SOME ALKALOIDAL CONSTITUENTS OF THE STEM BARK OF PACHYPODANTHIUM STAUDTII ENGL & DIELS

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ABSTRACT

Liriodenine an oxoaporphine and discretine a tetrahydroprotoberberine isolated from the stem bark of Pachypodanthium staudtii and characterised by physicochemical data.

The Plant, Pachypodanthium staudtii is a tropical annonaceous plant found in the closed evergreen forest from Sierra Leone to Zaire. The bark especially is claimed to have medicinal properties and is so used in folk medicine.

The Chemotaxonomic significance of the isolated alkaloids and the medicinal importance of liridonine in relation to the folk-loric use of the plant are discussed.

KEYWORDS

Pachypodanthium staudtii, Annonaceae, alkaloids, isoquinoline, liriodenine, discretine, chemotaxonomy, folk-lore.

INTRODUCTION

Pachypodanthium staudtii Engl and Diels. (Fam. Annonceae) is known locally as Paeaduasa or Okyra (Asante), Duawisa (Twi) and Fale (Nzema).

It is widely distributed in the tropical closed forest of the West Africa coast stretching from Sierra Leone as far down as Zaire.

It has a rich folk-lore heritage as a traditional herbal remedy in traditional medicine in West Africa. Among its several uses is lower abdominal pain relief especially when the bark decoction is drank after childbirth (1). The stem bark in conjunction with other ingredients is indicated for the treatment of benign tumours (2).

The plant Pachypodanthium staudtii has been the subject of several Phydtochemical studies and over 11 alkaloids have been characterised from the alkaloidal isolates, of the stem bark. All these alkaloids belong to the isoquinoline group of alkaloids and are either tetrahydroprotoberberines, oxoaporphines or aporphines (3,4,5,6).

Because of known variation, both quantitative and qualitative, in secondary metabolic products in some plant species due to geographical chemotypes and ontogenetic states [7], it was thought useful to examine the alkaloid constituents and to correlate them to the claimed folk-lore uses and also to investigate the chemotaxonomic significance of the alkaloids.

EXPERIMENTAL

Melting points (m.p) were measured in a Gallenkamp Electrothermal Melting Point apparatus and are uncorrected.

Thin layer Chromatographic (TLC) analysis were carried out on silica gel G. (Merck) plates using the following solvent systems:

(i) Methycyclohexane: Chloroform: Diethylamine (7:2:1)

(ii) Chloroform: Diethylamine (9:1)

The alkaloids were visualised in U.V. (Camag Universal U.V. lamp) at 254nm and 366nm and revealed with Dragendorff's spray reagent.

Ultraviolet (U.V) specta were obtained spectrophotometer SP 1800 spectrophotometer using

96% ethanol as solvent. Infra-red IR Spectra were obtained from KBr discs on a Beckmann IR spectrophtometer while Nuclear magnetic resonance (NMR) date were obtained on a Varian NMR spectrophotometer using deuterochloroform as solvent and tetramethylsilane as internal standard. Mass spectra were determined on a double focusing mass spectrometer.

Plant Material

The stem bark of P. staudtii was obtained from the Bobiri Forest Reserve near Ejisu-Ashanti in may 1984. Field identification and collection of the material were done by Mr. Martin Buntugu of the FPRI, Kumasi and authenticated by comparison with a herbarium specimen in FPRI.

Extraction of Alkaloids

Dried and coarsely powdered stem bark of Pachypodanthium staudtii (3.9kg) was macerated and extract with ammoniacal ethylacetate over 7 days.

The cold extract was filtered and concentrated in vacuo to a syrup mass.

The residue was acidified with aqueous acetic acid and filtered. The filtrate was basified (pH9) with strong ammonia solution and extracted with chloroform: ethanol (95:5 v/v mixture). The solvent was removed in vacuo to give an alkaloidal residue (36g).

Isolation of Alkaloids

24g of the alkaloidal extract was dissolved in dichloromethane and shaken with sodium hydroxide (5%) solution in successive small portions. The dichloromethane fraction was washed several times with water till alkali free (neutral to litmus) and evaporated in vacuo to give a non-phenolic alkaloid residue (12.2g).

The alkaloid residue (10.5g) was chromatographed over a column of alumina (Aluminium oxide 60, active, basic type Merck) and eluted successively with petroleum spirit (bp 60°C - 80°C), petroleum spirit: ethylacetate mixtures and ethylacetate to give 2 compounds designated PS (np)1 and PS (np)2. PS (np) 2 was recrystallised from diethyletther as yellowish microcrystals (amorphous).

The bulked sodium hydroxide extract was acidified with 5% sulphuric acid and them made distinctly alkaline with strong ammonia solution. The alkaloids were then extracted with chloroform which after drying with sodium sulphate (anhydrous) was evaporated to dryness in vacuo to give 4.1g of phenolic alkaloids.

4g of the phenolic alkaloids was chromatographed on a silica column (silica gel, extra pure BDH) and eluated with the same solvents used for the non-phenolics. The eluates yielded two compounds which were designated PS (np)1 - 11mg and PS (np) 2 - 30mg in order of eluation.

RESULTS AND DISCUSSION

Compound PS (np)2 had the following characteristics:

Yellowish microcrystals (recrystallised from) mp 232 -234°C.

U.V. λmax nm : 274, 268, 308, 400 (logε 4.21, 4.16, 3.67, 3.92).

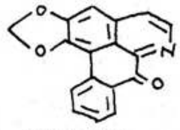
L.R. ν max cm^{-1} : 1645 (conjugated c=o, c=c).

Ms. m/z (rel. intensity): 275 (100)M^+

219(9), 217(19), 189(15), 188(21), 162(14).

NMR δ (protons) : 6.33(2H); 7.12(H) 7.70-8-90 (4H, aromatic).

Based on the above data the structure I was proposed i.e liriodenine.



I = Liriodenine.

The complex U.V. absorption peaks and the yellow colour suggested a highly conjugated aromatic system indicative of an oxoaporphine compound which normally shows peaks in the 245-270nm region [8].

The NMR signal at δ 6.33 which integrated for downfield methylene protons indicated the presence of the methylenedioxy substituent which was confirmed by the reddish-brown colour formed on the addition of conc. sulphuric acid to a chloroform solution of the compound. The signal at δ 7.70-8.90 which integrated that ring D was unsubstituted [9]. The signal at δ 7.12 integrated for 1 proton (aromatic) which appeared at a higher field than other aromatic protons and suggested that ring A was substituted at 2 position i.e C_1 and C_2 - the methylenedioxy substituent.

The mass specta showed peaks at m/z 217 and 247 which are typical of oxoaporphines and in agreement with the literature [8]. Also, the base peak (M^+) at m/z 275 agrees with that for liriodenine [10].

Further justification of the structure and identify of compound PS (np) 2 was obtained by co-chromatography with authentic liriodenine which were identical and mixed melting point determination which was not depressed.

Compound PS (np)1 was characterised as follows: Yellow needle (recrystallised from petroleum spirit b.p 60 - 80°C) m.p 170 - 172°C.

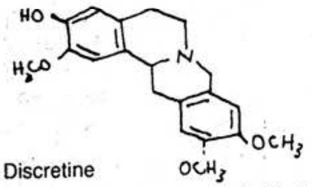
U.V. max nm : 286 (log 4.06)

M.S m/z : 341 (M+), 326, 324, 310, 176, 164

(base peak), 149, 135

NMR δ (protons) : 3.87 (9H); 5.54 (1H); 6.59, 6.62 6.7 6.85 (4 H, aromatic).

On the basis of the above characteristics data. Structure II was proposed and justified as follows:



II = Discretine

The yellow coloured compound indicated a compound with chromophoric groups. The U.V absorption peak at 286nm indicated either a tetrahydrobenzylisoquinoline or a tetrahydroproberberine structure

The NMR signal at δ 5.54 indicated the presence of a phenolic (OH) group on the base structure. This was confirmed when on adding a solution of 1% ferric choride solution to a sample of PS (np)1 and PS (np)2(p)1 a deep green solution was obtained. The signal at δ 3.87 integrated for protons and established 3 methoxy groups while those at δ 6.59, 6.62, 6.67 and 6.85 integrated for 4 aromatic protons the signal occurring further downfield than the others indicates an adjacent deshielding group, an OH.

The mass spectral peaks at m/z 341, 176, 164, are typical of tetrahydroprotoberberine (8). The peaks at 310 (M-31) and 324 (M-7) indicated the loss of a methoxy and hydroxy moities respectively from the molecule. The peaks at m/z 176 and 178 indicate a fragment comprising of rings A and B substituted with a hydroxy and methoxy moities while the base peak or m/z 164 represents ring D, with 2 methoxy groups (14). The absence of an AB quartet around δ 3.65 and δ 4.35 suggested that the methoxy groups on ring D are at C - 10 and C - 11 (15).

Work continues on compounds PS (np)1 and PS (np)2(np)1 to establish their identities.

CONCLUSION

The oxoaprophine alkaloid liriodenine appears to be of common occurrence in the Annonaceae family. So far it has been isolated from 16 genera out of 41 genera examined (11). The family has about 120 genera comprising 150 plant species which Hutchinson (12) has classified into 2 subfamilies: the Annonoideae and the Monodoroideae, the compound liridenine occurs in both subfamilies. Thus, liriodenine may only be important chemotaxonomically in the delineating of members of the Annonaceae and not at the subfamilial taxonomic levels. Certainly a lot more of the alkaloids would have to be characterised to enable a more comprehensive discussion on their chemotaxonomic significance.

The tetrahydroprotoberberines appear to be restricted in occurrence to species in the tribe Xylopineae - sub family Monodoroideae. This would lend support to the phytogenetic grouping of plant in the Xylopineae among which discretine has been isolated from only two genera, Pachypodanthium and Xylopia (11).

One the medical use of P. staudtii, it is the use in the treatment of benign tumours (12) which is outstanding and the demonstrated cytotoxic activity of liriodenine (13) seems to justify the folk-lore uses of P. staudtii.

It should be of interest to examine the pharmacological activities of liriodenine to ensure toxicological safely. If this is done it will be possible to utilise the crude drug or its extracts in formulated products in the treatment of susceptible tumours.

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