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Structural Analysis of the Bioactive Compounds in *Momordica charantia* (Bitter Melon) Leaf and Its Potential Medicinal Properties

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Abstract

Bioactive compounds present in Momordica charantia extract were isolated and characterized in order to investigate the relationship of the structure's functional groups and their medicinal properties. Soxhlet extraction method was used to isolate bioactive compound using preferred solvents, both organic and aqueous extract were characterized using GC-MS, while the bioactive compounds were identified based on the chirality of elucidated compounds and the Structural activity relationship of each identified bioactive compound present in Momordica charantia. The result revealed two identified bioactive compounds (squalene and Pyrimidine-4-fluoro-6-dimethylamine obtained in the plant's petroleum ether solvent. Four bioactive compounds were obtained in the ethanol solvent namely: neophytadiene, 9,12,15-Octadecatrien-1-ol-(Z,Z,Z), 3,5,7-triamino-1-azaadamantane, Pyrimidine-4-fluoro-6-dimethylamine and 2-Dicyanomethylene-8H-pyrrolo[2,3-b]indole-3-carboxamide. The SAR study provide valuable insights of the specific functional groups in each bioactive compounds and their potential therapeutic applications. The study shows the bioactive molecules may serve as lead molecules for new drug screening, for various diseases, including infections, cancer, and inflammatory disorders. The study verified the traditional medicine hypothesis that Momordica charantia extract has numerous medicinal properties and it is a rich source of bioactive compounds.

Keywords: Phytochemicals, *Mormodica charantia*, GC-MS, structural activity relationship, medicinal properties, bioactive compounds.

Introduction

Momordica charantia is basically a medicinal plant which belongs to the family Cucurbitaceae and was first discovered by a renowned botanist Linnaeus. It is tropical vine with phytochemical rich in alkaloids, polypeptides, and terpenes, which can help when in tackling various health issues [1]. The fruit of the plant is consumed in Asia and Africa continents, as food due to rich source of vitamins, minerals, and flavonoids and phenolic compounds. The phenolic compounds and phytosterols such as β-sitosterol present in the Bitter melon plant extract has been reported to show high antioxidant and anti-inflammatory activity, which can help protect pancreatic β-cells and increase insulin levels [2].

Some of the phytochemical bioactive compounds have been identified in the plant's leaves, fruit, and seeds, exhibit various biological activities, and health benefits [3].

Specific functional groups and molecular structures are key to medicinal properties exhibited by a bioactive compound. SAR study helps identify important functional group responsible for the bioactivity of the compound. While variation of some of these functional groups, can result to different analogues with either less or more bioactivities. Hence this study provides a good insights into the medicinal properties of bioactive compounds in *Momordica charantia* plant. QSAR studies also help identify specific functional groups and molecular structures that are attributed to a compounds' medicinal properties, SAR studies identify these key components of the compound [4].

Momordicin and Cucurbitacins are some of the major phytochemicals identified in *M. charantia*. The cucurbitacins has tetracyclic ring and it is a triterpene. Momordicin I is a specific type of cucurbitacins which is a triterpenoid, which is responsible for the anti-diabetic and hypoglycaemia activities of the plant [5]. For instance, goyaglycosides, goyasaponins and momordicosides are Cucurbitacins identified from the methanolic extract of *M. charantia* fruits.

Cucurbitane triterpenoids: identified in *M. charantia* dried gourds, were reported to lower blood sugar in diabetic mice indicating *M. charantia* may have insulin-like activity [6, 7, 8]. Cucurbitane-type triterpenoids has also shown that *M. charantia* exhibit anti-inflammatory and antioxidant activities due to their unique molecular structure

Steroids, tannins, and glycosides, phlobatannins, tannins, and cardiac glycosides are also of the phytochemicals identified in the plant. A study analyzing the aqueous and ethanolic leaf extracts of *M. charantia* reported the presence of glycosides in significant amounts, with cardiac glycosides being the most abundant (42.55±0.02 mg/100g in aqueous extract and 61.44±0.01 mg/100g) in ethanol extract [9].

Materials and Methods

Sample Preparation

Momordica charantia leaves used for this study was obtained from the plant which was yet to produce the bitter melon in Igbesa community in Ado Odo LGA of Ogun Sate in May 2021. The plant leaves samples were identified by a botanist at University of Lagos with herbarium number 100527. The plant's leaves were dried at room temperature for a week.

Petroleum Ether and Ethanol Soxhlet Extraction:

A Soxhlet apparatus was used to extract 50 g of leaf powder with petroleum ether. The extraction process was repeated for three hours, allowing the solvent to reflux and extract the desired

compounds. The procedure was repeated using ethanol solvent. The extracts were then concentrated using a distillation process, and the solvent was removed.

GCMS Analysis

Each *Mormodica charantia* extract was characterized by GCMS (Perkin-Elmer GC Clarus 500 system) using electron ionization to produce fragmentation pattern that can easily identify bioactive phytochemicals present.

Results and Discussion

Table 1: GC-MS analysis of bioactive compounds found in *Mormodica Charantia* leaf ethanolic and petroleum extract and its potential medicinal properties

Bioactive Compounds in *M. charantia*	**Class / Molc. Formula**	**Medicinal Properties**	**Ref.**
Neophytadiene	Diterpenoid C20H38	Antibacterial activity.	[10]
9,12,15-Octadecatrien-1-ol, (Z,Z,Z).	Fatty Alcohol C18H32O	Anti-inflammatory, antioxidant, hepatoprotection	[11]
3,5,7-Triamino-1-azaadamantane	Heterocyclic C9H18N4	Anti-cancer.	[12]
2-Dicyanomethylene-8H-pyrrolo[2,3-b]indole-3-carboxamide	Heterocyclic	Anti-inflammatory, antimicrobial, anti-cancer.	[13]
Pyrimidine-4-fluoro-6-dimethylamine	Alkaloid C6H8FN3	Anti-inflammatory, antimicrobial, anticancer.	
Squalene	Triterpene C30H50	Anti-oxidant Cardioprotective	[12]

Mass spectrum of bioactive compounds:

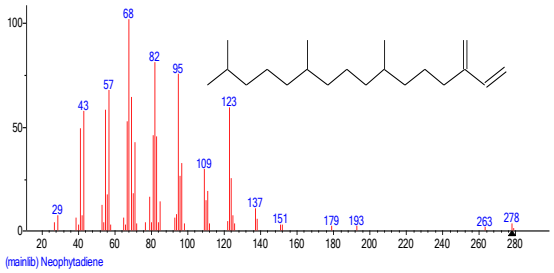


Figure a: Mass spectrum of Neophytadiene

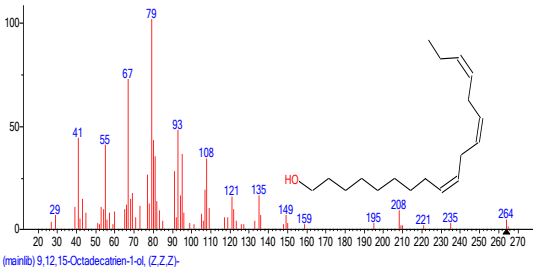


Figure b: Mass spectrum of 9,12,15-Octadecatrien-1-ol, (Z,Z,Z)

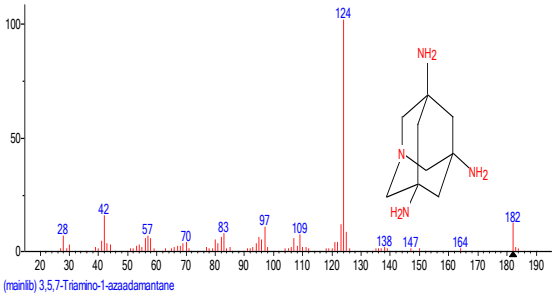


Figure c: Mass spectrum of 3,5,7-Triamino-1-azaadamantane

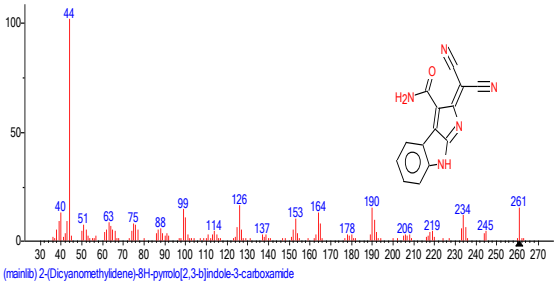


Figure d: Mass spectrum of 2-Dicyanomethylene-8H-pyrrolo[2,3-b]indole-3-carboxamide

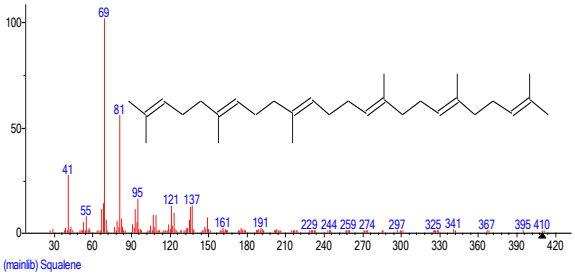


Figure f: Mass spectrum of Squalene

Discussion

Neophytadiene structure and its biological activities: Figure A, indicates that the mass spectrum and elucidated structure of Neophytadiene is a di-terpene with terminal double bonds and methyl groups. These features influence its biological activity, including its anxiolytic-like and anticonvulsant effects [9] Studies have shown that the presence of these functional groups is crucial for the biological activity of Neophytadiene

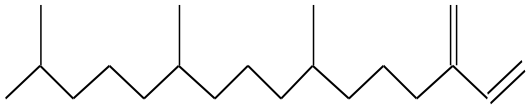


Figure 1: Neophytadiene elucidated by GCMS.

SAR of Functional Groups and their Biological activity:

- Double Bonds (C=C): The presence of multiple double bonds in neophytadiene makes it an unsaturated hydrocarbon. These double bonds contribute to the molecule's reactivity and can be involved in various chemical reactions.
- Methyl Groups (CH_3): Neophytadiene has several methyl groups attached to the main carbon chain. These methyl groups can affect the molecule's polarity, solubility, and overall biological activity.
- Isoprenoid Units: Neophytadiene is a diterpene, meaning it's built from multiple isoprenoid units. This structural feature is common in many natural products and can influence how the molecule interacts with biological targets.

Biological Activity

The result was also consistent with a previous research in which Neophytadiene, was reported to

interact with GABA receptors, leading to its anxiolytic-like, anti-depressant-like, anticonvulsant, and sedative effects [9]. The Neophytadiene bioactive identified structure in M. charantia was similar to the report on the biological activities of Neophytadiene exhibiting antibacterial activity in the methanolic leaf extract of Abutilon Pannosum [15].

The prenyl groups in neophyte diene are crucial for binding to GABA receptors, thereby mediating its neuropharmacological activity [16].

9,12,15-octadecatrien-1-ol (Z,Z,Z) structure and its biological activities

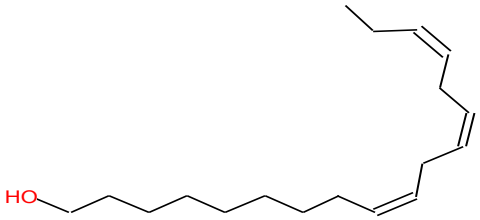
Important functional groups responsible for the bioactivities of 9,12,15-Octadecatrien-1-ol, (Z,Z,Z) can be attributed to the following: 1) An alcohol (-OH) at the 1st carbon position and three double bonds (alkene) at the 9th, 12th, and 15th carbon positions. Alcohol (-OH):

or hydroxyl group (OH) at the 1st carbon makes the molecule hydrophilic and contributes to its ability to interact with water and participate in hydrogen bonding.

The hydroxyl group (-OH) at the end of the chain is the primary functional group, making it an alcohol.

Alkenes (Double Bonds): The (Z,Z,Z) designation indicates that these double bonds are in a cis (Z) configuration. The three double bonds (C=C) at positions 9, 12, and 15, indicated by "(Z,Z,Z)", impacts the molecule's shape, reactivity, and potential biological activities which is believed to be responsible for its antimicrobial and antioxidant properties when bounded to complimentary functional group of its biological target.

C18 Hydrocarbon chain Lipophilicity: The long hydrocarbon chain (18 carbon atoms) and the presence of double bonds contribute to the molecule's lipophilicity, meaning it has a higher affinity for lipids (fats) and non-polar environments. Making the compound a safe therapeutic bioactive drug compound that can cross most cell fat membranes.



9,12,15-Octadecatrien-1-ol, (Z,Z,Z)

Previous Research has shown that the unique structure of 9,12,15-octadecatrien-1-ol (Z,Z,Z) is responsible for its anti-inflammatory, antioxidant, and hepatoprotective effects [10]. 9,12,15-Octadecatrien-1-ol (Z,Z,Z) has also been reported to possess antioxidant activity and protected against oxidative damage [7]. A study by Singh et al. (2019) found that this compound protected the liver against damage caused by toxins and reduced liver inflammation. These findings suggest that 9,12,15-Octadecatrien-1-ol (Z,Z,Z) may be useful in the treatment of liver diseases [2].

3,5,7-Triamino-1-azaadamantane structure and its biological activities

The compound's unique structure and amino group is important for its anti-inflammatory properties. [13].

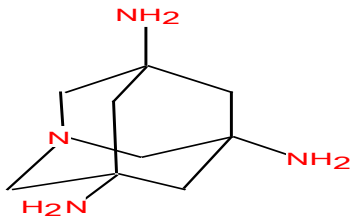


Figure c: 3,5,7-Triamino-1-azaadamantane

Functional Groups:

Primary amino groups:

The amino groups (NH_2) are essemtial for the compound's interactions.. Modifying or removing these groups could significantly alter its bioactivity.

2-dicyano-methylene-8H-pyrrolo-(2,3-b)-indole-3-carboxamide structure and its biological activities

The compound 2-Dicyanomethylene-8H-pyrrolo[2,3-b]indole-3-carboxamide (2-DCM-PI-3-carboxamide) is a complex molecule with a fused ring system. Functional groups include: Indole ring which is a bicyclic benzene ring fused to a pyrrole ring. Dicyanomethylene Group: A substituted methylene group with two cyano groups attached. And carboxamide group: which is a carbonyl group attached to a nitrogen atom, which is also part of a pyrrole ring.

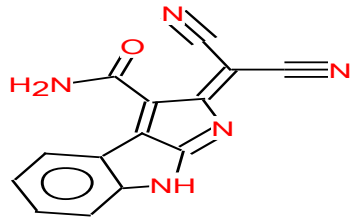
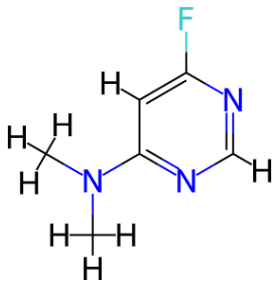


Figure d: 2-Dicyanomethylene-8H-pyrrolo [2,3-b]indole-3-carboxamide

Importance of the Indole/Pyrrole Framework: The presence of either an indole or a pyrrole ring is crucial for biological activity, particularly for binding to specific receptors like CB1. The carboxamide moiety can affect the activity and selectivity toxicity to foreign cells.

Pyrimidine-4-fluoro-6-dimethylamine structure and its biological activities

Pyrimidine-4-fluoro-6-dimethylamine contains a pyrimidine ring, a fluorine atom, and a dimethylamino group. The pyrimidine ring is a six-membered ring with two nitrogen atoms. The fluorine and dimethylamino positions on the ring are likely to enhance its biological activity.



Pyrimidine-4-fluoro-6-dimethylamine

Functional Groups and its Structure:

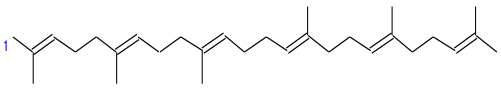
- The presence of N-methyl group class this structure as an alkaloid.
- The stereo-chemical structure shows more than one chiral carbon atom.
- Hence the absolute configuration of this bioactive enantiomers and diastereomers can serve as potential lead compounds for drug development.
- Pyrimidine ring is crucial for its biological activity, as seen in DNA/RNA bases.
- Fluorine (F): modifies electronic properties, potentially enhancing potency or specificity.
- Dimethylamino group acts as an electron-donating, influencing basicity and interactions with acidic sites.

Squalene structure and its biological activities.

Squalene, with unique structure, has six double bonds and a triterpene backbone, contributing to its diverse biological activities.

Squalene's Structure:

- The double bonds in squalene helps to neutralize free radicals and impacts its antioxidant properties:
- Squalene as important precursor in cholesterol and steroid biosynthesis in plants
- Squalene can serve as a moisturizer due to its emollient properties and ability to enhance skin hydration and protect against lipid peroxidation.



Squalene is well known precursor to cholesterol and other sterols. Squalene is a tri-terpenoid with 6 isoprene units, and 6 double bonds. The first C15 part of the molecule is joined head to tail to the other C15 molecule. In the biosynthesis of squalene from pre-squalene. Two molecules of FPP is isomerized to presqualene. Presqualene is alkylated undergoes rearrangement, and reduction to give the squalene compound in plant. Squalene has been reported to exert great antioxidant activity.

Summary:

The findings of the study of the structurally important functional group of bioactive compounds identified *M. charantia* leaves extracts, indicate the following:

- Two bioactive compounds Pyrimidine-4-fluoro-6-dimethylamine and squalene were identified by the GCMS in the petroleum ether extract of the plant.
- Pyrimidine-4-fluoro-6-dimethylamine showed anti-inflammatory, and anticancer properties
- Squalene is reported to show anti-oxidant properties and a potential lead compound for cardio-health.
- Four bioactive compounds were found in the ethanol extract namely: neophytadiene, 9,12,15-Octadecatrien-1-ol-(Z,Z,Z), 3,5,7-triamino-1-azaadamantane, and 2-

Dicyanomethylene-8H-pyrrolo[2,3-b]indole-3-carboxamide

- Neophytadiene was reported to exhibit anti-bacterial effects.
- 9,12,15-Octadecatrien-1-ol-(Z,Z,Z) shows anti-inflammatory, antioxidant, hepatoprotection effects.
- 3,5,7-triamino-1-azaadamantane indicates an anti-tumor or anti-cancer activity.
- Pyrimidine-4-fluoro-6-dimethylamine is reported to show, antimicrobial, and anticancer activities
- 2-Dicyanomethylene-8H-pyrrolo[2,3-b]indole-3-carboxamide identified shows important functional groups responsible for its anti-inflammatory, antimicrobial, anti-cancer, antioxidant, and neuro protective effects.

This study provides valuable insights into the phytochemical profile of *Mormodica charantia* leaves suggesting potential use of the for drug screening, drug development and further structural activity relationship study.

Recommendations:

These compounds may be useful in developing treatments for various diseases, including cancer, inflammatory disorder, and bacterial infection:

- **Cancer**: 3,5,7-Triamino-1-azaadamantane and Pyrimidine, 4-fluoro-6-dimethylamine show potential as anticancer agents.
- **Inflammatory disorders**: Neophytadiene, 9,12,15-Octadecatrien-1-ol, (Z,Z,Z), and 2-Dicyanomethylene-8H-pyrrolo[2,3-b]indole-3-carboxamide maybe help alleviate inflammation.
- **Infections**: Neophytadiene,2-Dicyanomethylene-8H-pyrrolo[2,3-b]indole-3-carboxamide, and Pyrimidine, 4-fluoro-6-dimethylamine exhibit antimicrobial properties.
- The identification and characterization of these compounds provide a scientific basis for the traditional use of *Momordica charantia* in medicine.
- The study's findings have significant implications as a good source to screen bioactive compounds with promising medicinal properties.
- The identified bioactive compounds may serve as lead molecules for understanding impact of important group in a compounds bioactivity.

The study concluded that the plant a good source of bioactive phytochemical compounds with medicinal properties as suggested by ancient traditional medicine.

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