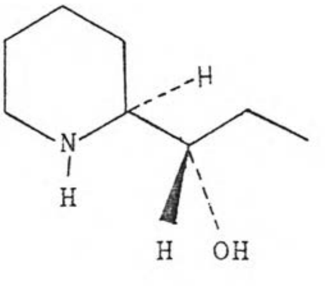


(82) Isokuraramine

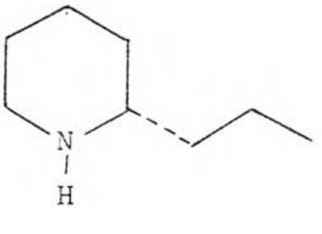
Conhydrine (83, 84), coniine (85) and γ-coniceine (86) are isolated from *Conium maculatum*, poison hemlock (64,65). Coniine and γ-coniceine are extremely toxic and induce paralysis of the motor nerve ending; after acceleration, respiration is slowed , and death results due to paralysis of the respiratory system (64).



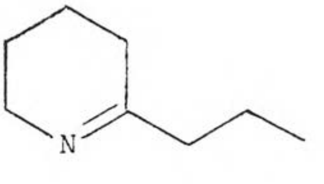
(83) (+)-α-Conhydrine



(84) (+)-β-Conhydrine

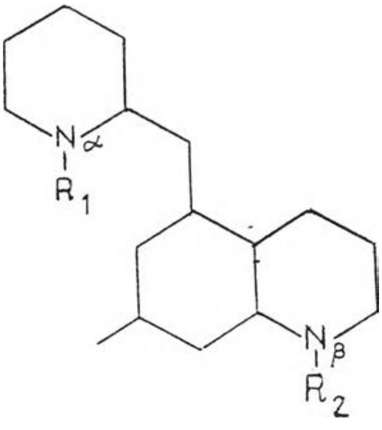


(85) (+) Coniine



(86) γ-Coniceine

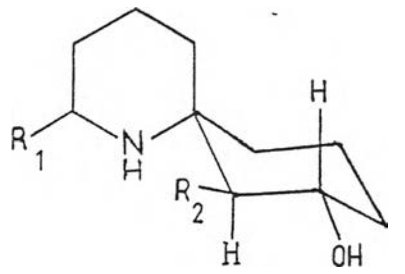
Four novel alkaloids from *Lycopodium* species, phlegmarine(87) and N_β-methylphlegmarine(88) were obtained from *L.phlegmaria* while N_α-methylphlegmarine (89) was isolated from *L.cernuum* and N_α-acetyl-N_β-methylphlegmarine (90) from *L.clavatum* (66).



(87)	$R_1 = R_2$ = H	Phlegmarine
(88)	R_1 = H, R_2 = CH_3	N_β-Methylphlegmarine
(89)	R_1 = CH_3 , R_2 = H	N_α-Methylphlegmarine
(90)	R_1 = $COCH_3$, R_2 = CH_3	N_α-Acetyl-N_β-methyl-phlegmarine

10.2 Piperidine Alkaloids from Animals

The spiropiperidine, histrionicotoxin (91) and dihydrohistrionicotoxin (92) were isolated from the skin of the poisonous Colombian frog *Dendrobates histrinicus*. In addition, a number of new related minor base (93, 94) have been found in the same source and it has been learned that the nature of side chain is an important factor for cholinolytic activity and sodium-potassium ion membrane phenomena (67).



(91) R_1 = CH_2 CH$\overset{cis}{=}$CH C≡CH R_2 = CH$\overset{cis}{=}$CH C≡CH

(92) R_1 = CH_2 CH_2CH=C=CH_2 R_2 = CH$\overset{cis}{=}$CH C≡CH

(93) R_1 = CH_2 $CH_2CH_2CH_2CH_3$ R_2 = $CH_2CH_2CH_2CH_3$

(94) R_1 = $CH_2CH_2CH_2$CH$\overset{cis}{=}$$CH_2$ R_2 = CH_2CH_2CH$\overset{cis}{=}$$CH_2$

Recently it has been reported the isolation of 2,6-dipentylpiperidine from this source (68).

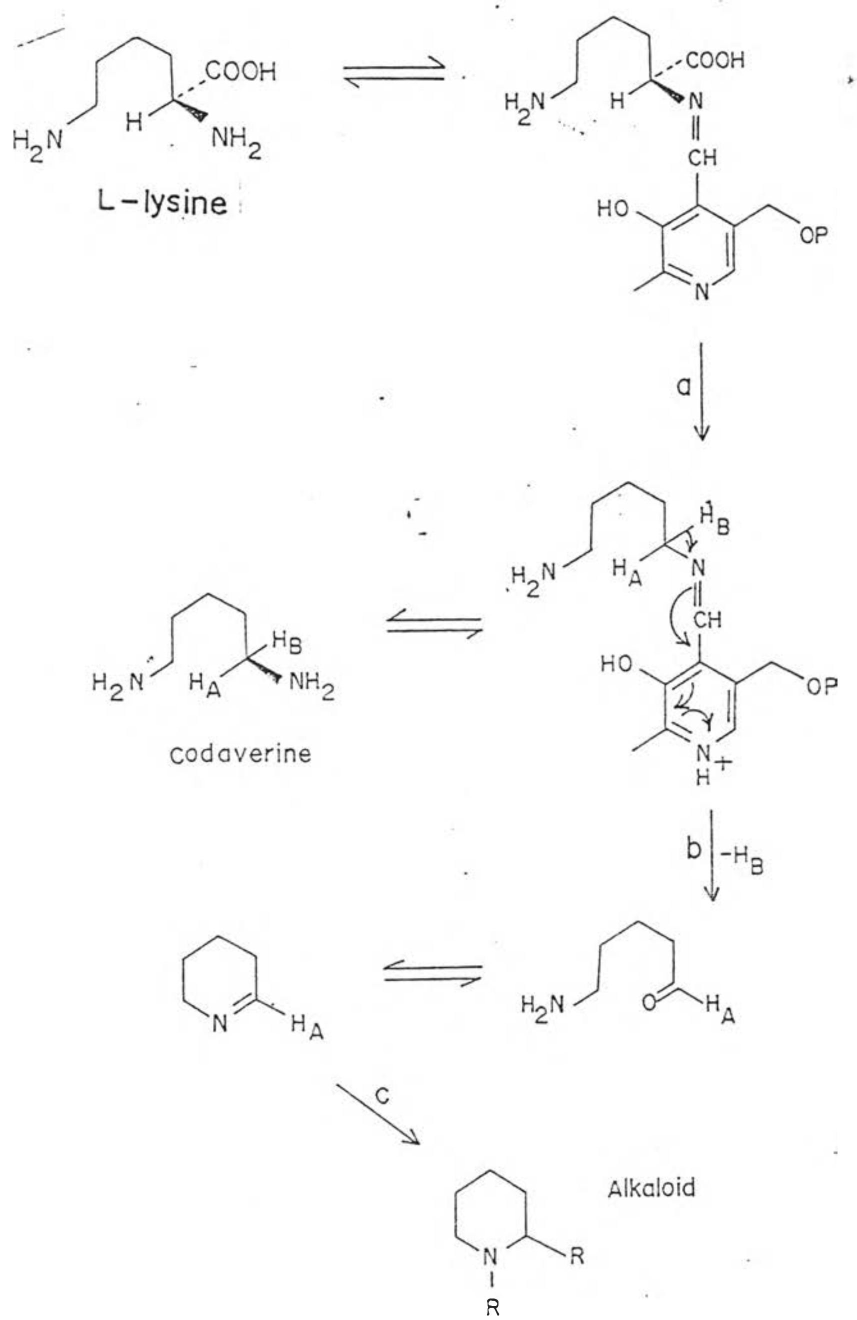
Biosynthesis of Piperidine Alkaloid

Piperidine alkaloids have more than one biosynthetic routes. The piperidine ring arises by at least two biosythetic routes. One is derived from amino acid lysine, the other from polyacetate (64).

1. Biosynthesis from Lysine

The amino-acid Lysine serves as the precursor of piperidine ring, *via* Δ^1-piperideine or 1,2-dehydro piperidine as a key intermediate, in the biosythesis of a large number of piperidine alkaloids (69). Piperidine alkaloids which have biosynthesis from lysine are included Nicotiana alkaloids; such as anabasine , Sedum and Lobelia alkaloids , Lythraceae alkaloids , and pipecolic acid together with its derivatives (69-73).

A general scheme of the biosynthesis of piperidine alkaloids from Lysine is show in scheme 1 (70).



Scheme 1. The Biosynthesis of piperidine alkaloids from Lysine

(a) L-Lysine decarboxylase (sterospecific decarboxylation)

(b) Diamine oxidase (specific oxidative deamination)

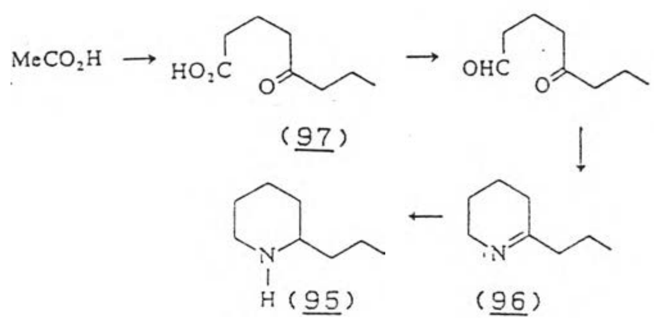
(c) Stereospecific entry of side chain at C-2:benzoyl acetic acid (re-face)→sedamine, acetoacetic acid(si-face)→ pelletierine, dihydronicotinic acid(re-face)→anabasine

2. Biosynthesis from Polyacetate

There are several piperidine alkaloids which structurally quite similar to lysine-derived, that have different biosynthetic routes from polyacetate.

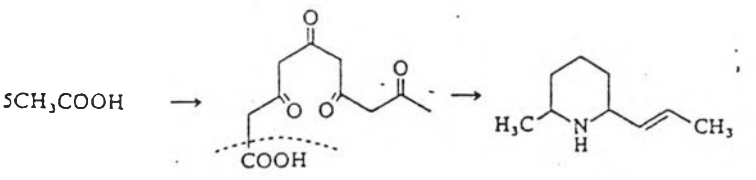
Piperidine alkaloids in this group are included Pinus alkaloids; such as pinidine, Hemlock alkaloids; such as coniine, nigrafactine from several *Streptomyces* straine, carpaine, cassine and related compounds,and fire ant venom (64).

Coniine(95) and related compound; such as γ-coniceine (96) were found that all carbon atoms derived from acetate, and Lysine are not their precursor(74). Octanoic acid (97) is also a specific precursor by incorporation experiments (75) with 5 - keto - [6-^{14}C] octanoic acid and the corresponding [6-^{14}C] aldehyde (scheme 2).



Scheme 2. Biosynthesis of Coniine

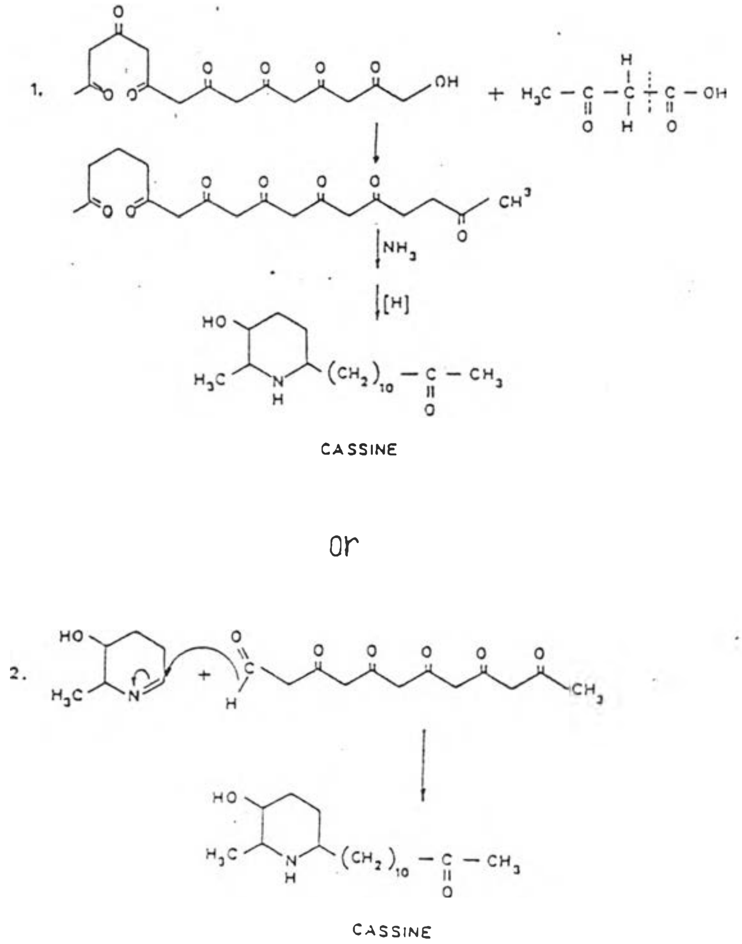
Pinidine(98), the biosynthetic pathway similar to the hemlock alkaloid coniine, is derived from a linear combination of five acetate units (scheme 3) (75).



(98)

Scheme 3. Biosynthesis of Pinidine

N.B. Mulchandani and S.A. Hassarajani (15) postulated biogenesis of cassine, cassinicine and anthraquinones could be derived from acetate unit only. (scheme 4) (15).



Scheme 4. Biogenesis of Cassine

Synthesis of Piperidine Alkaloids.

A large number of piperidine alkaloids were reported to be synthesized for example cassine (76), carpaine (77), pinidine (78), pseudoconhydrine (79), solenopsin A (80), anhydronupharamine (81), histrionicotoxin(82), perhydrohistrinicotoxin (83), (-)-deoxoprosopinine and (-) - deoxoprosophylline (84), piperine and isochavicine(85),and etc.

A new appoarch of synthesis of piperidine alkaloids is deal with the asymmetric synthesis (86). A general method for the steroselective synthesis of *cis-* and *trans-* 2,6- dialkyl piperidine alkaloid has been described (87).

Distribution of Piperidine Alkaloids in Nature Sources.

Piperidine alkaloids are widely distributed in higher plants, frequently found in *Piper* spp.(Piperaceae) (42, 88-91) most of which are conjugated piperidide derivatives, piperine is the basic constituent in this species; *Nicotiana* spp. (Solanaceae) (42); *Lobelia* spp. (Lobeliaceae) (42, 92-99); *Conium* spp. (especially *Conium maculatum*, (Umbelliferae) (64) and *Sedum* spp. (Crassulaceae) (41,50). They are also occur throughout *Achillea* spp. (Compositae)(42,100,101); *Anabasis aphylla* (Chenopodiaceae)(42); *Bochmeria* spp.(Urticaceae)(102,103), *Carica* spp. (Caricaceae)(41,44); *Lytrum anceps*(Lythraceae) (54); *Nuphar japonicum*(Nymphaeaceae)(104,105); and *Pinus* spp. (Pinaceae)(64).

Many species of Leguminosae were reported to contain piperidine alkaloids as following.

Subfamily Caesalpinoideae :- *Cassia* spp. (39), *Baikiae plurijuga* (106) and *Ceratonia siliqua* (106).

Subfamily Mimosioideae :- *Acacia* spp.(42,107), *Albizzia lophanta* (42), *Galliandra haematocephala* (108), *Leucaena glauca* (109), *Lysiloma bahamensis* (107) and *Prosopis* spp. (39,110,111).

Subfamily Papilionoidae :- *Adenocarpus* spp. (42, 112-116), *Ammodendron conollyi* (117), *Coelidium fourcadei* (90), *Cytisus* spp.(41), *Gernista* or *Retama* spp.(41, 94, 118), *Laburnum vulgare* (119), *Lathyrus* spp.(119), *Lupinus formosus* (53), *Medicago sativa* (120), *Phaseolus vulgaris* (121), *Pongamia glabra* (57), *Trifolium pratense* and *T. repens* (119).

Pipecolic acid and its derivatives are distributed among the family :- Alliaceae (119), Leguminosae (42,106,119), Moraceae (122), Palmae (109), Plumbaginaceae (123), Strelilziaceae (42), Violaceae (42, 124) and Zygophyllaceae (125).

The other families that containing some piperidine alkaloids are family Aizoaceae (41,42), Annonaceae (41), Apocynaceae (41,126), Campanulaceae (61), Chenopodiaceae (41, 42, 127-129), Compositae (58, 59), Ericaceae (41), Euphorbiaceae (41, 129-133), Himantadraceae (131,134), Lauraceae (135), Rhamnaceae (40), Rubiaceae (52), Salvadoraceae (41), Saxifragaceae (136), Solanaceae (135) and Zygophyllaceae (137).

New piperidine alkaloids are recently reported in *Amoora rohituka*, *Tecoma stans* (44), *Achillea* spp. (138), *Excoecaria agallocha* (139), *Rhazya stricta* (140) and *Andrachne aspera* (141).

Piperidine alkaloids are also distributed in animals; fire ants (*Solenopsis* spp.)(46,47) and poisonous Columbian frogs (*Dendrobates* spp.)(67,68). Moreover, in bacteria, *Pseudomonas* spp. (39) and *Streptomyces* spp.(64) were reported the presences of piperidine alkaloids.