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RESEARCH ARTICLE
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BIOAVAILABILITY AND PHARMACOKINETICS, DRUG LIKELINESS PREDICTIONS OF BIOACTIVE COMPOUNDS OF MUSA ACUMINATA USING SWISS ADME AND PHYRE 2.0 SOFTWARE

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ABSTRACT

This study presents an in silico evaluation of bioactive compounds from *Musa acuminata*, focusing on their pharmacokinetic behavior, bioavailability, and drug-likeness using SwissADME and Phyre2.0 tools. Selected phytochemicals were analyzed for absorption, distribution, metabolism, and excretion (ADME) properties, alongside key medicinal chemistry filters such as Lipinski's Rule of Five. Swiss ADME predictions revealed promising oral bioavailability, favourable lipophilicity, and minimal cytochrome P450 inhibition for several compounds. Phyre2.0 was employed to model target protein structures, enabling preliminary insights into ligand-protein compatibility. Compounds like ferulic acid, catechin, and β-sitosterol demonstrated optimal drug-likeness profiles, suggesting potential for further pharmacological exploration. This integrative computational approach streamlines early-stage screening and supports the identification of natural leads for future drug development.

MATERIALS AND METHODS: The current study will be the first to use the free online tool SWISS ADME to report the ADME characteristics of Musa acuminata. The ADME properties of five bioactive compounds from licorice were screened and the results were evaluated.

RESULT: Six bioactive compounds were identified to have good gastrointestinal absorption and can penetrate the brain . These compounds include Dopamine showing better lipophilicity, hydrogen bond donor and hydrogen bond acceptor.

CONCLUSION: This method is for determining the ADME characteristics of the bioactive compounds in Licorice. Based on the information, it was predicted that licorice would be effective in managing the disease. To validate these findings, it is advisable to conduct further controlled experimental research exploring the bioactive compounds' pharmacological effects.

KEYWORDS: ADMET LAB 3.0, Musa acuminata, bioactive compounds, medicinal plant, SWISS ADME, drug likeliness.

INTRODUCTION:

Medicinal plants, also referred to as medicinal herbs, are botanical sources rich in bioactive compounds. These plants have been used since prehistoric times in both traditional and modern medicine to treat and prevent a wide spectrum of health conditions. Their therapeutic potential stems from active constituents such as alkaloids, polyphenols, glycosides, and terpenes, which exhibit antimicrobial, anti-inflammatory, analgesic, and other pharmacological properties. For centuries, these naturally occurring compounds have served as the foundation for developing pharmaceutical drugs and health-promoting formulations [1-4].

Musa acuminata, a banana species indigenous to Southern Asia, is primarily found across the Indian subcontinent and Southeast Asia. It serves as the genetic foundation for many modern dessert bananas, though some varieties are hybrids involving *Musa balbisiana*.[5] Archaeological evidence suggests that humans began cultivating this plant as early as 8000 BCE, making it one of the earliest domesticated crops in agricultural history. [6,7]

Botanically, *Musa acuminata* is identified as a herbaceous, evergreen, and perennial plant, though it is not classified as a tree. Its trunk, referred to as a pseudostem, consists of densely layered leaf sheaths that arise from corms, which may be either fully or partially buried. [8] The plant's leaves emerge from the top of these sheaths or petioles. Notably, in the subspecies *M. acuminata truncata*, the leaf blade (lamina) can reach dimensions of up to 6.7 meters (22 feet) in length and 0.99 meters (39 inches) in width.

BIOACTIVE COMPOUNDS:

There are some bioactive compounds from Musa acuminata

1. Myricetin
2. Apigenin
3. Glycosides
4. Dopamine
5. N-Acetyl serotonin
6.Rutin

*1.*MYRICETIN: Myricetin belongs to the flavonoid subclass of polyphenolic compounds and is recognized for its potent antioxidant activity. It is commonly found in a variety of dietary sources such as vegetables (e.g., tomatoes), fruits (e.g., oranges), nuts, berries, tea, and red wine. Structurally, myricetin shares similarities with other flavanols like fisetin, luteolin, and quercetin, and exhibits comparable biological functions.The average daily intake of myricetin varies with dietary habits; studies conducted in the Netherlands report an estimated consumption of approximately 23 mg/day. Biosynthetically, myricetin is derived from taxifolin via the intermediate (+)-dihydromyricetin. This intermediate can be further metabolized into laricitrin and syringetin, both of which are flavonols. Alternatively, myricetin may also be synthesized directly from kaempferol. Notably, dihydromyricetin is marketed as a dietary supplement and has been investigated for its potential role as a partial GABAA receptor modulator, particularly in the context of Alcohol Use Disorder (AUD), though its efficacy remains debated.[9-14]

2. APIGENIN: Apigenin (4′,5,7-trihydroxyflavone) is a naturally occurring flavone compound widely distributed in various fruits, vegetables, and herbs. Structurally, it serves as the aglycone component of several glycosides. This yellow crystalline substance has historically been utilized as a dye for wool

due to its pigmentation properties. Among dietary sources, parsley—both fresh and dried—contains the highest concentrations of apigenin, with fresh parsley offering approximately 215 mg per 100 grams and dried parsley reaching up to 45 mg per gram. Other notable sources include celery, celeriac, and chamomile tea. Chamomile flowers, in particular, are rich in apigenin, comprising nearly 68% of their total flavonoid content. While apigenin is present across a wide range of plant-based foods, these specific herbs and vegetables are considered its most potent sources. [15-16]

3. GLYCOSIDES: A **glycoside** (/ˈglaɪkəsaɪd/) is a type of molecule where a sugar unit is chemically bonded to another functional group through a glycosidic linkage, typically involving the sugar's anomeric carbon. This bond can occur via different atoms, resulting in various classes: O-glycosides (oxygen-linked), N-glycosides (nitrogen-linked or glycosylamines), S-glycosides (sulfur-linked or thioglycosides), and C-glycosides (carbon-linked). However, the IUPAC advises using the term C-glycosyl compound instead of "C-glycoside" and recommends the Haworth projection for accurate stereochemical representation.In biological systems, glycosides serve multiple roles. Plants often store bioactive compounds in the form of inactive glycosides, which become active upon enzymatic hydrolysis—a process that cleaves the sugar moiety and releases the aglycone. These plant-derived glycosides are widely used in pharmaceuticals due to their therapeutic properties.Some insects, such as Heliconius butterflies, utilize plant glycosides as a chemical defense mechanism, incorporating them into their bodies to deter predators. In mammals, including humans, glycosylation of toxic substances facilitates their detoxification and excretion, as the sugar attachment enhances solubility and aids in elimination.[17-20]

4.DOPAMINE : Dopamine (DA), short for 3,4-dihydroxyphenethylamine, is a key neuromodulator involved in various cellular functions. Belonging to both the catecholamine and phenethylamine chemical families, dopamine is classified as an amine. It is biosynthesized through the decarboxylation of its precursor, L-DOPA, which is produced in the brain and kidneys. Beyond humans, dopamine synthesis also occurs in plants and across many animal species.In the central nervous system, dopamine acts as a neurotransmitter, facilitating communication between neurons by transmitting signals across synapses. The brain contains multiple dopamine pathways, each serving distinct roles. One prominent pathway is associated with the motivational aspects of reward-driven behaviour—dopamine levels typically rise in anticipation of rewarding stimuli. This mechanism is also exploited by many addictive substances, which either stimulate dopamine release or inhibit its reuptake, prolonging its action. Additional dopamine circuits are crucial for regulating motor functions and hormonal release. Collectively, these pathways constitute the brain's dopamine system, which exerts broad neuro modulatory effects across physiological and behavioural domains.[21-25]

5. N-ACETYL SEROTONIN: N-Acetyl serotonin (NAS), also referred to as normelatonin, is a naturally occurring intermediate in the biosynthetic pathway that converts serotonin into melatonin within the body. While it serves as a precursor in melatonin synthesis, NAS also exhibits distinct biological activities. It functions as an agonist at melatonin receptors—specifically MT1, MT2, and MT3—similar to melatonin itself, and is considered to have neurotransmitter-like properties. Beyond its role in melatonin production, NAS activates TrkB receptors, contributes to antioxidant defense, and is found in brain regions where serotonin and melatonin are absent, implying it may have unique central nervous system functions. Research has highlighted its antidepressant, neurotrophic, and cognitive-enhancing effects, positioning NAS as a potential therapeutic target for conditions such as age-related cognitive decline and depression.[26-33]

6. RUTIN: **Rutin**, also known as **Ruto side**, **quercetin-3-O-rutinoside**, or **sophorin**, is a flavonoid glycoside formed by the combination of the flavanols **quercetin** and the disaccharide **rutinose** (α-L-rhamnopyranosyl-(1→6)-β-D-glucopyranose). This compound is widely distributed across various plant species, particularly in **citrus fruits**, where it contributes to their phenolic profile. The name "rutin" originates from **Ruta graveolens** (commonly known as rue), a plant recognized for its high rutin content. It is also present in **Carboborites edulis**, a succulent plant known for its medicinal properties. **Citrus peels** are especially rich in rutin.[34-38]

MATERIALS AND METHODS :

Modelling platform The SwissADME and Admetlab3.0 :Computational modelling platforms such as SwissADME and ADMETlab 3.0 have become essential tools in modern drug discovery, particularly for screening natural compounds. **SwissADME**, developed by the Swiss Institute of Bioinformatics, provides rapid predictions of physicochemical properties, pharmacokinetics, drug-likeness, and medicinal chemistry friendliness. It evaluates parameters like gastrointestinal absorption, blood-brain barrier permeability, lipophilicity, solubility, and compliance with rules such as Lipinski's and Veber's. **ADMETlab 3.0**, on the other hand, offers a more comprehensive suite of predictions, including absorption, distribution, metabolism, excretion, and toxicity (ADMET) profiles. It integrates machine learning models to assess CYP enzyme interactions, P-glycoprotein substrate status, half-life, and multiple toxicity endpoints such as Ames mutagenicity and carcinogenicity. When applied to phytochemicals from *Musa acuminata*, these platforms enable researchers to identify promising drug candidates by predicting their pharmacokinetic behaviour and safety profiles before experimental validation. This approach streamlines the selection process and supports the integration of traditional plant-based remedies into evidence-based pharmaceutical development.

ADME TOXICITY : The pharmacokinetic behaviour of bioactive compounds from *Musa acuminata*—including flavonoids like myricetin, apigenin, and rutin, as well as neuroactives such as dopamine and N-acetyl serotonin—can be evaluated through ADME parameters: Absorption, Distribution, Metabolism, and Excretion. These properties determine how a compound behaves in the human body and influence its therapeutic potential.

- **Absorption**: Compounds like apigenin and N-acetyl serotonin show high gastrointestinal absorption, suggesting good oral bioavailability. In contrast, rutin and myricetin exhibit poor absorption due to high polarity and molecular weight.
- **Distribution**: Most banana-derived compounds are moderately distributed in tissues. Lipophilic molecules like apigenin may cross the blood-brain barrier, while polar compounds such as rutin are less likely to do so.
- **Metabolism**: Flavonoids and glycosides undergo extensive phase I and phase II metabolism, primarily through cytochrome P450 enzymes. Apigenin and myricetin are known to inhibit CYP1A2, CYP2C9, and CYP3A4, which may affect the metabolism of co-administered drugs.
- **Excretion**: These compounds are typically eliminated via renal and biliary routes. Their half-life varies depending on metabolic stability and conjugation patterns.

MEDICINAL PROPERTIES: *Musa acuminata* exhibits a wide range of medicinal properties attributed to its rich phytochemical composition. Its **antioxidant activity** helps neutralize free radicals and reduce oxidative stress in cells. The **anti-inflammatory effect** aids in lowering inflammation by modulating cytokine production. **Antimicrobial properties** inhibit the growth of bacteria, fungi, and other pathogens, supporting infection control. Its **antidiabetic potential** improves glucose metabolism and enhances insulin sensitivity. The **neuroprotective action** supports brain health by regulating neurotransmitters and protecting neurons from damage. **Wound-healing properties** accelerate tissue regeneration and reduce healing time. Additionally, its **cardioprotective effects** help maintain heart function by reducing lipid accumulation and improving vascular health. Beyond these, *Musa acuminata* also demonstrates **anti-ulcer activity**, which helps protect the gastric lining and reduce the formation of peptic ulcers. Its **anti-diarrheal effect** stabilizes intestinal motility and reduces fluid loss, making it useful in managing gastrointestinal disturbances. The plant's **hepatoprotective properties** support liver function by minimizing oxidative damage and enhancing detoxification pathways. **Antianaemic potential** is attributed to its iron-rich content, which may aid in improving haemoglobin levels and combating fatigue. Moreover, its **immunomodulatory effects** help regulate immune responses, potentially enhancing resistance to infections and inflammatory conditions. These diverse therapeutic actions make *Musa acuminata* a valuable candidate for natural remedy development and integrative medicine.

IN-SILICO MODELLING:

INTRODUCTION OF SWISS ADME : SwissADME is a freely accessible web-based tool developed by the Swiss Institute of Bioinformatics, designed to evaluate the pharmacokinetic and physicochemical properties of small molecules. It plays a crucial role in early drug discovery by predicting key parameters such as gastrointestinal absorption, blood-brain barrier permeability, lipophilicity, solubility, and drug-likeness based on established medicinal chemistry rules. When applied to phytochemicals derived from *Musa acuminata*, including flavonoids like myricetin, apigenin, and rutin, as well as neuroactive compounds such as dopamine and N-acetyl serotonin, SwissADME provides valuable insights into their potential as therapeutic agents. By analysing molecular descriptors and ADME-related features, researchers can identify compounds with favourable oral bioavailability, minimal toxicity, and suitable pharmacokinetic profiles. This predictive capability supports the rational selection of banana-derived bioactive for further experimental validation and development in pharmaceutical research.

DRUG LIKENESS: The concept of drug-likeness refers to the structural and physicochemical properties that make a compound suitable for development as an orally active drug. Phytochemicals derived from *Musa acuminata*, such as flavonoids (myricetin, apigenin, rutin), glycosides, and neuroactive agents like dopamine and N-acetyl serotonin, exhibit promising drug-like characteristics. Many of these compounds comply with key medicinal chemistry filters including Lipinski's Rule of Five, which evaluates molecular weight, lipophilicity (LogP), hydrogen bonding potential, and solubility. For instance, apigenin and N-acetyl serotonin demonstrate favourable gastrointestinal absorption and blood-brain barrier permeability, while maintaining low toxicity profiles. Although some compounds like rutin and myricetin may violate one or more drug-likeness criteria due to high polarity or molecular weight, their bioactivity and therapeutic relevance justify further investigation. Overall, the phytochemical spectrum of *Musa acuminata* offers a rich foundation for identifying lead compounds with acceptable drug-likeness for future pharmacological applications.By using Swiss ADME software we can also produce the 2D & 3D structures of TUG8.

INTRODUCTION OF ADMET LAB 3.0 : ADMETlab 3.0 is a cutting-edge computational platform designed to predict the pharmacokinetic and toxicological properties of chemical compounds, including those derived from natural sources like *Musa acuminata* (banana). This tool plays a pivotal role in early-stage drug discovery by evaluating key ADMET parameters—Absorption, Distribution, Metabolism, Excretion, and Toxicity—using advanced machine learning models and curated datasets. For phytochemicals found in *Musa acuminata*, such as myricetin, apigenin, rutin, dopamine, and N-acetyl serotonin, ADMETlab 3.0 enables researchers to assess drug-likeness, gastrointestinal absorption, blood-brain barrier permeability, cytochrome P450 interactions, and potential toxicity risks including mutagenicity and carcinogenicity. Its user-friendly interface and batch processing capabilities make it ideal for screening complex plant matrices, bridging traditional ethnobotanical knowledge with modern pharmacological evaluation. By providing reliable predictions, ADMETlab 3.0 supports the rational selection of bioactive compounds from *Musa acuminata* for further experimental validation and therapeutic development.

FLOW CHART OF MUSA ACUMINATA:

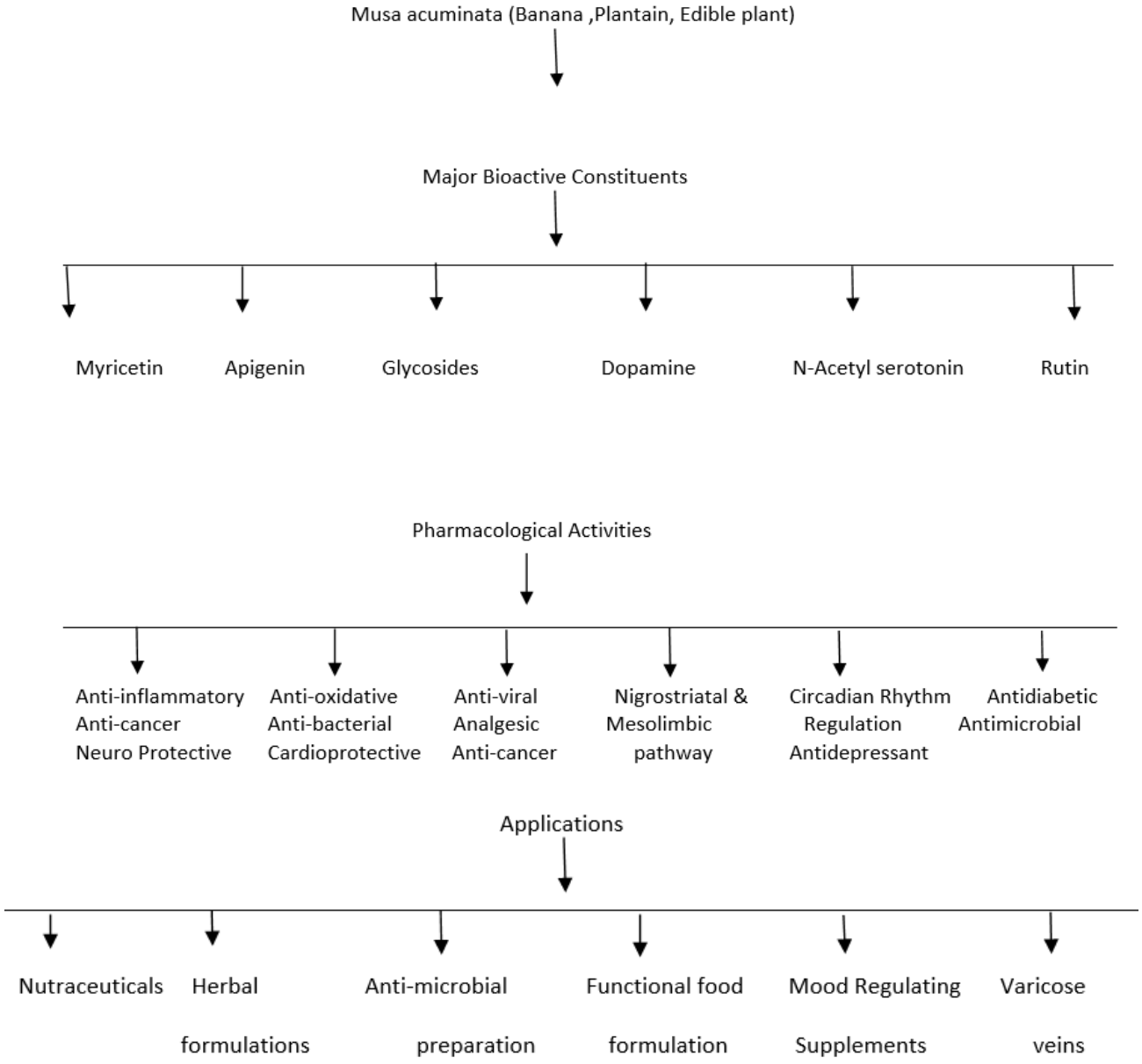
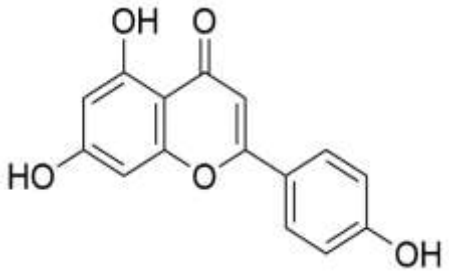
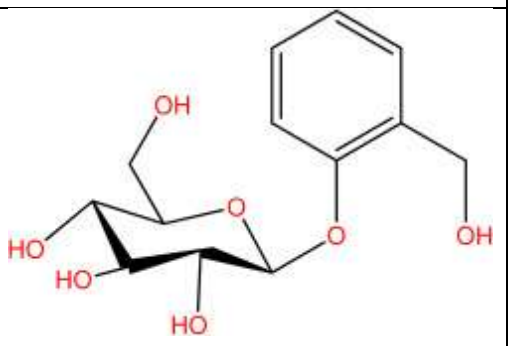
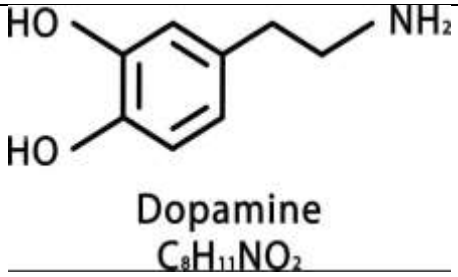
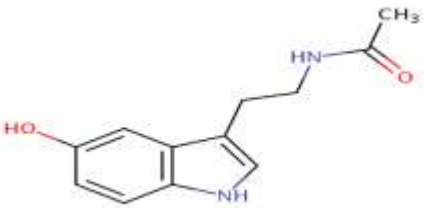
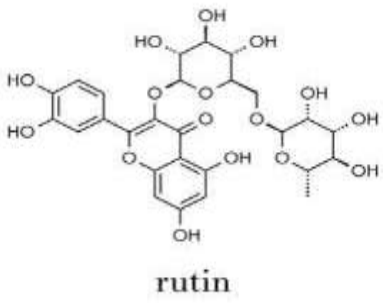


Table 1: General characteristics and PubChem ID of the bioactive compounds of Musa acuminata:

S.no	Bioactive compound	Pub chem ID (CID)	Plant part	Structure
1	Myricetin	5281672	Peel, Pulp	 myricetin

2	Apigenin	5280443	Peel, Pulp, Leaves	
3	Glycosides	Generic term – no single CID	Peel, Stem, Leaves	
4	Dopamine	681	Fruit pulp	
5	N Acetyl Serotonin	903	Fruit pulp	
6	Rutin	5280805	Fruit pulps	

METHODOLOGY:

SwissADME-Based Profiling of Bioactive Compounds from *Musa acuminata*

The SMILES representations of selected bioactive compounds from *Musa acuminata* were retrieved

using PubChem. These molecular descriptors were then input into the SwissADME platform (http://www.swissadme.ch/) to evaluate their pharmacokinetic behavior and physicochemical characteristics. The analysis yielded detailed insights into lipophilicity, water solubility, drug-likeness, and gastrointestinal absorption (Boiled Egg model). The results are visually summarized in the figure below.

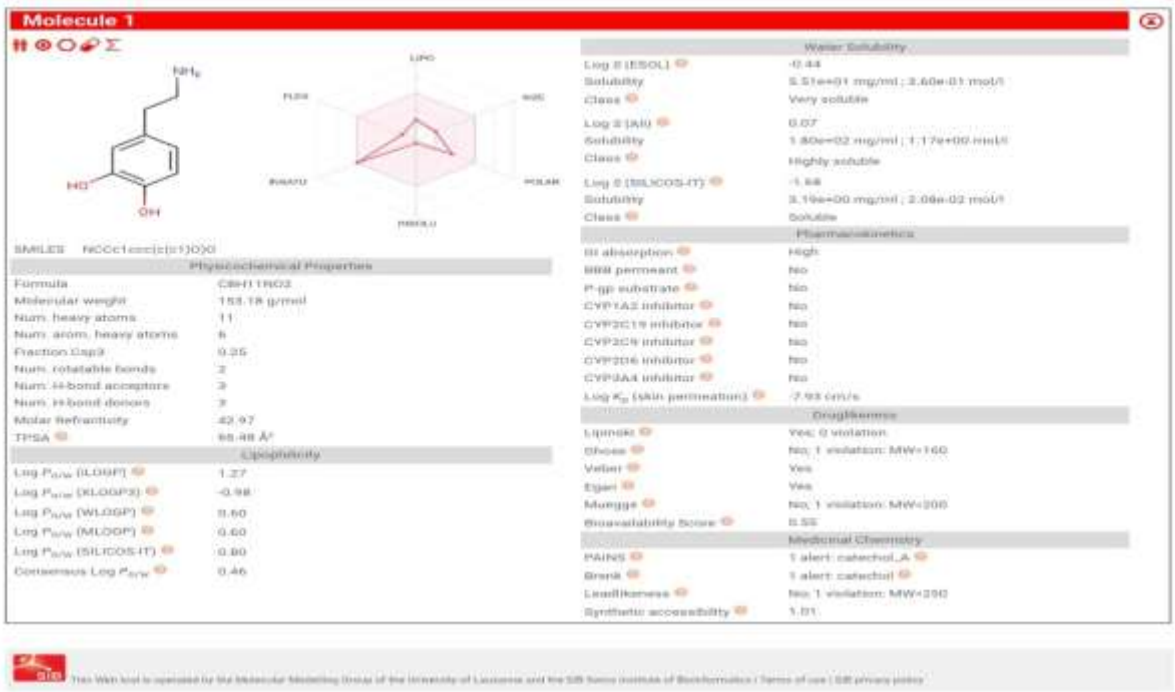


Figure: 1

The SMILES representations of bioactive compounds were retrieved using the PubChem database. These SMILES strings were then input into the ADMETlab 3.0 platform (https://admetlab3.scbdd.com/) to evaluate their toxicity profiles. The analysis provided predictions for various toxicity endpoints, including Ames mutagenicity, carcinogenicity, genotoxicity, and ototoxicity, as illustrated in the figure below:

Figure:2-physicochemical properties of Dopamine

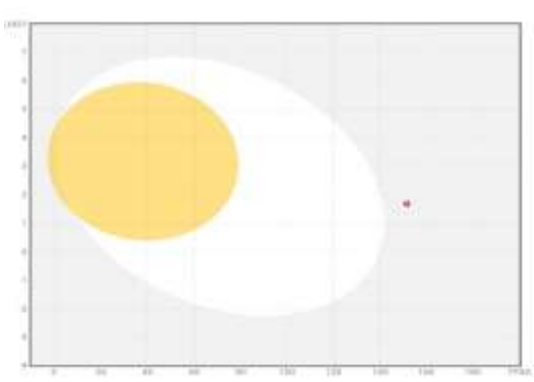


Figure: A(myricetin)

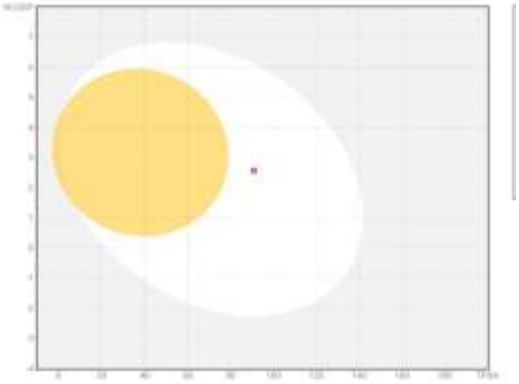


Figure : B(apigenin)

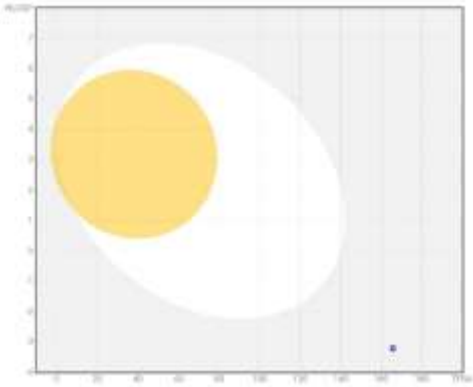


Figure: C(glycosides)

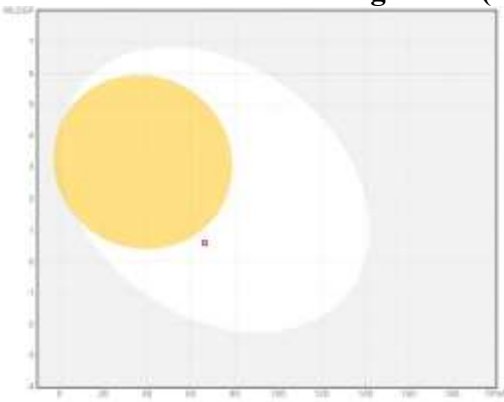


Figure : D(dopamine)

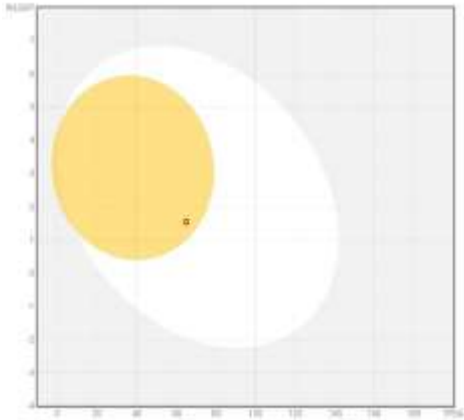


Figure: E (n-acetyl serotonin)

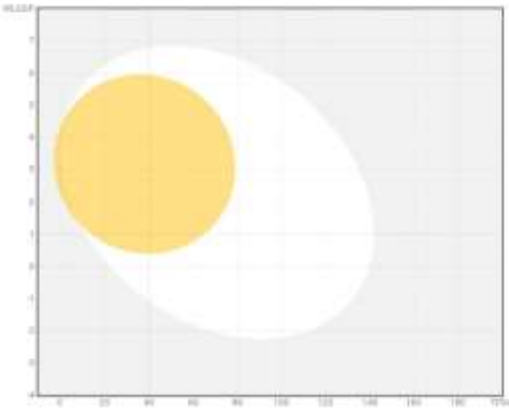


Figure: F(rutin)

Figure-4:A-Myricetin, B-Apigenin ,C-Glycoside, D-Dopamine, E-Rutin, F-Musa acuminata

Figure:A

Figure:B

Figure: C

Figure: D

Figure: E

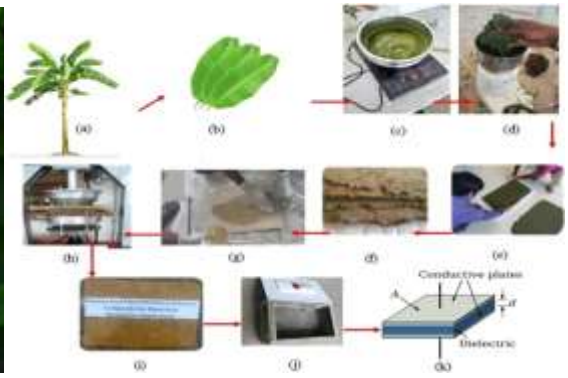


Figure:F

Table:2 Physicochemical properties of the bioactive compounds of Musa acuminata:

Bioactive compounds	Molecular weight	Lipophilicity	No.H-bond donor	No.H-bond acceptor	TPSA	No.of Lipinski rule violation
Myricetin	318.24g/mol	~1.6	6	8	$181A^2$	3
Apigenin	270.24g/mol	~2.5	3	5	$90A^2$	0
Glycosides	180g/mol	~1.0	Highly variable	Highly variable	Highly variable	2-3
Dopamine	153.8g/mol	~0.9	2	3	$66A^2$	0
N-Acetyl serotonin	218.24g/mol	~1.4	2	4	$66A^2$	0
Rutin	610.2g/mol	~1.0	9	13	269 A^2	3

Table:3 Drug likeliness of the bioactive compounds of Musa acuminata:

Bioactive compounds	Pgp substrate	CYP_1A_2	CYP_2C_{19}	CYP_2C_9	CYP_3A_4	CYP_2D_6
Myricetin	No	Inhibitor	Inhibitor	Inhibitor	Inhibitor	Inhibitor
Apigenin	No	Inhibitor	Inhibitor	Inhibitor	Inhibitor	Inhibitor
Glycosides	Variable	Variable	Variable	Variable	Variable	Variable
Dopamine	No	No effect	No effect	No effect	No effect	No effect
N-Acetyl serotonin	No	No effect	No effect	No effect	No effect	No effect
Rutin	No	Inhibitor	Inhibitor	Inhibitor	Inhibitor	No effect

Table:4 Pharmacokinetics of the bioactive compounds of Musa acuminata:

Bioactive compounds	Molecular Formula	Water solublility	GI Absorption	BBB Permeant	Abbot bioavalibility score
Myricetin	$C_{15}H_{10}O_8$	Poorly soluble	Low	No	0.11
Apigenin	$C_{15}H_{10}O_5$	Moderately soluble	High	Yes	0.55
Glycosides	Variable	Moderately soluble	Low to moderate	No	0.17-0.55
Dopamine	$C_8H_{11}O_2$	High soluble	High	No	0.55
N-Acetyl serotonin	$C_{12}H_{14}O_2$	Moderately soluble	High	Yes	0.55
Rutin	$C_{27}H_{30}O_{16}$	Poorly soluble	Low	No	0.17

Table:5 Ames mutagen and carcinogen toxicology properties of the bioactive compounds of Musa acuminata:

Bioactive compound	Ames toxicity	Geno toxicity	Carcino toxicity	Ototoxicity
Myricetin	Negative	No toxic	Low toxic	No toxic
Apigenin	Negative	Low toxic	Low toxic	No Toxic
Glycosides	Negative	Mild to moderate toxic	Variable	No toxic
Dopamine	Negative	Low toxic	Low toxic	No toxic
N-Acetyl serotonin	Negative	Low toxic	Low toxic	No toxic
Rutin	Negative	Mild toxic	Low toxic	No toxic

Result:

The rule also recommends that the number of hydrogen bond donors should not exceed 5. Dopamine contains 2 hydrogen bond donors, which is within the acceptable range. Similarly, the number of hydrogen bond acceptors should be 10 or fewer; dopamine has 3, again complying with the rule. The topological polar surface area (TPSA) should ideally be between 0 and 140 Å² for good oral bioavailability. Dopamine's TPSA is 49.33 Å², which supports efficient absorption. Dopamine shows zero Lipinski rule violations, making it a highly compliant compound. Regarding water solubility, dopamine has a LogS of -2.52, indicating good solubility in aqueous environments. It also demonstrates high gastrointestinal (GI) absorption, which is advantageous for oral formulations. Furthermore, dopamine is capable of crossing the blood-brain barrier (BBB), making it suitable for central nervous system (CNS) applications, unlike some larger or more polar compounds. In summary, dopamine aligns well with all major drug-likeness criteria and outperforms several other bioactive compounds in terms of compliance, solubility, and CNS accessibility.

Discussion and conclusion:

Utilizing in silico profiling offers a rapid and efficient strategy for identifying bioactive compounds, predicting their biological activities, and optimizing them for conventional drug development pipelines. In this study, computational tools such as SWISSADME and ADMETlab 3.0 were employed to evaluate the ADMET properties and drug-likeness of phytochemicals derived from *Musa acuminata*. A total of six compounds—myricetin, apigenin, glycosides, dopamine, N-acetyl serotonin, and rutin—were selected based on their promising pharmacokinetic profiles and favourable safety attributes. These compounds demonstrated encouraging drug-like characteristics, supported by their chemical descriptors, drug-likeness scores, and predictive ADMET models. Notably, dopamine exhibited superior lipophilicity, which may enhance membrane permeability and central nervous system accessibility. Furthermore, pharmacophore modeling was applied to predict potential therapeutic targets, revealing a spectrum of disease-modifying possibilities associated with these bioactives. Overall, the computational data suggest that *Musa acuminata* harbors compounds with significant therapeutic potential. However, to substantiate these findings, controlled experimental validation is essential to confirm the pharmacological efficacy and safety of these candidates in biological systems**.**

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