CHEMICAL STUDY OF *KNEMA* SPECIES FROM THAILAND

Madalena M.M. Pinto
Laboratório de Química Orgânica, Faculdade de Farmácia, Universidade do Porto, 4000 Porto – Portugal.
Anake Kijjoa
Laboratório de Química, Instituto de Ciências Biomédicas Abel Salazar, Universidade do Porto, 4000 Porto – Portugal.

Dedicated to Prof. Dr. Otto R. Gottlieb on the occasion of his 70th birthday

Key Word Index – *Knema elegans; Knema furfuraceae; Knema laurina; Knema tunuinervia;* Myristicaceae; stem bark; neolignans; dehydroguaiaretic acid; (+)-*trans*-1,2-dihydrodehydroguaiaretic acid; 8-hydroxy-3-(12-phenyldodecyl)-isocoumarin;8-hydroxy-6-methoxy-3-pentylisocoumarin; 3-(12-phenyldodecyl)-phenol; 3-(12-phenyldodec-8-enyl)-phenol; 3-(8-pentadecenyl)-phenol; 2,4-dihydroxy-6-(10-phenyldecyl) acetophenone; 2-hydroxy-6-(12-phenyldodecyl)-benzoic acid.

The new lignan (+)-*trans*-1,2-dihydrodehydroguaiaretic acid, two new isocoumarins and a new acetophenone have been isolated together with dehydroguaiaretic acid, anacardic acid derivative and three cardanols from stem bark of *Knema elegans* Pierre (*K. laurina* Warb.) *K. furfuraceae* Warb. and *K. tunuinervia* ssp. *setosa* W. J.J.O. de Wilde.

INTRODUCTION

Little is known about the chemistry of the genus *Knema* which comprises approximately sixty southeast Asian species. Of these, twelve are endemic to Thailand and are known by the common names as buffalo blood or horse blood because of their dark red resin exuded from the bark. Some of the *Knema* species are mentioned to be used in the traditional medicine for curing cancer.

So far, only five species of *Knema* have been investigated chemically and three of them in our laboratories. Indian coworkers have isolated an optically active 1-aryltetralin type lignan attenuol from the bark of *K. attenuata* (Wall) Warb[1,2] while the seed oil of *K. elegans* Warb[3] was found to contain a series of homologous anacardic acids, cardanols and resorcinols as well as three diaryltetrahydrofuran type lignans.

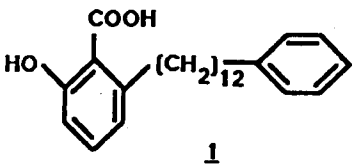
Because of their popular use in Thai traditional medicine, three *Knema* species namely *K. furfuraceae* Warb[4], *K. elegans* Pierre (*K. laurina* Warb) and *K. tunuinervia* ssp. *setosa* W.J.J.O. de Wilde[5] have been investigated in our laboratories.

CHEMICAL CONSTITUENTS

The constituents of three *Knema* species isolated in our laboratories can be divided into 5 groups.

a) Anacardic acid

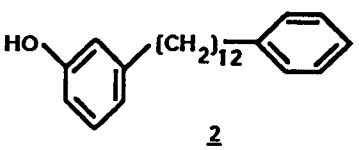
2-Hydroxy-6-(12-phenyldodecyl)-benzoic acid (*1*) was the only anacardic acid derivative isolated from stem bark of *K. elegans, K. furfuraceae* and *K. tunuinervia*. This compound seems to be a common constituent for the genus *Knema*, eventhough it has not been reported to be isolated from *K. attenuata (1)*.



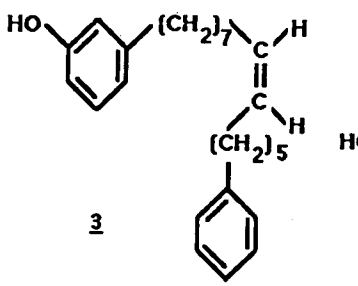
1

b) Cardanols

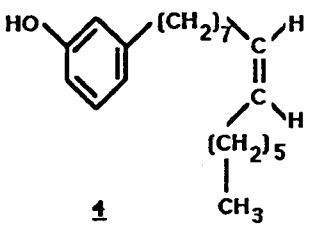
Both saturated and unsaturated cardanols have been isolated from stem bark of *Knema*. Hence, 3-(12-phenyldodecyl)-phenol (*2*) was isolated from *K. furfuraceae* while 3-(12-phenyldodec-8-enyl)-phenol (*3*) and 3-(8-pentadecenyl)-phenol (*4*) were isolated from *K. elegans* and *K. tunuinervia* respectively.



2



3

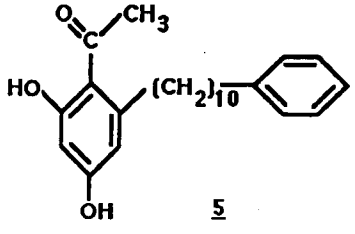


4

The *cis* configuration of the double bond in compounds *3* and *4* was established by the characteristic coupling constant of the olefinic protons in the ^{1}HNMR spectra together with the typical chemical shift values of the vinylic carbons in ^{13}C NMR[6].

c) Acetophenone derivative

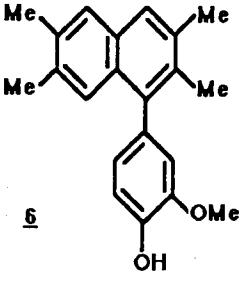
The new acetophenone, 2,4-dihydroxy-6-(10-phenyldecyl)-acetophenone (*5*) was isolated from both *K. elegans* and *K. tunuinervia* ssp. *setosa*. It is the first acetophenone known to be isolated from Myristicaceae.



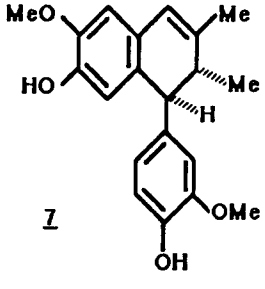
5

d) Neolignans

No neolignans have been isolated from *K. elegans* and *K. tunuinervia* while dehydroguaiaretic acid (*6*) and (+)-*trans*-1,2-dihydrodehydroguaiaretic acid (*7*), a new neolignan have been isolated from *K. furfuraceae*.



6



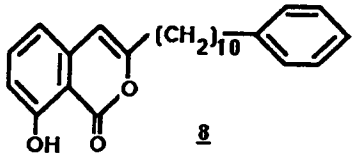
7

The neolignan *7* is dextrorotatory. Its relative configuration *trans* of C-1,2 was assigned by the coupling constants of their protons.

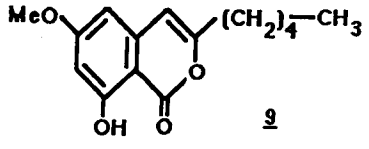
e) Isocoumarins

Although a majority of isocoumarins have been isolated from fungi (*Aspergillus* spp., *Penicillium* spp. and *Streptomyces* spp.), a number of them have been known to be constituents of a few higher plant families. Among these, Bignoniaceae, Compositae, Leguminosae, Myricaceae and Saxifragaceae, but not Myristicaceae, were reported the isolation of isocoumarins[7].

So far, 8-hydroxy-(12-phenyldodecyl)-isocoumarin (*8*) and 8-hydroxy-6-methoxy-3-pentylisocoumarin (*9*) have been isolated from *K. furfuraceae* and *K. tunuinervia* respectively. These two new isocoumarins are distinguished from all simple isocoumarins previously reported by their comparatively long side chains.



8



9

BIOSYNTHESIS

The compounds isolated from *Knema* spp. in our laboratories showed a very interesting biogenetic point of view. While cardanol *4* and isocoumarin *9* are purely acetate derived, the neolignans *6* and *7* are from shikimate pathway. The anacardic acid *1*, cardanols *2* and *3*, acetophenone *5* and isocoumarin *8* are mixed acetate-shikimate origin. It is remarkable that in the same group of compounds the enzyme systems mediating their biosynthesis can be completely different.

AKNOWLEDGEMENTS

We want to thank Instituto Nacional de Investigação Científica (I.N.I.C.) for support of this work. We are also indebted to Department of Pharmaceutical Botany, Faculty of Pharmaceutical Sciences, Chulalongkorn University, Bangkok, Thailand, for ethnobotanical studies.

REFERENCES

1. Joshi, B.S.; Ravindranath, K.R.; Viswanathan, N.; *Experientia* (1978), **34**, 422.
2. Joshi, B.S.; Viswanathan, N.; Balakrishman, Y.; Gawad, D.H.; Ravindranath, K.R.; *Tetrahedron* (1979), **35**, 1665.
3. Spencer, G.F.; Tjarks, L.W.; Kleiman, R.; *J. Nat. Prod.* (1980), **43**, 724.
4. Pinto, M.M.M.; Kijjoa, A.; Mondranondra, I.; Gutierrez, A.B.; Herz, W.; *Phytochemistry*, (1990), **29**, 1985.
5. Kijjoa, A.; González, M.J.T.G.; Pinto, M.M.M.; Mondranondra, I..; Herz, W.; *Plant. Med.* (in publication).
6. Mudd, A.; *J. Chem. Soc. Perkin Trans. 1*(1983), 2161.
7. Hill, R.A.; *Progress in the Chemistry of Organic Natural Product*, (1986), **49**, 1.