

Chemical investigation of bioactive secondary metabolites from *Allamanda cathartica*

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INTRODUCTION: Natural Products

❖ A natural product

- A chemical substance produced by a living organism in nature
- Has pharmacological or biological activity for use in pharmaceutical drug discovery and drug design.

❖ Nature's biosynthetic pathways produces innumerate secondary metabolites with distinct biological properties that make natural products as valuable health products (nutritional/medicinal) or as structural templates for drug discovery.

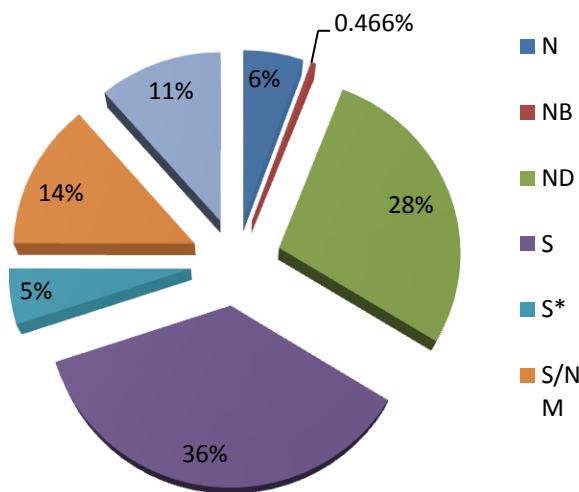
❖ Natural products always remain a consistent source of very simple to extremely complex structured molecules which plays an important role in human dietary function as well as in prevention of human disease .



Source of Natural Products and their Role

- ❖ Common sources: plants, microbes (bacteria, fungi), animals and marine organisms.
- ❖ As per WHO report, 65% population relies on Natural Products (80% of drug derived from ethno-medicinally important plant species).
- ❖ Plant based drugs have been used worldwide in traditional medicines for the treatment of various diseases^[2] .

Sources of Approved New Drugs^[3]



- N:** Unmodified NP
- NB:** Recently approved NP
- ND:** Modified NP
- S:** Totally synthetic drugs (modification of an existing agent)
- S*:** Total synthesis (NP pharmacophore)
- S*/NM:** Synthetic drug showing competitive inhibition of NP substrate
- S*/NM:** Synthetic drug with NP pharmacophore showing competitive inhibition of NP substrate

Allamanda cathertica

- Plant name:** *Allamanda cathertica*.
- Family:** Apocyanaceae
- Parts used:** Stem & Leaves
- Common name:** Allamanda Yellow, Golden Trumpet
- Hindi name:** Pilaghanti, Saithani phool.
- Local Name:** Malatilata, Ghanta Phul, Harkakra
- Distribution:** Native to Brazil, in India mostly distributed in the eastern costal region of Odisha and some parts of southern region.
- Traditional Uses:** Ayurvedic and Unani system of medicine for healing of wounds and ulcers^[4,5].
- Bark - hydragogue in ascites
- Leaves - valuable cathartic in moderate doses.
- Root - remedy for snake-bites.
- Whole plant - used against jaundice, malaria, fungal infections and antiseptic for the treatment of skin burns.^[6,7,8]



Biological activity: Antileukemic, wound healing, hepatoprotective activity^[7,8,9]

Type of compounds reported : Iridoids and triterpenes^[7,8,9]

Long chain esters, isoplumericin, plumericin, and plumeride are reported from roots while the leaves contained hydrocarbons, long chain esters, triterpene esters isoplumericin, plumericin, and plumeride and ursolic acid^[7,8,9] .

Isolated compounds : 8 compounds reported so far from this plant from literature search.

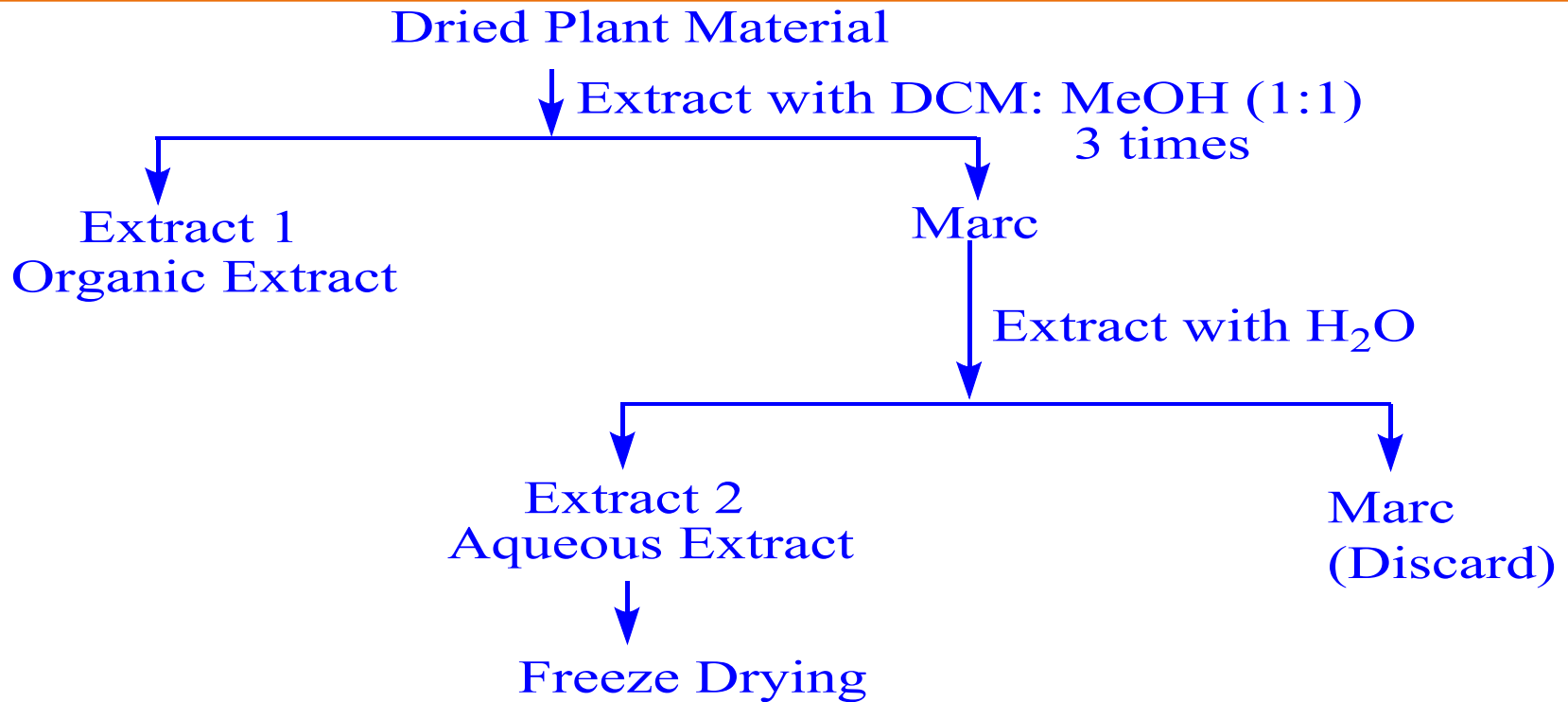
Presence of antileukemic iridoids lactone from *Allamanda cathertica* has shown anticancer activity of the species.^[7,8,9]

Therefore the plant has been taken up for detailed chemical investigation.

Chemical Investigation of *Allamanda cathartica*

- ✓ Isolation of natural products from the plant.
- ✓ Characterization of isolated natural products
- ✓ Structural modification of major bioactive molecules to create a library of molecules.

NCI Protocol for Extraction



Extraction of *Allamanda cathertica*

Parts Used: **Leaves**

Weight of dried Leaves: 892.44g

Weight of Organic Extract: 106.69g

Extractive Value: 11.95%

Parts Used: **Stem**

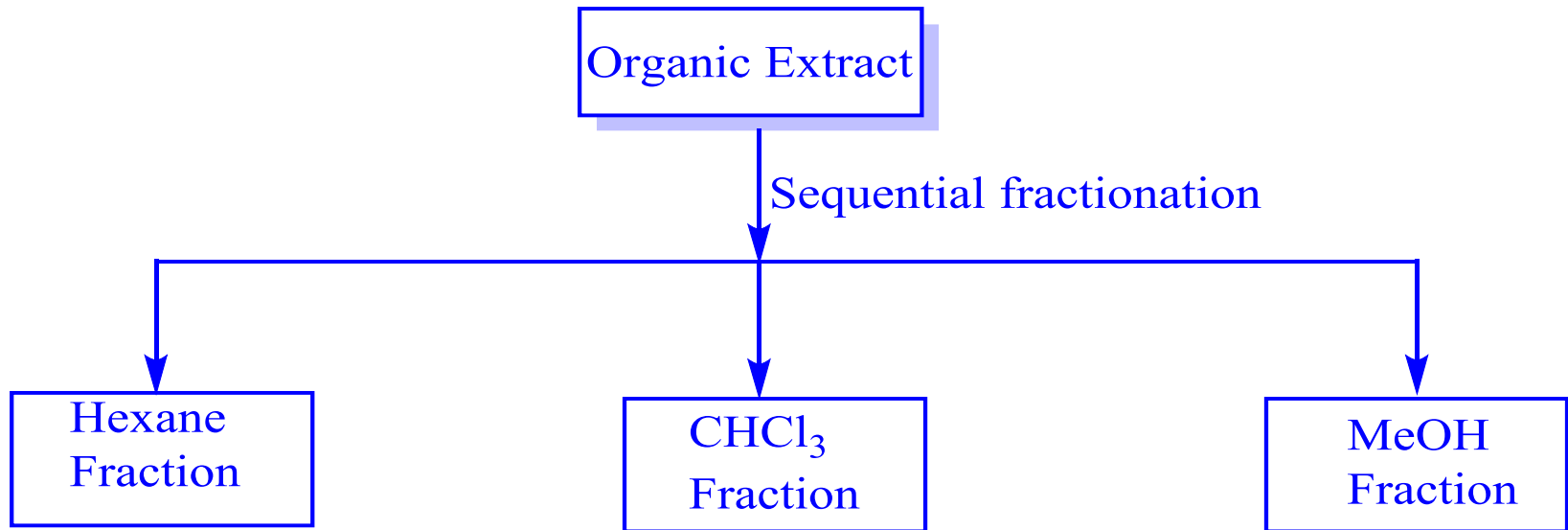
Weight of dried Stem: 1.9 kg

Weight of Organic Extract: 120.14g

Extractive Value: 6.32%

FRACTIONATION

Fractionation of Organic Extract



Fractionation of *Allamanda cathertica*

Parts Used: Leaves

Hexane extract: 32.54g

Chloroform extract: 52.44g

Methanol extract: 17.8g

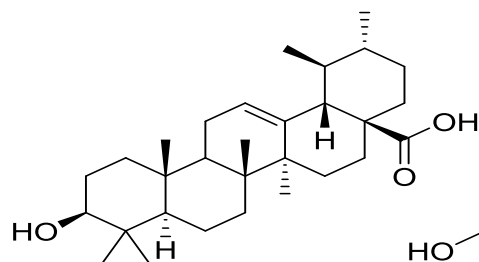
Parts Used: Stem

Hexane extract: 35.2g

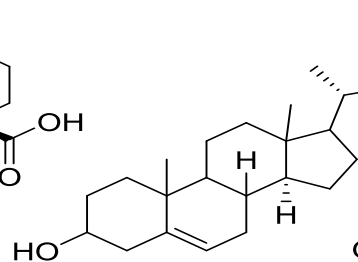
Chloroform extract: 62.5g

Methanol extract: 20.8g

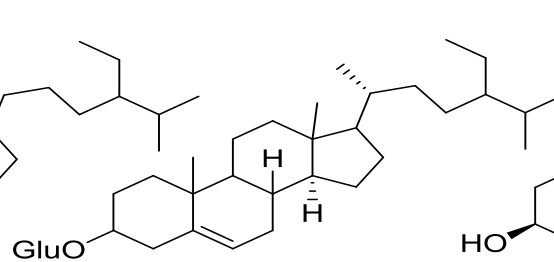
Compounds isolated from *Allamanda cathartica*



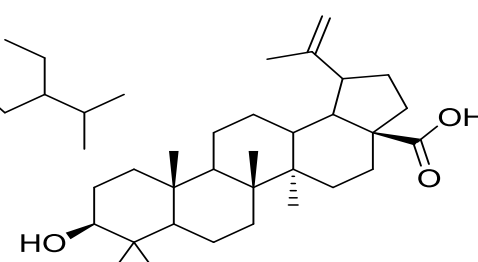
Ursolic acid



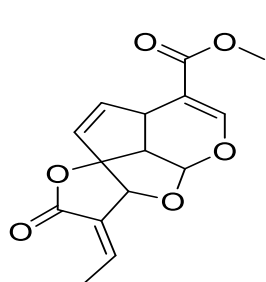
β-Sitosterol



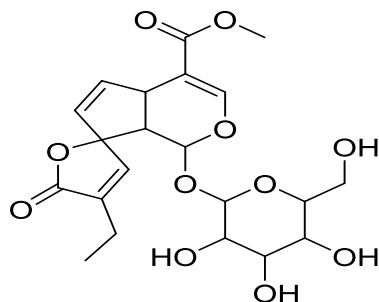
β-Sitosterol glucoside



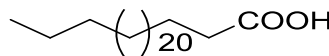
Betulinic acid



Plumericine



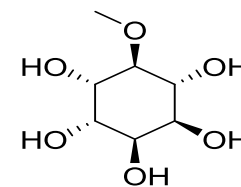
Allamadin glucoside



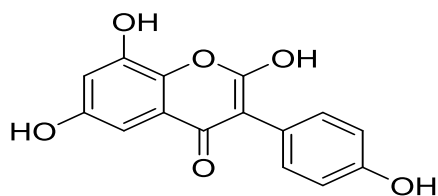
Heptacosanoic acid



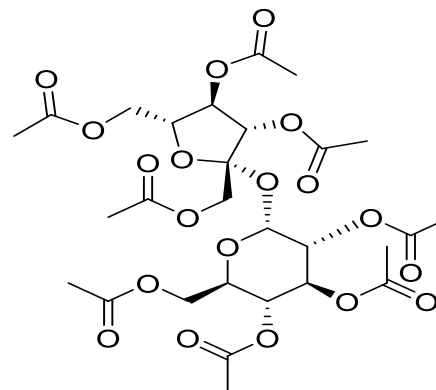
Heptacosane



D-(+)-Pinitol

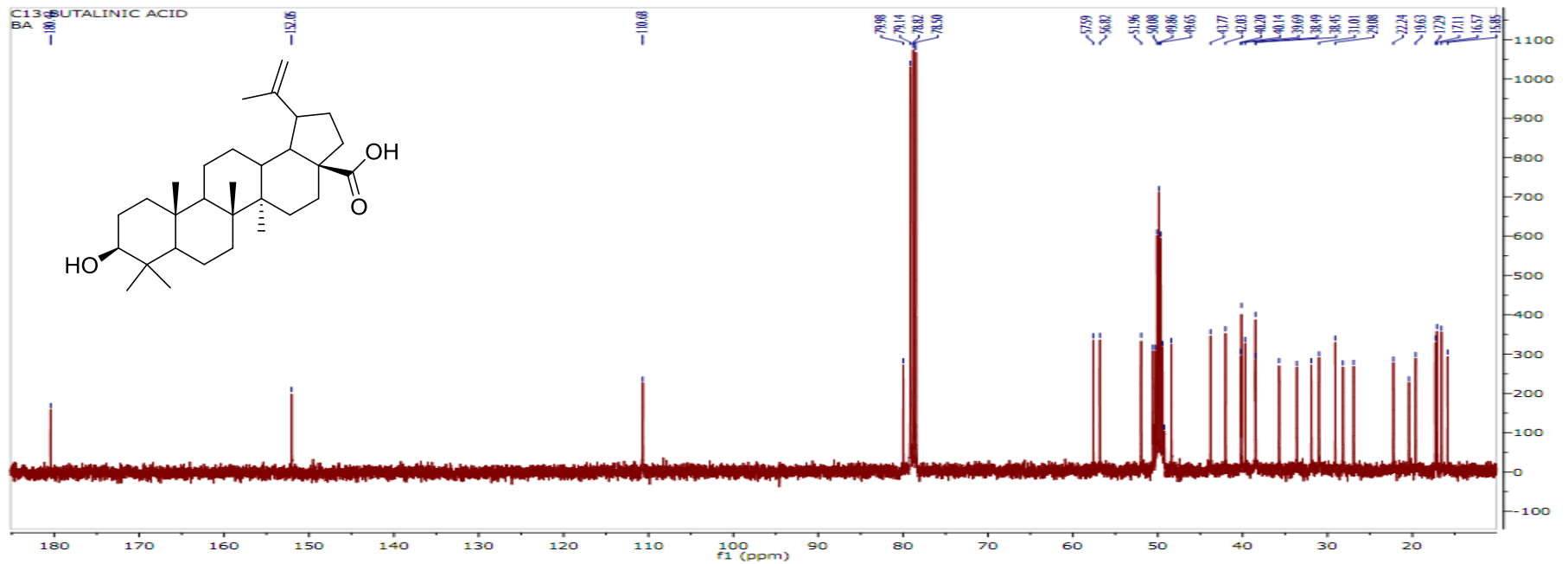
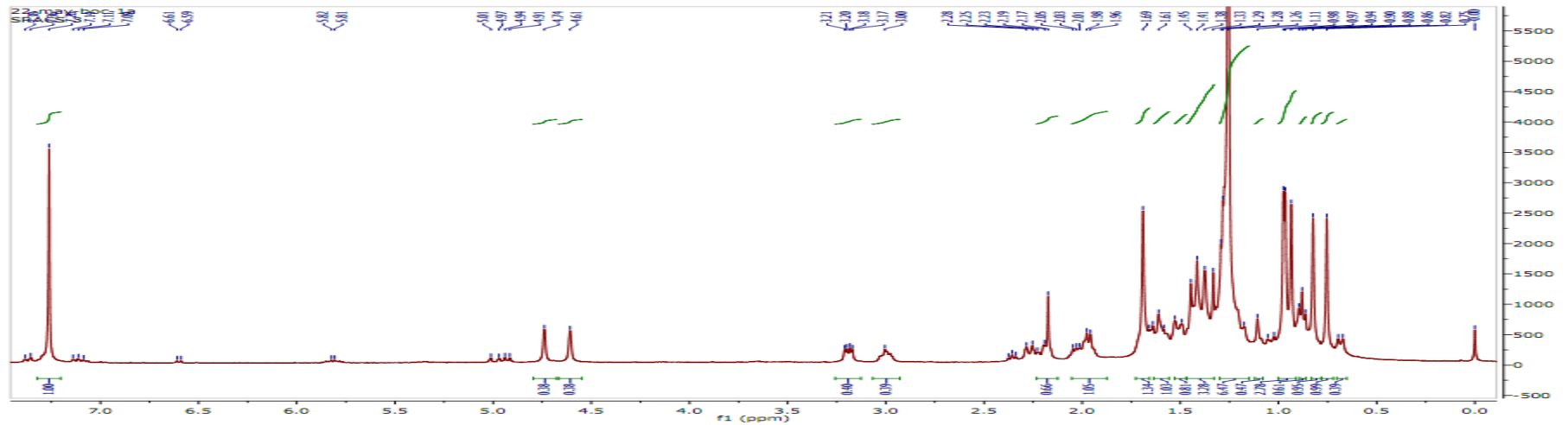


2,6,8-trihydroxy-3-(4-hydroxyphenyl)-4H-chromen-4-one

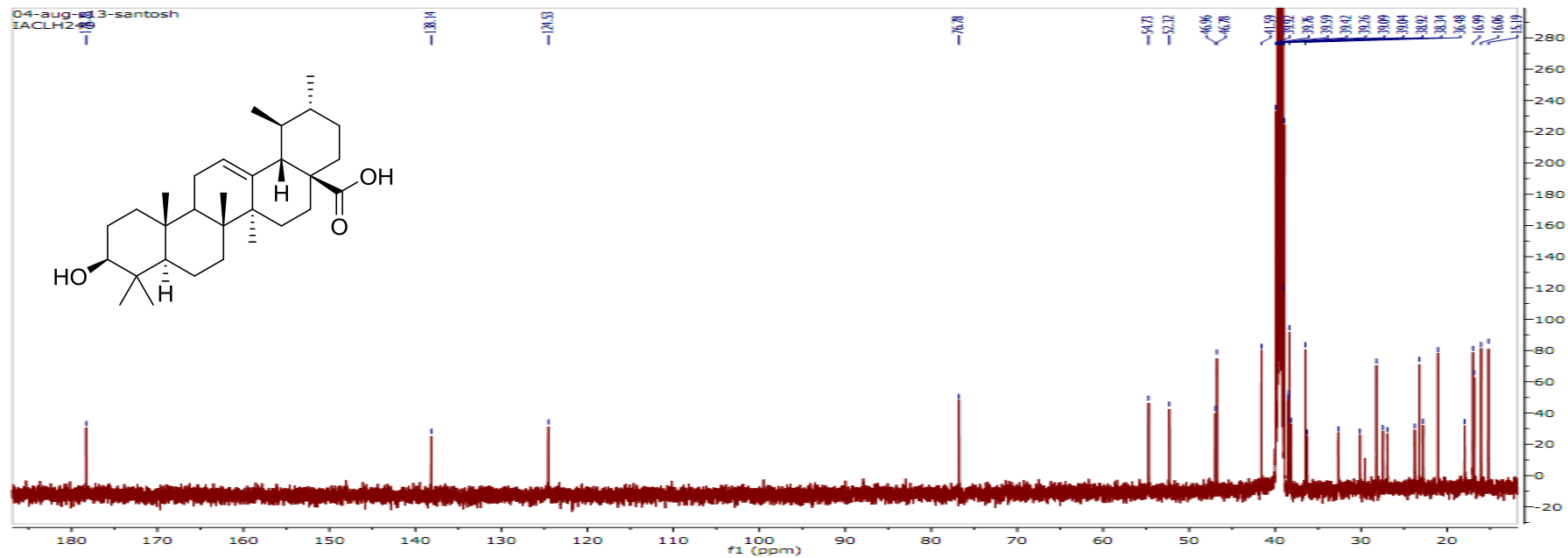
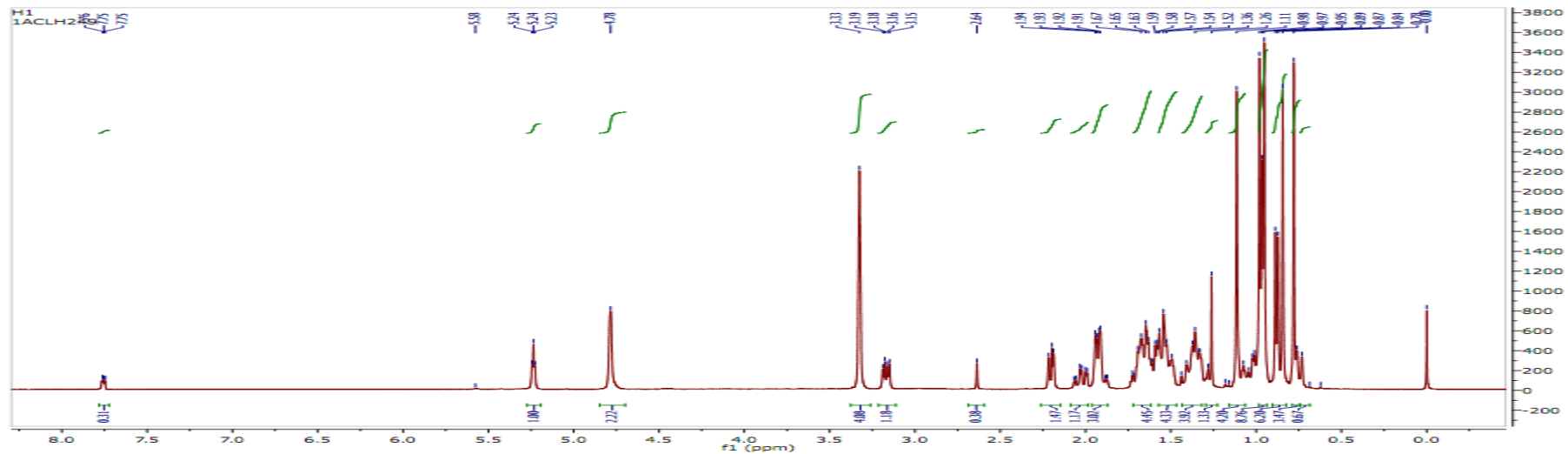


Sucrose Octaacetate

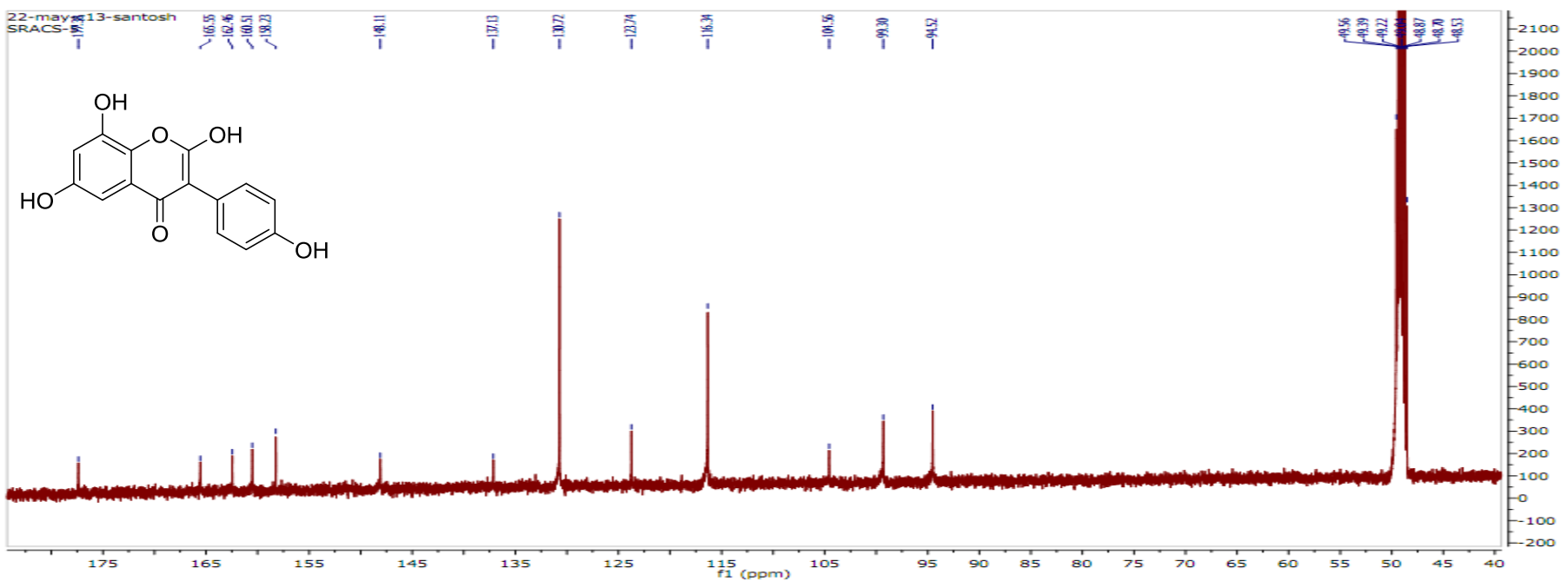
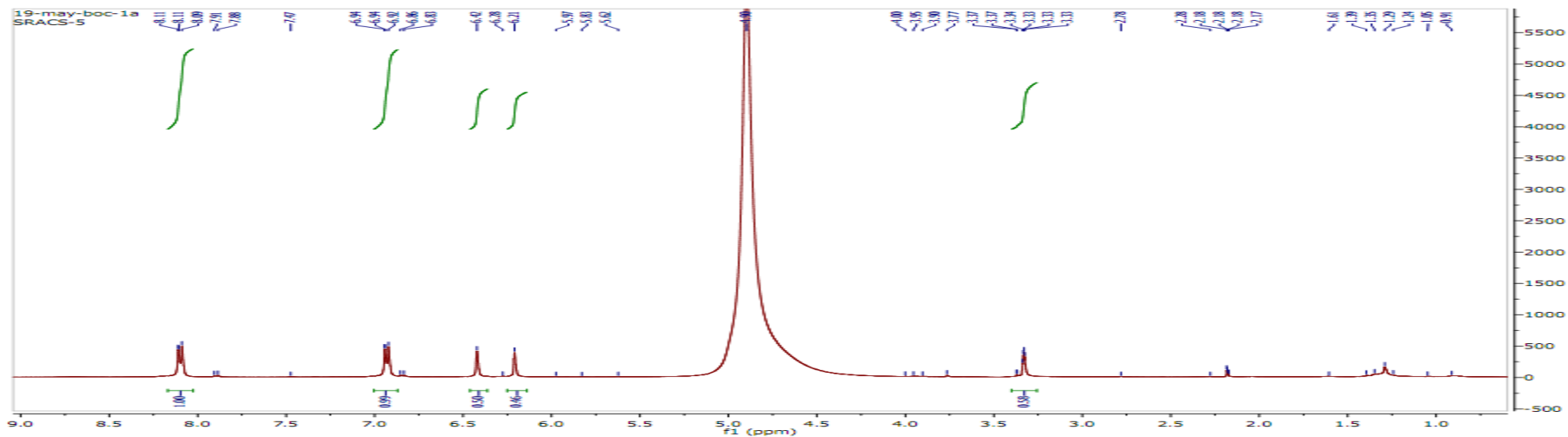
^1H NMR & ^{13}C NMR of Betulinic acid



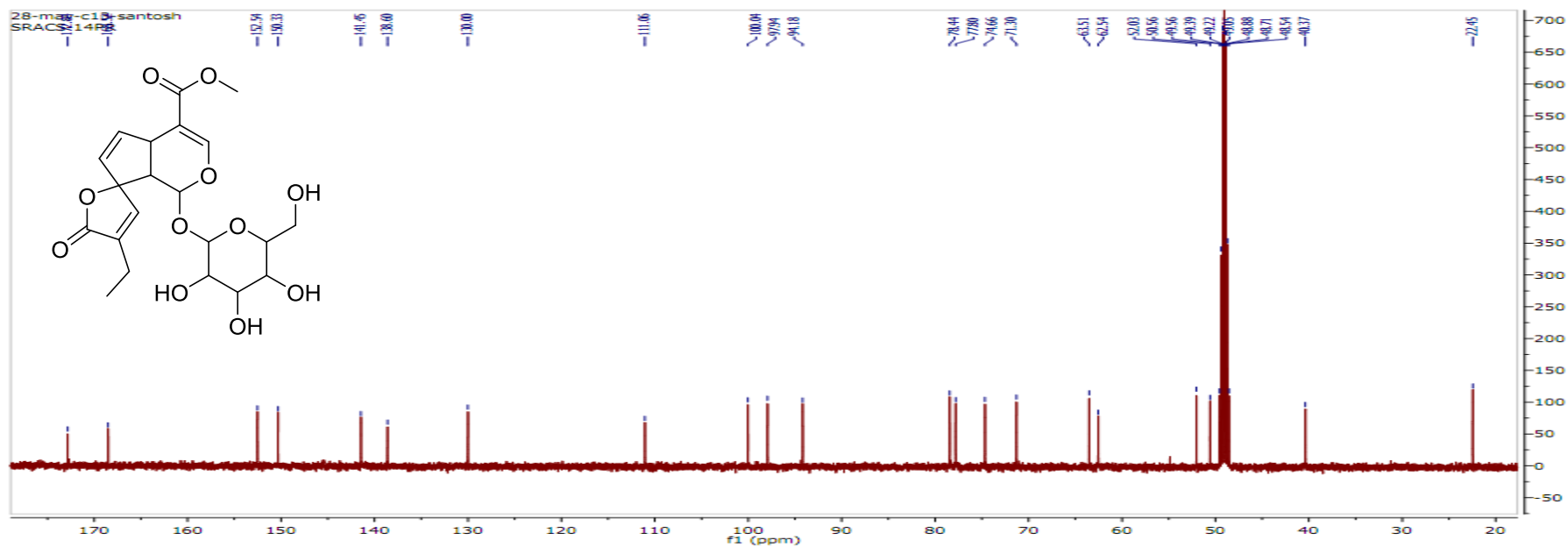
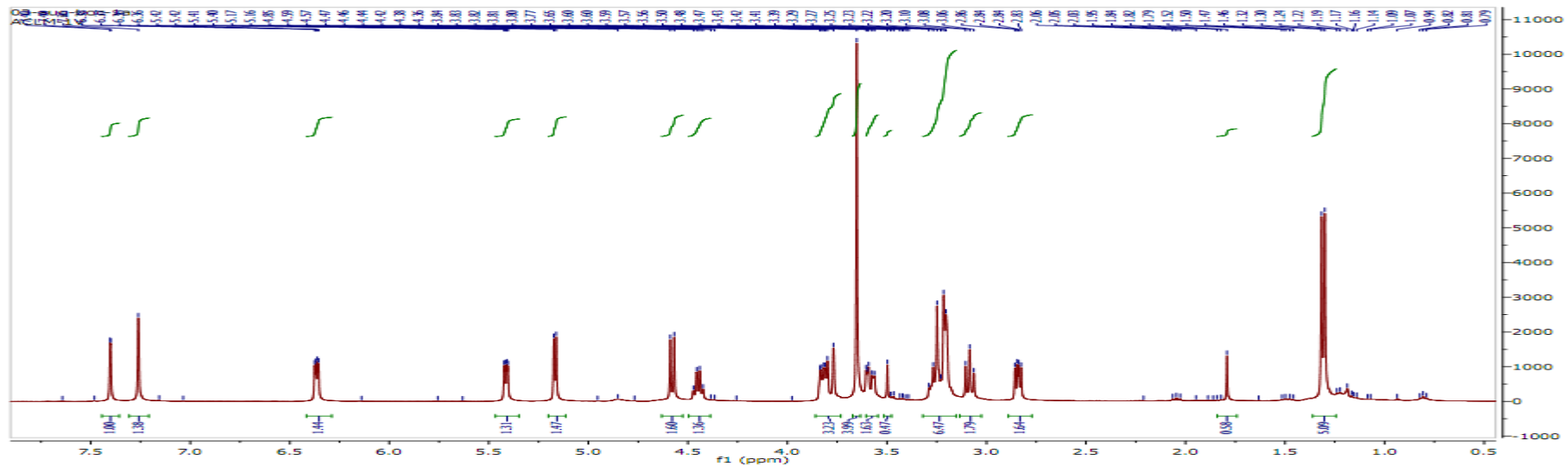
^1H NMR & ^{13}C NMR of Ursolic acid



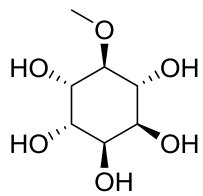
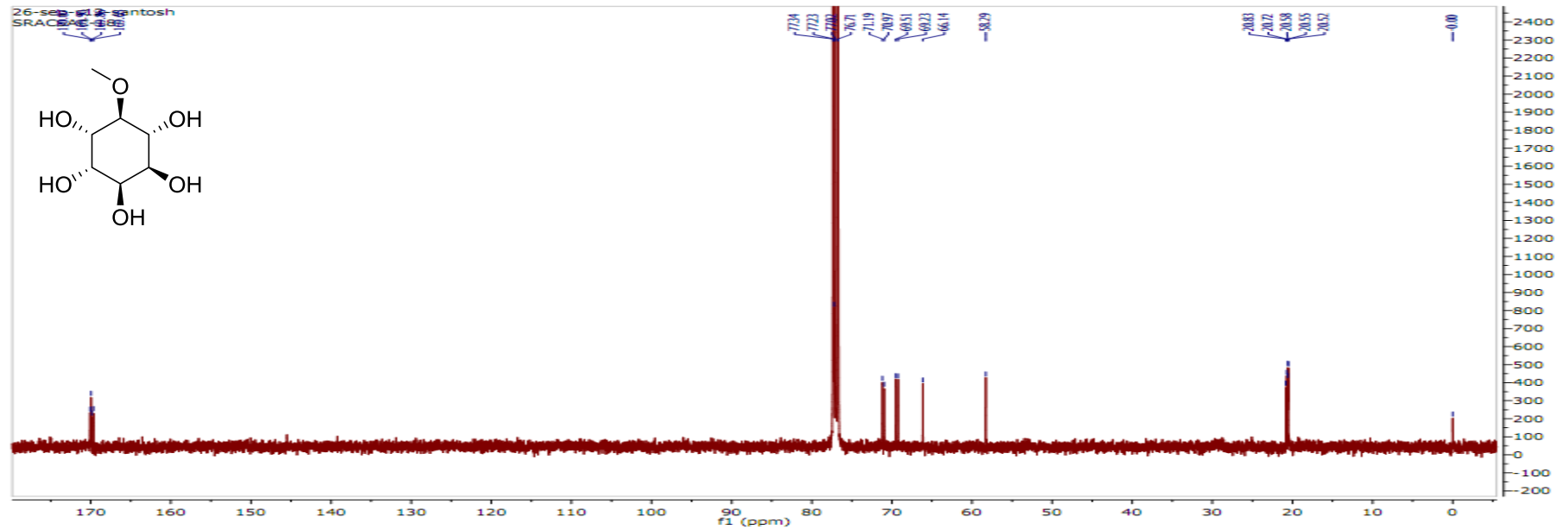
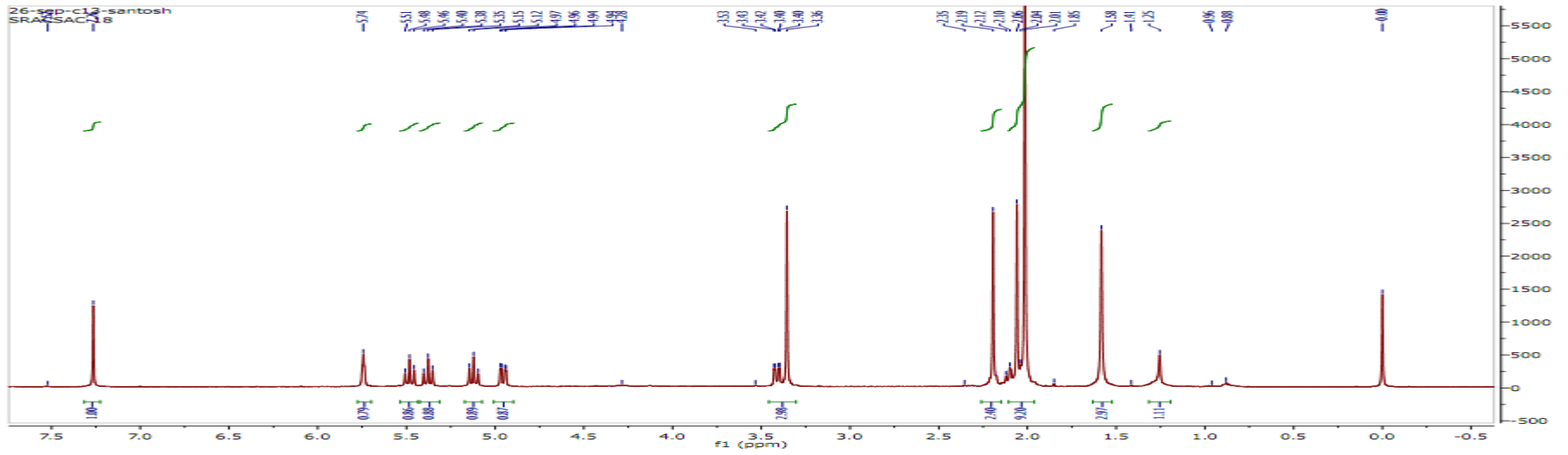
^1H NMR & ^{13}C NMR of 2,6,8-trihydroxy-3-(4-hydroxyphenyl)-4H-chromen-4-one



^1H NMR & ^{13}C NMR of Allamandin glycoside



^1H NMR & ^{13}C NMR of Pinitol acetate



RESULT & DISCUSSION

1. Considering the importance the species in Indian System of Medicine (ISM) and traditional use, the chemical investigation of whole plant was carried out which resulted in the isolation of eleven medicinally noteworthy secondary metabolites.
2. Betulinic acid, pinitol and a flavonoid are reported first time from this plant.
3. The structures of isolated compounds were elucidated mainly by one-dimensional, two-dimensional NMR, MS studies and by comparison with the spectral data in literature.
4. Ursolic acid (4) was found major component (natural abundance: 1.118%), allamdin glucoside (2) (0.0353%) and betulinic acid (3) (0.019%) the least which is advantageous as all are known for potent anticancer, anti-microbial activities.

REFERENCES

1. Kishore et al., Alkaloids as potential anti-tubercular agents, *Fitoterapia (Elsevier)*, (2009), 80: p. 149-163.
2. Gautam et al., Indian medicinal plants as a source of antimycobacterial agents, *Journal of Ethnopharmacology*, (2007), 110(2): p. 200-234.
3. Khazir et al., Natural products as lead compounds in drug discovery, (2007), *Journal of Asian natural product research*, 15(7): p. 764-788
4. Nayak et al., A. Evaluation of wound healing activity of *Allamanda cathartica*. L. and *Laurus nobilis*. L. extracts on rats. *BioMed Central Complementary Alter. Med.* 2006; 5: 6-12.
5. Chakraborty et al., Miracle of herbs in antibiotic resistant wounds and skin infections: treasure of nature – a review/ perspective, *Pharma science monitor*, Vol - 4, Issue - 4, Jul-Sept 2013
6. Pothan et al., In vitro hepatoprotective activity of *Allamanda Cathartica* on the BRL3A cell line, *International journal of Institutional Pharmacy and Life sciences*, (2014), 4(3).

7. Jewers et al., Constituents of *Allamanda Cathartica*, *Asian Journal of Pharmacy*, (1971), 2(1): p. 5-8.
8. Coppen et al., Iridoids with algicidal from *Allamanda Cathartica*, *Phytochemistry* (Elsevier), (1983), 22(1): p. 179-182.
9. Kupchan et al., Isolation and structural elucidation of Allamandin, an antileukemic iridoid lactone from *Allamanda Cathartica*, *Journal of Organic Chemistry*, (1974), 39(17): 2477-2482.

A scenic view of a coastline with a bright sun reflecting on the water and mountains in the background. The sun is positioned in the upper left, creating a strong lens flare and a shimmering path of light across the blue water. The coastline features dark, rocky shorelines and green hills in the distance under a clear blue sky.

THANK YOU
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