The genus *Gelsemium*: An update

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**ABSTRACT**

The review includes 103 references on the genus *Gelsemium*, and comprises ethnopharmacology, morphology, phytoconstituents, pharmacological reports, clinical studies and toxicology of the prominent species of *Gelsemium*. Alkaloids and iridoids constitute major classes of phytoconstituents of the genus. Most popular species of the genus are the Asian *G. elegans* and the two North American related species, *G. sempervirens* and *G. rankinii*. *Gelsemium* species are categorized under medicinal as well as poisonous plants. Amongst various species, *G. elegans* and *G. sempervirens* possess medicinal value, and have been traditionally used as nervous system relaxant. These plants have been explored exhaustively for their anticancer activity. In the concluding part, the future scope of *Gelsemium* species has been emphasized with a view to establish their multifarious biological activities and mode of actions

**Key words:** Alkaloids, anticancer, *gelsemium*, iridoids

**INTRODUCTION**

The literature review on *Gelsemium* has been compiled using references from major databases such as Chemical Abstracts, Medicinal and Aromatic Plants Abstracts, PubMed, King’s American Dispensatory, Raintree Nutrition Incorporation, Henriette’s Herbal Homepage, National Agricultural Library (AGRICOLA), Duke’s Phytochemical and Ethnobotany database, UK Cropnet Ethnobotany database, Archives of American Folk Medicine and USPTO Patent Full Text and Image database.

The available information on *Gelsemium* has been divided into six sections, that is, ethnopharmacology, morphology, phytoconstituents, pharmacological studies, clinical studies, toxicology, covering prominent species of *Gelsemium*. The ethnopharmacological section has been further subdivided into two sections, that is, traditional uses, and alternative and complementary medicinal uses. The reports, in which *Gelsemium* species have been used as domestic remedy by common men without any prescription for the treatment of various ailments, have been discussed under traditional uses. The subhead ‘alternative and complementary medicinal uses’ highlights *Gelsemium* species as medicine prescribed by medical practitioners for the treatment of various ailments. It also mentions uses for which *Gelsemium* species or their preparations are available in the market. Under every section, *Gelsemium* species have been arranged in an alphabetical order.

**THE GENUS GELSEMIUM**

**Taxonomic classification**

- **Kingdom**: Plantae (plants)
- **Superkingdom**: Tracheobionta (Vascular plants)
- **Superdivision**: Spermatophyta (Seed plants)
- **Phylum**: Embryophyta ( Higher plants)
- **Class**: Magnoliopsida (Dicotyledons)
- **Order**: Gentianales
- **Family**: Loganiaceae
- **Genus**: Gelsemium
- **Species**: elegans, rankinii, sempervirens

The genus *Gelsemium* belongs to family Loganiaceae, and comprises about five species that are widely distributed throughout Central America. *Gelsemium elegans* known as Lemuan is an extremely poisonous plant that is indigenous to the South East Asian countries and found predominantly in Malaysia and Sarawak. Most popular species of the genus are the Asian *G. elegans* and the two North American related species, *G. sempervirens* and *G. rankinii*. *Gelsemium* is a climbing plant with dark evergreen leaves and all parts are poisonous.

**ETHNOPHARMACOLOGY**

**Traditional uses**

*Gelsemium elegans* has been traditionally used as a nervous system relaxant to treat various types of pain including headache and
pain associated with inflammatory conditions.\cite{16,6} *Gelsemium* is one of homeopathy’s important remedy for influenza.\cite{3} *Gelsemium sempervirens* Ait. Syn. *G. nitidum*, commonly known as Yellow jasmine, has been used in the treatment of restlessless, mental irritability, insomnia, headache, irritation of the urinary tract, hyperemia and convulsions.\cite{8} The roots of *G. sempervirens* have been used in the treatment of migraine, neuralgia, rheumatism, and in ovarian and uterine pain.\cite{9} In the US, it has been extensively used as an arterial sedative and febrifuge in various fevers. It has been used in treatment of spasmodic disorders such as asthma and whooping cough. The plant has been used in hysteria, dysmenorrhea, chorea, pneumonia and bronchitis.\cite{10}

**Alternative and complimentary medicinal uses**

An herbal preparation containing *G. sempervirens* has been used for evening cold and influenza.\cite{11} Pharmaceutical formulations containing *G. sempervirens* as one of the constituents have been used for the treatment of psoriasis and neurodermatitis.\cite{12} Nebera et al. reported that homeopathic preparations, containing *G. sempervirens* in the form of sugar granules, are used in treating myopia of I, II or III degree.\cite{13} Fluid extract of the plant has been used for its spasmylytic actions.\cite{14}

**MORPHOLOGY**

*Gelsemium* includes three species of shrubs and climbers from United States and Central America and one species from China, South East Asia and Indo-Malaysia. *Gelsemium elegans* Benth. is a large, woody evergreen climber with corky bark; leaves ovate or ovate-lanceolate; flowers golden yellow; sepals ovate, margin minutely ciliate; corolla funnel shaped, lobes imbricate in bud; ovules numerous in each cell; style filiform, at the apex with four short stigmatic branches.\cite{15,16} *Gelsemium sempervirens* is a climbing shrub indigenous to the Southern United States from Virginia to Florida and Texas.\cite{17} The plant is supplied commercially as segments of the cylindrical rhizome with attached wiry roots;\cite{18} rhizome horizontal, the segments 3 to 20 cm in length and 3 to 30 mm in diameter, externally moderate brown to dark yellowish-orange, frequently spirally twisted, longitudinally wrinkled, with purplish-brown longitudinal lines and transverse fissures, upper surface with few stem scars, the under and lateral portions with several roots and root scars, fracture of rhizome tough, splintery, internally exhibiting a narrow purplish-brown bark, a broad, pale yellowish orange to light yellow, finely radiate and eccentric wood, a minute disintegrated pith; roots up to 20 cm in length and 2 to 8 mm thick, light brown, nearly smooth and wiry; fracture one-half transverse, the other oblique and splintery, fractured surface showing a broad, radiate, yellow wood and a thin bark.\cite{19}

**PHYTOCONSTITUENTS**

A survey of literature reveals that alkaloid constitutes the major class of phytoconstituents in *Gelsemium* species. Table 1 summarizes phytoconstituents reported from various species of *Gelsemium*.

**PHARMACOLOGICAL STUDIES**

It has been reported that alkaloidal fraction isolated from *G. elegans* exhibits analgesic and anti-inflammatory activities.\cite{20} A growth stimulant for pig has been prepared from gouwen (*G. elegans*) that served to promote nutrient absorption of organism, to increase immunity, and raise lean-to-fat pork ratio.\cite{7} Cuéllar et al. reported that *Gelsemium* tincture at higher concentration inhibits dopamine, noradrenaline and serotonin uptake into synaptosomal preparations from different parts of the rat brain, whereas lower concentrations enhances noradrenaline and serotonin uptake into mesencephaline preparation.\cite{21,22} Methanol extract of *G. elegans* leaves exhibited high cytotoxicity against the human ovarian cancer cell lines CaOV-3 with an IC50 value of 5 µg/ml after 96 h of incubation while less toxicity against the human breast cancer cells MDA-MB-231 suggesting its selectivity towards CaOV-3 cells.\cite{23} Uncaricin acid E, isolated from *G. elegans*, reported to exhibit antitumor effects due to its growth inhibitory activity for HepG2 cells in dose-dependent manner.\cite{24} Gelescide type alkaloids of *G. elegans* exhibited potent cytotoxic activity in an A431 human epidermoid carcinoma cell line.\cite{25,26} Koumine (50 mmol/L) induced apoposis of human colon adenocarcinoma LoVo cells in a time-dependent manner, and inhibited DNA synthesis in LoVo cells in vitro.\cite{27} Koumine (20–320 µg/ml) dose dependently inhibited concanavalin A or phytohemagglutinin-induced proliferation of murine lymphocytes determined by MTT colorimetry.\cite{28} It also decreased IL-2 level in the cell culture supernatant measured by enzyme-linked immunosorbent assay. Koumine showed remarkable inhibitory effect on mouse vaginal epithelial cell mitosis and promoted the formation of epidermal glandular layer in the scales at the mouse tail.\cite{29} It also decreased serum IL-2 level in mice at concentrations 6, 30, 150 mg/kg. These activities infer that the therapeutic effect of Koumine against psoriasis is related to the inhibition of epidermal cell proliferation, promoting the formation of glandular cells and decreasing the serum level of IL-2. Koumine injection significantly decreased mouse spontaneous activity in moderate and high doses but did not produce any effect on the respiratory and cardiovascular system of dogs.\cite{30}

Low doses of *G. sempervirens* and *Atropa belladonna* showed significant neurotropic and protective effects on behavioral and gastric alterations induced by foot shock stress in mice.\cite{31} Ethanolic extract of *G. sempervirens* has been reported to increase the resistance of rabbits to pneumococcus toxin.\cite{32} *G. sempervirens* alkaloidal fraction possessed anticancer activity as evidenced by significant inhibition of hepatic carcinoma HepG2 cells using crystal violet dyeing method.\cite{33} Sempervirine nitrate, isolated from *G. sempervirens*, exhibited antimitotic activity in mice bearing several types of tumors.\cite{34} Sempervirine has also been reported to possess vasoconstrictor action in the perfused isolated rabbit ear.\cite{35} In an experiment performed by Hinsdale on isolated rat intestine, *G. sempervirens* produced an immediate relaxation of the intestine tissue.\cite{36} *G. sempervirens* and *Datura stramonium* in appropriate concentration reported to prevent development of spontaneous seizures induced in rats by lithium or picrocarpine.\cite{37}
CLINICAL STUDIES

Gouwen injection, prepared by using alkaloids extracted from G. elegans roots, has been reported to exhibit antitumor effect against esophageal cancer in humans.[80] An injection containing G. sempervirens extract as one of the ingredients when given to patients suffering from neurodermatitis, resulted in subsidence of itching associated with neurodermatitis after 1 week, disappearance of large erythema after 3–4 weeks and elimination of disease after 6 weeks.[12]

TOXICOLOGY

Gelsemium acts in the similar manner as nicotine and conine. Sometimes small doses of G. sempervirens can produce toxic symptoms.[9] A drachm of fluid extract of the plant can cause death, and 30 minims are dangerous. An alkaloid gelsemine from G. sempervirens is toxic, and symptoms of toxicity are depressed respiration, tremors, paralysis of extremities, convulsions, urination, defecation, erection, retching and salivation. [90] Gelsemine, in small doses, stimulates respiration and paralyses the respiratory centers in larger doses.[91] The minimum lethal dose is 0.02 to 0.03 mg/g, s.c. for frogs, 0.00010 to 0.00012 mg/g, s.c. for rats, 0.00005 to 0.00006 mg/g, i.v. for rabbits and 0.0005 to 0.0001 mg/g, i.v. for dogs. E-Bay website rated extracts of Gelsemium ‘extremely toxic’.[92] The roots of G. sempervirens contain a resin, which is poisonous in very small doses. A tincture prepared by digesting it in undiluted alcohol is fatal. Small doses of G. sempervirens relax the muscles but larger doses cause dropping of the lower jaws and difficulty in managing the eyelids. The continued administration of it affects the brain spinal centers and medulla, causing marked feebleness of muscular movements, confusion of vision and vertigo. Large doses paralyze the spinal cord and cause almost complete loss of muscular power. These effects are due to its action upon the spinal marrow. The characteristic toxic symptoms are peripheral relaxation, disturbance of the ocular muscles, drooping of the lower jaw and profound prostration and muscular relaxation. When applied locally to the eye, it dilates the pupils. Overdose of the plant may cause death due to asphyxia. Alkaloid fraction, isolated from G. elegans leaves, at a lethal dose produced violent clonic convulsions that led to respiratory failure. Authors suggested that alkaloids act centrally against GABA as evidenced by prevention of convulsions by pentobarbital or diazepam and potentiation by reserpine.[93]

Persons are reported to have been poisoned by eating honey gathered by the bees from G. sempervirens flowers. Gelsemium when administered to rabbits and guinea pigs produced a marked generalized congestion of all organs, depressive action on heart and respiration and severe toxic action on liver, kidney and testes.[94] Histological studies showed neurological signs characterized by marked progressive weakness and convulsions culminating in death in three goats over a 24-h period after ingestion of G. sempervirens leaves.[95] Aqueous extract of the plant greatly depressed the activity of the isolated frog heart muscles.[96] It has been reported that single intravenous injection of gelsemine (0.2 mg/kg), isolated from G. sempervirens, in chloralosed dog produced a marked and prolonged decrease in blood pressure.[96] Alkaloids gelsemine, sempervirine and gelsemicine, isolated from G. sempervirens, increased the hypertensive action of adrenaline[97] and inhibited the cholinesterases of nervous tissue and serum.[97] The drug is used as poison as its effects vary rapidly.[98,99]

Table 1: Phytoconstituents of various species of Gelsemium

| Species          | Phytoconstituents                                                                 |
|------------------|----------------------------------------------------------------------------------|
| G. elegans       | Alkaloids koumine,[1] kouidine, koumine, kouminidine, koumicine, kouminicine,[19-28] 19-(R)- and 19-(S)-hydroxydihydrokoumine,[2,29] 19-(R)- and 9-(S)-kouminol,[5,32] humantine,[6] 11-hydroxyhumantinen,[7] 15-hydroxyhumantinen, 11-methoxy-humantinen,[8] N-desmethoxyhumantinen,[9] rankidine,[10] 11-hydroxyrankidin,[11] N-desmethoxy-rankidin,[12] 20-hydroxydihydrorankidin, humantiniren,[13] humantinidene,[14] gelsemoxinone,[51,52,53] gelsemidyne,[15,51,53] 19 α-hydroxygelsemydine,[16] 14 -hydroxygelarsemasaine,[17] Gelsebanine,[19,53,54] koumidine,[20] 19-(Z)-akuamidin,[21] 16-epi-voacarpine,[22] 19-hydroxy-dihydrogeloseervine (40), gelserine,[20-22,23] gelsevirine,[24] 19-(R)-acyethylhydrogeloseervine, 19-(R)-hydroxydihydgeloseervine,[25] gelserine,[25,55,56] gelsedine,[25,57,58] elegansamine,[27,58] N-methoxy-anhydrovobasinediol,[28,64] gelsemande,[29] 11-methoxygelseramamide,[30] 11-methoxy-19-(R)-hydroxygeloseeline,[30,32] sempervirine,[33] Gelsediam,[31] 14-acetoxygelselediam,[32] gelserufaridine,[33] gelserinedione,[34,51] 14 acetoxygelserene,[35] 14 acetoxy-15-hydroxygeloseveline,[36] 14-acetoxy-19-oxogelseveline,[37] 19-acetoxy-19-oxogelseveline,[37] 19-acetoxy-19-goelseveline,[38,55] humantinen N(4)-oxide,[39] iridois (53) gelserime,[40] GEIR-1,[41] GRIR-1,[41] GEIR-2,[42] GEIR-3,[43,44] Di(2-ethylhexyl) phthalate, 3β-hydroxy-27-(p-Z)-coumaroyloxy urson-12-en-28-ocic acid, 3β-hydroxy-27-p-(E) coumaroyloxy urson-12-en-28-ocic acid, uncarinic acid (Wei et al., 2007), β-sitostreol, stigmastereol, daucosterol, stigmasterol, β-D-glucopyranoside, ursolic acid, gallic acid, ferulic acid, protocatechuric acid,[101] Glycosides; Gelsemiunoside A and B[102] |

| G. rankini Small | Alkaloids 21-oxogelsevinne, 21-oxogelsentine, gelsivirine,[26] gelsevirine,[26] gelsemine,[26,54] rankidine,[10] humantiniren,[14] humantinidene,[5,55] iridois gelserime,[26] GEIR-1,[41] GRIR-1,[41] GEIR-2,[42] GEIR-3,[43,53] |

| G. sempervirens  | Alkaloids gelsermine,[23] gelserminine, gelserminoidine, gelseminicine,[25,56-62] 21-oxogelsevinne,[26] gelsevirine,[24,54] gelsedine,[24,48] 14β-hydroxygelsedine,[87,88] sempervirine,[60,61] gelseline type oxindole alkaloids,[62] gelseric acid,[70] iridois gelserime,[26] gelseremide-7-glucoside, gelseminol,[26] gelsemol 1- and 3-glucoside, 9-hydroxysempereperoxide,[71] 2008 Steroids pregna-4,16-diene-3,20-dione, 12 β-hydroxy-5α-pregna-16-ene-3,20-dione, 12 β-hydroxypregna-4,16-diene-3,20-dione,[86] Scopopletin, 7-0-beta-D-glucopyranosylscopolitin, 7-0-beta-D-apiofuranosyl-(1->6)-β-lucopyranosylscopoletin, Uvaol, 2-(4-hydroxyphenyl) ethylheptadecanoate,[102] |
Appendix (contd...)
Appendix (contd...)

28

29

30

31 R = H

32 R = OAc

33

34

35 R = H

36 R = OH

37

Appendix (contd...)

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CONCLUSION

About 05 species of the genus *Gelsemium* have been reported in various floras. An exhaustive survey of literature revealed that information is available on 03 species. Among these 05 species, most of ethnopharmacological reports are available on *G. elegans* and *G. sempervirens*. Further, these plants [Table 1] have been investigated for their phytocomstituents.

*Gelsemium sempervirens* has been included in a number of herbal and homoeopathic formulations, which are in clinical use for the treatment of various ailments. Mother tinctures of the
plant are available in Indian market, and are frequently used for the treatment of CNS disorders, but no pharmacological work supports its efficacy in CNS disorders. Keeping in view the traditional, alternative and complimentary medicinal uses, and frequency of use in homeopathic formulations, *G. sempervirens* seems to hold great potential for in-depth investigation on various biological activities, especially its effect on the central nervous systems.

A close scrutiny of literature on *Gelsemium* reveals that two species have been investigated pharmacologically. Pharmacological studies infer that *G. elegans* exhibits analgesic, antiinflammatory and cytotoxic properties; *G. sempervirens* exhibits neurotropic and antitumor activities. Koumine, gelsedine type alkaloids and uncarinic acid E have been considered bioactive constituents of *G. elegans*. Toxicological studies have confirmed high toxicity of *Gelsemium* species at higher doses. These plants have narrow therapeutic index, that is, margin between therapeutic efficacy and toxic value is very less. Although the plants of the genus *Gelsemium* hold great potential to be developed as antitumor drugs, their toxicity could not be ruled out.

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REFERENCES

1. Latiff A, Ibrahim AZ, Mat-Salleh K. An account and checklist of the flowering plants at Kelabit Highlands. Baro Sarawak: ASEAN Review of Biodiversity and Environmental Conservation; 1999. p. 15.
2. Ridley HN. The Flora of the Malay Peninsular. Ashford, London: Reeve and Co.; 1925.
3. Perry LM. Medicinal plant of East and Southeast Asia: Attributed properties and uses. Cambridge, MA: MIT Press; 1980.
4. Burkhil JA. A Dictionary of the economic products of the Malay Peninsular. Kuala Lumpur: Ministry of Agriculture and Cooperatives; 1966.
5. Ponglux D. Wongseripipatana S, Subhadhirasakul S. Studies on the indole alkaloids of Gelsemium elegans (Thailand): Structure elucidation and proposal of biogenetic route. Tetrahedron 1988;44:5075-4.
6. Watson L, Dallwitz MJ. Families of Flowering Plants: Descriptions, Illustrations, Identification, and Information Retrieval; 2002.
7. Blackwell WH. Poisonous and Medicinal plants. Prentice Hall, New Jersey: Englewood and Cliff; 1990. p. 329.
8. Felter HW, Lloyd JU. Gelsemium (U.S.P.). King’s American Dispensatory; 1898.
9. Chopra RN. Poisonous plants of India. India: Council of Agricultural Research; 1940. p. 692.
10. Grieve M. A Modern Herbal (first Published in 1931). London: Tiger Books International; 1994. p. 249.
11. Voorhees J, Nachman L. inventors: Herbal composition for treating symptoms of influenza. US patent 6455070; 2002. P. 3.
12. Calarasu C, inventor: Pharmaceuticals containing diphenhydramine and Echinacea and Eupatorium and Gelsemium and Lachesris extracts for the treatment of Psoriasis and neurodermatitis. German patent 3641220; 1988. P. 4.
13. Nebera SA, Nebera OA, Pakhomova NN. inventors: Homoeopathic preparation for treating myopia. RU patent 2203674; 2003.
14. Uhlenbroock K, Schweer M, Maschmann L. Spasmolytic effect of the ingredients of Gelsemium fluid extract. Arzneimittelforschung 1959;9:419-22.
15. The Wealth of India. A Dictionary of Indian Raw Materials and Industrial Product. New Delhi: Council of Scientific and Industrial Research; 1956. p. 123.
16. Brandis D. Indian Trees. In: singh B, Singh MP editors. Dehradun, India; 1987. p. 476.
17. Wallis T. Textbook of Pharmacognosy. 5th ed. New Delhi: CBS Publishers and Distributors; 1999. p. 387, 568-62.
18. Gahalot A, Patra A, Sharma A. Pharmacognostical studies on Gelsemium sempervirens Alt. Roots P’ Cog Mag; 2008.
19. Chou TQ. The alkaloids of Gelsemium elegans Benth. III. Zhangguo Shenglixue Zazhi 1981;5:345-52.
20. Chou TQ, Wang CH, Cheng WC. The alkaloids of Chinese gelsemium. Ta-ch’a-yeh Zhangguo Shenglixue Zazhi 1936; 10: 70-84.
21. Chi YF, Kao YS, Huang YT. Alkaloids of Chinese gelsemium, Kou-wen. J Am Chem Soc 1938;60:1723-4.
22. Liu CT, Loh JY, Liu CC, Lu JY, Chu TC, Wang CH. Gelsemium alkaloids. I. Reinvestigation of the alkaloids of Gelsemium elegans and the constitution of koumine. Huaxue xuebao 1961;27:47-58.
23. Khuong-Huu F, Chiaroni A, Riche C. Structure of koumine, an alkaloid from Gelsemium elegans Benth. Tetrahedron Lett 1981;22:733-4.
24. Jin H, Xu RS. Studies on the alkaloids of Gelsemium elegans Benth. The structure of koumidine. Acta Chim Sin 1982;40:1129-35.
25. Lounasmaa M, Koskenen A. A plausible biogenetic proposal for koumine. Planta Med 1982;44:120-1.
26. Yang J, Chen Y. Chemical studies on the alkaloids from Hu Man Teng (Gelsemium elegans Benth). II. structure of humantenidine. Yaoxue Xuebao 1984;19:437-40.
27. Zhang L, Lin J, Wu Z. Advances in the study on chemical constituents and pharmacology of Gelsemium elegans (Gardn. et Champ.) Benth. Zhong Yao Cai 2003;26:451-3.
28. Zhang LL, Wang ZR, Huang CQ, Zhang ZY, Lin JM. Extraction and separation of koumine from Gelsemium alkaloids. Di Yi Jun Yi Da Xue Xue Bao 2004;24:1006-8.
29. Lin LZ, Cordell GA, Ni CZ, Clardy J. Two oxindole alkaloids from Gelsemium elegans. Phytochem 1990;29:3013-7.
30. Sun F, Xing QY, Liang XT. Structure of (19R)-kouminol and (19S)-kouminol from Gelsemium elegans. J Nat Prod 1989;52:1180-2.
31. Yang J, Chen Y. Chemical study of the alkaloids of Gelsemium elegans. Yaoxue Tongbao 1989;52:1180-2.
32. Yang J, Chen Y. Chemical studies on the alkaloids from Hu Man Teng (Gelsemium elegans Benth.) II. structure of humantenidine. Yaoxue Xuebao 1982;17:633-4.
33. Yang JS, Chen YW. Chemical studies on the alkaloids of Hu-
Man-Teng (Gelsemium elegans Banth.). I. Isolation of the alkaloids and structure of humanemine. Yao Xue Xue Bao 1983;18:104-12.

34. Lin LZ, Cordell GA. New humanemine-type alkaloids from Gelsemium elegans. J Nat Prod 1989;52:588-94.

35. Lin LZ, Cordell GA, Ni CZ, Clardy J. Oxindole alkaloids from Gelsemium elegans. Phytochemistry 1991;30:1311-5.

36. Kitajima M, Kogure N, Yamaguchi K, Takayama H, Aimi N. Structure reinvestigation of gelsemoxonine, a constituent of Gelsemium elegans, reveals a novel azetidine containing indole alkaloid. Org Lett 2003;5:2075-8.

37. Lin LZ, Cordell GA, Ni CZ, Clardy J. Gelsemamine, an indole alkaloid from Gelsemium elegans with two monoterpenic units. J Org Chem 1989;54:3199-202.

38. Lin LZ, Hu SF, Cordell GA. 19 α-Hydroxygelsemansydine from Gelsemium elegans. Phytochemistry 1996;43:723-6.

39. Xu YK, Yang SP, Liao SG. Alkaloids from Gelsemium elegans. J Nat Prod 2006;69:1347-50.

40. Sakai S, Wongseripipatana S, Ponglux D, Wangseripipatana S, Takayama H, Ogata K, Aimi N. Isolation of a new indole alkaloid from Gelsemium rankinii. J Nat Prod 1986;49:483-7.

41. Lin LZ, Cordell GA, Ni CZ, Clardy J. Three oxindole alkaloids from Gelsemium elegans species. Phytochemistry 1991;30:879-83.

42. Du X, Dai Y, Zhang C, Lu S, Liu Z. Studies on the Gelsemium alkaloids. 1. The structure of gelsenicine. Huaxue Xuebao 1982;40:1137-41.

43. Ponglux D, Wangseripipatana S, Takayama H, Ogata K, Aimi N, Sakai S. A new class of indole alkaloid, elegansamines, constructed from a monoterpenoid indole alkaloid and an indoid. Tetrahedron Lett 1988;29:5395-6.

44. Lin LZ, Cordell GA, Ni CZ, Clardy J. N-methoxyanhydrobasinediol from Gelsemium elegans. Phytochemistry 1989;28:2827-31.

45. Lin LZ, Cordell GA, Ni CZ, Clardy J. Gelsemamide and 11-methoxy gelsemamide, two novel secoindole alkaloids from Gelsemium elegans. Tetrahedron Lett 1989;30:1177-80.

46. Stevenson AE, Sayre LE. Third alkaloid of Gelsemium. J Am Pharm Assoc 1915;4:60-2.

47. Stevenson AR, Sayre LE. Semprevirine from Gelsemium root. J Am Pharm Assoc 1915;4:1458-63.

48. Sayre LE. Final report on the alkaloids of Gelsemium. J Am Pharm Assoc 1919;8:708-11.

49. Hasenfratz V. The presence of an oxygen-free alkaloid in Gelsemium sempervirens. Comptes Rendus des Seances de la Societe de Biologie et de ses Filiales 1933;196:1530-2.

50. Janot MM, Gautarol R, Friedrich W. Gelsemicine. Ann Pharm Fr 1951;9:305-7.

51. Kogure N, Ishii N, Kitajima M, Wongseripipatana S, Takayama H. Four novel gelsemicine-related oxindole alkaloids from the leaves of Gelsemium elegans benth. Org Lett 2006;8:3085-8.

52. Kitajima M, Nakamura T, Kogure N, Ogawa M, Mitsuno Y, Ono K, et al. Isolation of gelsemicine-type indole alkaloids from Gelsemium elegans and evaluation of the cytotoxic activity of gelsemicine alkaloids for A431 epidermoid carcinoma cells. J Nat Prod 2006;69:715-8.

53. Kogure N, Ishii N, Kobayashi H, Kitajima M, Wongseripipatana S, Takayama H. New iridoids from Gelsemium species. Chem Pharm Bull 2008;56:870-2.

54. Schun Y, Cordell GA, Garland M. 21-oxogelsemansydine, a new alkaloid from Gelsemium rankinii. J Nat Prod 1986;49:483-7.
release of cytochrome C. Biol Pharm Bull 2006;29:1639-44.

77. Kitajima M. Chemical studies on monoterpenoid indole alkaloids from medicinal plant resources Gelsemium and Ophiorrhiza. J Nat Med 2006;61:14-23.

78. Chi DB, Lei LS, Jin H, Pang JX, Jiang YP. In vitro Study of koumine-induced apoptosis of human colon adenocarcinoma LoVo cells. Di Yi Jun Yi Da Xue Xue Bao 2003;23:911-3.

79. Wang ZR, Huang CQ, Zhang ZY, Zhang LL, Lin JM. In vitro Effect of koumine on proliferation of murine CD4+ T cells purified by magnetic-activated cell sorting. Di Yi Jun Yi Da Xue Xue Bao 2005;25:562-4.

80. Zhang LL, Huang CQ, Zhang ZY, Wang ZR, Lin JM. Therapeutic effects of koumine on psoriasis: an experimental study in mice. Di Yi Jun Yi Da Xue Xue Bao 2004;24:32-4.

81. Chi DB, Lei LS, Yang HX, Sun LS. General pharmacology of koumine parenteral solution. Di Yi Jun Yi Da Xue Xue Bao 2004;24:32-4.

82. Bousta D, Soulimani R, Jarmouni I, Belon P, Falla J, Froment N, et al. Neurotropic, immunological and gastric effects of low doses of Atropa belladonna L., Gelsemium sempervirens L., and Poumon histamine in stressed mice. J Ethnopharmacol 2001;74:205-15.

83. Baker WF. Gelsemium sempervirens and Bryonia alba in influenza. J Am Inst Homeopath 1920;12:695-8.

84. Wang Y, Fang Y, Lin W, Cheng M, Jiang Y, Yin M. In vitro Inhibitory effect of Gelsemium alkaloids extract on hepatic carcinoma HepG2 cells. Zhong Yao Cai 2001;24:579-81.

85. Bassleer R, Clerment D, Marnette JM, Caprasse M, Tits M, Angenot L. Effect of dihydroflavopereirine and sempervirine (β-carbolinium alkaloid) on cancer cells in culture. Ann Pharm Fr 1985;43:83-4.

86. Rothlin E, Raymond H. Vascular action of sempervirine, an oxygen-free alkaloid of Gelsemium sempervirens. Comptes Rendus des Seances de la Societe de Biologie et de ses Filiales 1934;117:754-6.

87. Hinsdale AE. Action of Gelsemium upon intestinal movement. J Am Inst Homeopath 1918;10:969-70.

88. Peredery O, Persinger MA. Herbal treatment following post-seizure induction in rat by lithium pilocarpine: Scutellaria lateriflora (Skullcap), Gelsemium sempervirens (Gelsemium) and Datura stramonium (Jimson Weed) may prevent development of spontaneous seizures. Phytother Res 2004;18:700-5.

89. Dai R. Preparation of Gouwen injection. Zhong Yao 1993;24:471-2.

90. Hou HC. The pharmacological action of gelsemicine, an alkaloid from Gelsemium. I. Acute toxicity. Zhangguo Shenglixue Zazhi 1931;5:181-90.

91. Raymond H. Gelsemicine. Comptes Rendus des Seances de la Societe de Biologie et de ses Filiales 1937;126:1151-4.

92. Cantrell FL. Look what I found. Poison hunting on e-Bay. Clin Toxicol (Phila) 2005;43:375-9.

93. Mitchell T. Gelsemium sempervirens. J Am Inst Homeopath 1926;19:707-13.

94. Thompson LJ, Frazier K, Stiver S, Styer E. Multiple animal intoxications associated with Carolina jasmine (Gelsemium sempervirens) ingestions. Vet Hum Toxicol 2002;44:272-3.

95. Espeas D, Moisset E. Action of extract of Gelsemium sempervirens on the isolated frog heart. Comptes Rendus des Seances de la Societe de Biologie et de ses Filiales 1938;127:1088-90.

96. Espeas D, Moisset E. Cardiovascular action of gelsemine. Action on the carotid pressure of the dog. Comptes Rendus des Seances de la Societe de Biologie et de ses Filiales 1938;127:1002-4.

97. Vincent D, Lagreu R. Action of the alkaloids of Gelsemium sempervirens on cholinesterases. Comptes Rendus des Seances de la Societe de Biologie et de ses Filiales 1951;145:348-50.

98. Kitajima M, Aray A, Takayama H, Aimi N. A chemical study on ‘Yakatsu’ stored in Shosoin repository: Isolation and characterization of four indole alkaloids from a 1250 year-old sample of the Chinese toxic medicine. Proc Japan Acad 1998;74:159-63.

99. Blaw ME, Adkisson MA, Levin D, Garriott JC, Tindall RS. Poisoning with Carolina jessamine (Gelsemium sempervirens [L.] Ait.). J Pediatr 1979;94:998-1001.

100. Yin S, He XF, Wu Y, Yue JM. Monoterpenoid indole alkaloids bearing an N4-Iridoid from Gelsemium elegans. Chem Asian J 2008;3:1824-9.

101. Qing-chun Z, Yan-Hui F, Tao G, Wei H, Li-jun W. Isolation and identification of non alkaloids constituents from G. elegans Benth. Yaoke Daxue Xuebao 2007;24:619-22.

102. Hua W, Zhao QC, Yang J, Shi GB, Wu LJ, Guo T. Two new benzofuran from lignan Glycosides. Chinese Chem Lett 2008;19:1327-9.

103. Zhang Z, Wang P, Yuan W, Li S. Steroids, alkaloids and coumarins from G. sempervirens. Planta Med 2008;74:1818-22.

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