SUMMARY

The thesis being submitted consists of three parts.

P A R T - I

This part deals with chemical investigations of a local plant Leucas aspera (Fam. Labiateae) to result in isolation and identification of three sterols and a triterpene, named leucolactone, for the first time from a natural source.

Chapter - I describes a brief review of pentacyclic triterpenes together with their biological activity ending with a list of pentacyclic triterpene lactones isolated and identified till date.

Chapter - II contains the morphological characters of plant of Labiateae family and Leucas aspera. Distribution of the plant has also been mentioned.

Details of chemical investigations of Leucas aspera have been included in Chapter - III. Aided by the results obtained from gas chromatography and GC-MS studies of the sterols and their acetate derivatives, it has been possible to identify them unambiguously as stigmasterol, β-sitosterol and campesterol.

Column chromatography of the extract of Leucas aspera also resulted in isolation of a pentacyclic triterpene lactone.

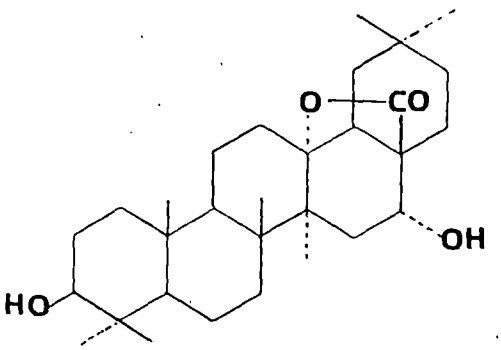
The triterpene, $C_{30}H_{48}O_4$, mp 310-12° was found to be a saturated pentacyclic one. IR spectrum (3607, 3540, and 1750 cm^{-1}) confirmed the presence of hydroxyl groups and a γ-lactone ring. Further informations about the compound was gathered by study of ^1H NMR, ^{13}C NMR and MS spectra of the compound and its acetate and ketone derivatives.

Comparison of ^{13}C NMR spectrum of the acetate derivative and that of 3β-acetyl oleanan-28→13β-olide revealed a close similarity between the two suggesting that the triterpene in question has an oleanane skeleton with a lactone ring between C-28 and C-13 with acetate function at C-3.

The signals in ^1H NMR of the triterpene and its acetate at δ 3.21 and 4.45 respectively with large coupling values are due to the axial proton at C-3 position while the triplet at δ 3.79 and 4.9 indicated that the proton attached to the hydroxyl bearing carbon is equatorially situated with two protons (axial and equatorial) present at α position.

Chromic acid-pyridine oxidation of the triterpene yielded a diketo-lactone whose IR spectrum suggested presence of a lactone ring (1760 cm^{-1}) and six membered ring ketones (1706 - 1710 cm^{-1}) implying that both the hydroxyl groups are susceptible to oxidation. ^1H NMR spectrum showed peaks at δ 2.15 and 2.8 integrated for five α protons to carbonyls. Earlier ^1H NMR spectrum of the triterpene had exhibited a doublet of a doublet at δ 2.81 with large coupling values of 14.5 and 5 Hz apparently due to a proton α to the lactone carbonyl. Hence it could now be stated that the newly formed ketone functions have four α -protons. Absence of a singlet

signal by C-18 proton discarded the possibility of oxygen function at C-19 in diketolactone. The doublets at δ 2.77 and 2.17 with J = 14 Hz are gem coupled having no neighbouring protons and are separated by 0.6 ppm due to the anisotropic effect of the carbonyl group. The results that the proton at δ 2.77 coupled with the methyl at δ 1.22 with a small J = 0.5 Hz, as confirmed by a decoupling experiment, show that the carbonyl group in diketolactone is either at C-15 or C-16 and C-3. The C-16 position is chosen because the methylene protons at C-15 would couple with methyl at C-14. Hence the hydroxyl functions are placed at C-3 and C-16 with the lactone ring between C-28 and C-13 as shown in the drawing. It was named leucolactone

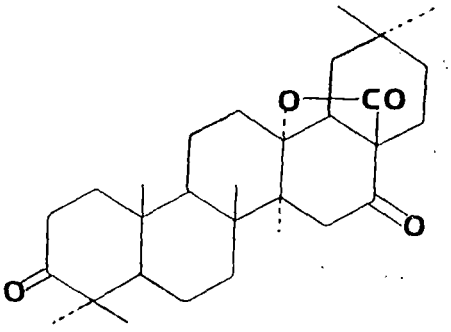


Application of 2D - NMR technique in structure elucidation of leucolactone:

Certain observations such as shifting of doublet at δ 2.8 upfield and appearance of a new doublet in this place compounded with the uncertainty whether the proton at δ 2.6 in leucolactone and its acetate really belonged to the α-proton to the lactone carbonyl necessiated the use of 2D-NMR for further clarification.

First of all the spectrum (discussed in the text) indicates the presence of a grouping $CO-CH_2-\overset{CH_3}{\overset{|}{C}}-\overset{|}{C}-CH_3$. where carbonyl function is assigned at C-16. Two pairs of methyls at 0.8266, 0.9433 ppm coupled to each other and 1.0733 and 1.1166 coupled to each other indicate that diketolactone (and therefore leucolactone) possesses oleanana skeleton. By studying the coupling of methyls protons with neighbouring protons, it was possible to specify signals to particular protons e.g. 1.12 and 1.36 ppm for C(19)-H2 and 2.59 ppm for C(18)-H.

The C-10 methyl (1.03 ppm) couples with C-1 proton (1.44 ppm) which further couples with protons at 2.02, 2.44 and 2.56 ppm. The last two downfield shifts of protons on the same carbon are appropriate for $-CH_2-$ adjacent to a carbonyl. These observations can be explained by the structure proposed for diketolactone.



A short description regarding biogenesis of pentacyclic triterpenes has also been included followed by experimental details at the end. Relevant references have been provided.

PART - II

This part consists of description of work on the study of oxidation reaction of selenium dioxide on lupanone

A review on the oxidation reaction of selenium dioxide has been provided followed by examples of oxidation of triterpenes with selenium dioxide.

Lupanone when oxidised by selenium dioxide has resulted in formation of seven products designated as compound A to G. Their identity has been established with the help of physico-chemical data.

Compound A has been identified as lup-1(2)-en-3-one . 424 [M$^+$] mp 176°, λ_{max} 228 nm ($\alpha\beta$ unsaturated ketone) identical with the authentic sample (mmp, IR).

Compound B has been identified as lup-1(2)-en-3-one-2-selenide. 504 [M$^+$], mp 300°. UV absorption was comparable with that of known compounds e.g. 1(2)-dehydro-lup-28-carbomethoxy -3-one-2-selenide, 1(2)-dehydro taraxerone-2-selenide. PMR and ^{13}C NMR spectra were also throughly examined for establishing the structure.

Compound C 582 [M$^+$] , mp 280°, was almost identical in PMR and ^{13}C NMR spectra with compound B. Hence it was given the structure as lup-1(2)-en-3-one-2-bisselenide.

Compound D, m/z 456 (M - H_2O), mp 284°, IR, 3490, 1709 cm^{-1} for hydroxyl and carboxyl group.

Methyl signals in ^{1}H NMR spectrum in the region δ 0.72 to 1.28, singlet at δ 4.03 (-CHOH), (C-1) 4.35 and (C-3) 5.20 for - OH protons were observed. Acetate derivative of the compound mp 260°, m/z 470 [M - AcOH - CO_2] , IR 1710 cm^{-1} (- COOH), 1740, 1250 cm^{-1} (acetoxyl groups). PMR singnals in the region δ 0.74 to 1.18 for eight methyls, singlet peaks at δ 2.01, 2.1 (acetoxyl methyls), δ 5.78 were observed. Identity of compound D as 1,3-dihydroxy-3-carboxy-A-nor-lupane was established with additional informations from its ^{13}C NMR spectrum.

Compound E 442 [M$^+$], mp 238°, IR 1800, 1750 cm^{-1} for anhydride. Informations from its ^{1}H NMR coupled with MS and IR data established its structure as A-nor-lupan anhydride.

Compound F, 472 [M$^+$], mp 320-22°. IR 1765, 1720 cm^{-1} for anhydride. In its PMR spectrum the singlet at δ 4.48 for a proton on C-1 geminal to oxygen function and without neighbouring proton appeared. With the help of added informations from its ^{13}C NMR spectrum the compound was identified as 1-hydroxy-lupan anhydride.

Compound G, 444 [M$^+$], mp 282-83°. IR 1740, 3400 cm^{-1} for a δ-lactone and hydroxy group. The singlet peek at δ 4.12 in its PMR spectrum was due to proton geminal to hydroxyl group. ^{13}C NMR exhibited signals from twentynine carbons, some with oxygen function. It was thus identified as 1-hydroxy-A-nor-lup-2-carb-4-olide.

Compound B and C were treated with H_2O_2 to yield a known compound 1α, 2α,-epoxy-lup-3-one.

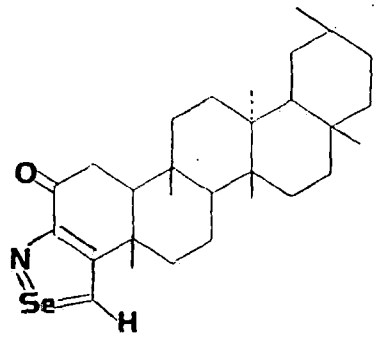
The experimental details has been described in the text.

PART - III

This part consists of description of studies on oxidation of oxime derivative of friedelin with selenium dioxide. Two products, compound A and compound B have been isolated and identified.

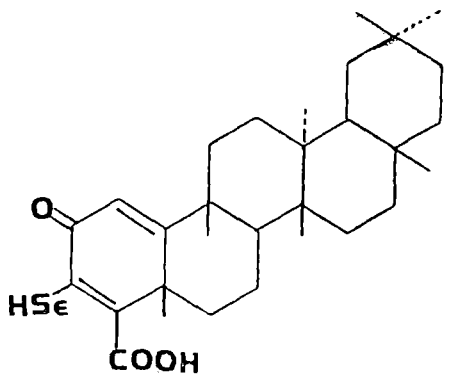
Compound A, mp 295-97°, $[\alpha]_D$ +60. IR 1675 cm^{-1} for $\alpha\beta$-unsaturated ketone. UV 254, 307 nm $\alpha\beta$-unsaturated ketone. PMR spectrum indicated seven tertiary methyls as singlets in the region δ 0.9 to 1.3, dd at δ 2.70 and 2.752, 1.91, doublet of a triplet at δ 2.37, singlet δ 9.04 for aldehydic type of proton.

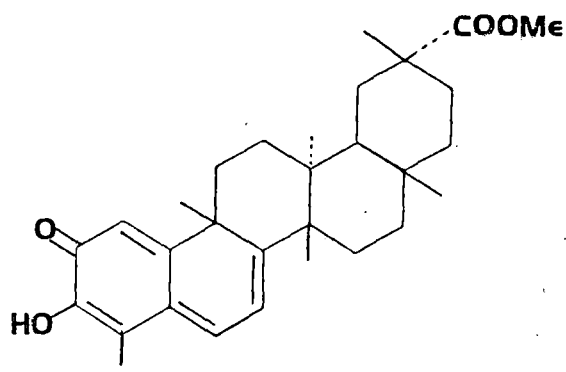
^{13}C NMR of the compound was compared with friedelin and pristimerin to confer the following structure for compound A.



Compound B, mp 296°. IR 1660-70, 2700-3500 cm^{-1} (-COOH). UV 274, 312 nm (quinone system). PMR spectrum of the compound indicated the presence of seven tertiary methyls in the region δ 0.9 to 1.6, singlet at δ 6.42 (olefinic proton α to ketone), δ 9.26 (carboxyl proton).

Comparison of its ^{13}C NMR spectrum with those of friedelin and pristimerin compoundec with the above mentioned data lend support to propose the following structure for compound B.





Pristimerin