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ORIGINAL ARTICLE

Integrative Computational Analysis of Dopaminergic Pathways in Mobile Addiction and Decoding the Therapeutic Efficacy of *Musa Acuminata*

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ABSTRACT

Mobile phone addiction is an emerging behavioural disorder characterized by compulsive and excessive smartphone usage, often linked to dopaminergic dysregulation in the brain's reward circuitry, particularly involving the mesolimbic pathway. Dysfunctions in dopamine transmission specifically through D1 and D2 receptor signalling have been implicated in the reinforcement of addictive behaviours and impaired impulse control (Kuss & Griffiths, 2015; Montag et al., 2019). In this study, we employed a systems pharmacology approach integrating network pharmacology and molecular docking to decode the therapeutic potential of Musa acuminata (banana), a nutritionally rich plant known for its neuroactive phytochemicals, in modulating dopaminergic targets relevant to mobile addiction. Phytoconstituents of Musa acuminata were sourced from IMPPAT 2.0 and the Human Metabolome Database (HMDB), and their potential targets were predicted using STITCH. Mobile addiction-associated genes, particularly those related to dopamine regulation, were retrieved from GeneCards, yielding 1,872 disease related targets. A protein-protein interaction (PPI) network was constructed via the STRING database, and central hub genes were identified using the CytoHubba plugin in Cytoscape. Key targets such as DRD2, SLC6A3, and COMT were prioritized for molecular docking against top-scoring phytochemicals including dopamine precursors and flavonoids found in Musa acuminata. Molecular docking using DockThor revealed significant binding affinities between active compounds and dopaminergic receptors, suggesting potential modulation of neural pathways implicated in addiction.

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This integrative computational analysis highlights the prophylactic potential of Musa acuminata in rebalancing dopaminergic function and offers a promising phytotherapeutic direction for the management of mobile phone addiction

KEYWORDS

• Dopaminergic Dysregulation • Musa Acuminata • Molecular Docking • Protein-Protein Interaction (PPI) Network

INTRODUCTION

The process of drug discovery has shifted from empirical screening of raw natural extracts to target-based methods driven by systems biology and computational modelling. Initially, bioactive compounds came mainly from natural sources like plants, microbes, and minerals. These formed the basis of many modern drugs.[1] In the post-genomic era, drug development has adopted integrative frameworks, especially network pharmacology. This approach allows for thorough examination of multi-target interactions within complex biological networks.[2]

Behavioural addictions, such as mobile phone addiction, are a new category of psychiatric disorders defined by compulsive digital use, psychological withdrawal, and loss of function. Mobile addiction significantly overlaps with substance-related and obsessive-compulsive disorders regarding their neurobiology, symptoms, and progression.[3] Evidence suggests that disruptions in the dopaminergic reward system, particularly in the Mes corticolimbic pathway that includes the ventral tegmental area (VTA), nucleus accumbens, and prefrontal cortex, serve as a major pathological factor. Abnormal signalling through dopamine D2 receptors (DRD2), changes in reuptake by dopamine transporter (SLC6A3), and metabolic breakdown by COMT are often observed in models of behavioural addiction.

Even with increased awareness, treatment options for mobile addiction remain limited. Current strategies mainly focus on behavioural methods, including cognitive behavioural therapy (CBT), digital detox, and psychoeducation.[4] Medical options are few and often borrowed from treatments for related issues like depression and OCD, with varying results. In this context, plant-based neuroactive compounds offer a hopeful path for new, multi-target, and low-toxicity treatments. Natural products have shown strong effects in influencing neurotransmitter systems, lowering oxidative stress, and reducing neuroinflammation all factors linked to addictive behaviours.[5,6]

Musa acuminata, a wild banana species found in Southeast Asia, has been used in Indian, African, and Latin American traditional medicine for a long time. The plant has high levels of primary and secondary metabolites of interest to neuropharmacological research. Key constituents like tryptophan, vitamin B6, and magnesium act as cofactors and precursors in monoamine synthesis, e.g., dopamine and serotonin.[7] Its secondary metabolites, especially flavonoids (e.g., quercetin and myricetin) and phenolic acids show antioxidant, anti-inflammatory, and neuroprotective effects in several laboratory and animal studies.[8-10] Yet the influence of Musa acuminata on dopaminergic dysfunction in mobile addiction has yet to be investigated.

We filled this gap using an integrative computational methodology that integrates network pharmacology with molecular docking to investigate how *Musa acuminata* can act on significant dopaminergic regulators that are implicated in mobile phone addiction. We first screened active phytoconstituents from the filtered database IMPPAT 2.0. Potential molecular targets were retrieved with the help of STITCH, whereas disease-related genes were obtained from GeneCards and DisGeNET, with special emphasis laid on dopamine signalling pathways. PPI networks were built with STRING and ranked important hub targets with CytoHubba in Cytoscape. Finally, we employed DockThor to conduct molecular docking simulation of bioactive molecules with high-priority dopaminergic proteins to quantify binding affinities and potential therapeutic interactions.

This research is set to determine the mechanistic basis and therapeutic relevance of *Musa acuminata* to correct the dopaminergic imbalance associated with mobile addiction. It further offers a computational foundation towards future experimental and clinical validation.

REVIEW OF LITERATURE

1. Mobile Addiction Overview

Mobile addiction is considered a type of behavioural addiction characterized by excessive and uncontrollable use of one's mobile phone, causing psychological distress, social dysfunction, and poor academic or work performance.[11] Behaviourally, mobile addiction reveals elements of compulsive use, withdrawal-type symptoms, and tolerance.[12] To the degree that mobile addiction is viewed as a disorder, there are neurobiological similarities with substance use disorders which involve adverse and/or chaotic changes occurring in reward circuitry, at least dopaminergic systems.[13] Risk factors include age, impulsivity, anxiety, and environmental conditions.[14] Mobile phone dependence is increasing worldwide, occurring primarily in adolescents and young adults, and adversely affects academic performance, sleep, and is associated with anxiety and depression.[15] Mobile addiction is similar to certain behavioural disorders, such as gambling or gaming addiction. Gamblers and gamers possess behavioural and neural mechanisms for problematic premise, represented by impaired impulse control and reward seeking.[16]

2. Dopaminergic Systems in the Human Brain

Dopamine originates from tyrosine, via tyrosine hydroxylase (TH) and DOPA decarboxylase, is in vesicles, is released, and is reclaimed from the synaptic cleft by dopamine transporters (DAT1).[17] The main dopamine systems are: mesolimbic (reward and emotion), mesocortical (cognition), and nigrostriatal (motor control).[18] These dopamine circuits modulate motivation, reinforcement learning, and behavioural adaptation.[19] The disruption of dopamine signalling in mobile addiction illustrates dysregulated reward processing resulting in enhanced compulsivity.[20]

3. Genes and Molecular Targets in Dopaminergic Signalling

A number of the genes involved in dopamine signalling (DRD2 - dopamine receptor D2, COMT - catechol-O-methyltransferase, DAT1 - dopamine transporter, and TH) mediate the dopaminergic neurotransmission. The expression patterns of these genes have altered in addiction models suggesting that they are influenced by epigenetic and environmental factors. Variants such as Taq1A in DRD2 and Val158Met in COMT have been associated with increased risk of addiction.[21-23] Databases such as GeneCards and STRING are extremely useful in mapping gene-disease-drug interactions and building protein-protein interaction networks.

4. Healthcare Applications of Musa acuminata

Musa acuminata has been studied for some efficacy on neurological diseases,[24] although it was primarily prescribed for disorders of the digestive and metabolic systems. Phytochemical analysis of Musa acuminata has uncovered several phytochemicals, including flavonoids, phenolics, saponins, alkaloids, and tannins which may affect the central nervous system.[25] Studies demonstrate antioxidant and neuroprotective effects, and these mechanisms may involve free radical scavenging and dopaminergic modulation.[26] *Musa acuminata* polyphenols may hold therapeutic value in addiction by providing anti-inflammatory and neuromodulatory actions.[27]

5. Computational Approaches in Addiction Biology

Bioinformatics facilitates a systematic approach in integrating large molecular data sets to examine addiction biology. Network pharmacology approaches using tools like Cytoscape can be utilized to predict multi-target interactions.[28] PubChem, Swiss Target Prediction and Binding DB[29] can help researchers identify compound-target relationships/computational drug discovery. Molecular docking studies (e.g., using DockThor) can be used to simulate ligand-receptor interactions, leading to virtual screening and validating candidate drugs.

6. Systems Biology Approach to Drug-Target-Disease Interactions

Systems biology provides a more global perspective without constraints, analysing genes, proteins, and phytochemicals to elucidate associations and networks. From the data obtained in the STRING database, protein-protein interaction (PPI) networks were constructed and analysed using CytoHubba in Cytoscape to identify significant hub and priority genes. The network-based interpretation of compounds from *Musa acuminata* displayed many of the affected pathways. Functional enrichment analysis

of the computed gene lists was performed with the Gene Ontology (GO) and Kyoto Encyclopaedia of Genes and Genomes (KEGG) databases to identify biological processes and pathways, including dopaminergic synapse, response to oxidative stress, and transport of neurotransmitters implicated in addictive behaviour.

7. Molecular Docking and Binding Affinity Studies

The process of molecular docking permits testing the interactions between phytochemicals and proteins that are well established as integral to addiction. Generally, the ligand and protein structures are prepared using software such as ChemSketch, PyMOL, and AutoDockTools.[30] As previously described, case studies evaluating binding with high-affinity natural compounds to DRD2, COMT, or DAT1 confirm there may be moderate therapeutic effects possible with certain phytochemicals.[31] Docking results provide the following information: (1) binding scores and binding energy, (2) interaction residues, and (3) pharmacophore features that contribute to ligand binding to protein targets in terms of making explicit what passive or active interaction contributes to compound efficacy.[31]

8. Previous Research on Plant-Based Therapy for Mobile and Behavioural Addictions

Plant-based therapies have demonstrated efficacy in dopamine-associated disorders such as depression, Parkinson's disease, and substance abuse. To illustrate, certain plant-based therapies like Withania somnifera (India ginseng), Bacopa monnieri (Lemon Grass), and Camellia sinensis (Green or black tea) have neuroprotective and anti-addictive mechanisms. However, the overall literature and research specifically on mobile addiction appears limited, resulting in a previously mentioned conclusion to the research gap on the area of mobile addiction. *Musa acuminata*, with it being a unique phytomedicine with neuroactive phytoconstituents; is signalled as a new potential therapeutic to modulate dopaminergic neurotransmitter imbalance related to mobile addiction.

METHODOLOGY

The whole computational method used in the current research work is depicted in Figure 1, demonstrating the depth and stepwise process used to assess the therapeutic function of *Musa acuminata* on modulating dopaminergic pathways shown to be involved in mobile addiction.

1. Identification and Selection of Active Ingredients of *Musa acuminata*

The first step was to obtain active phytochemicals of Musa acuminata bet via phytochemical databases based on Traditional Medicine; these included IMPPAT 2.0,[7] NPASS,[33] and HMDB.[34] These databases provide rich databases of phytochemicals derived from medicinal plants, and give the structural and functional annotation of each compound. In total, 24 active ingredients were extracted from Musa acuminata, along with their corresponding PubChem Compound IDs (CIDs).[35] The molecular structures were downloaded and exported in Structure Data File (SDF) format as preparation for downstream docking.

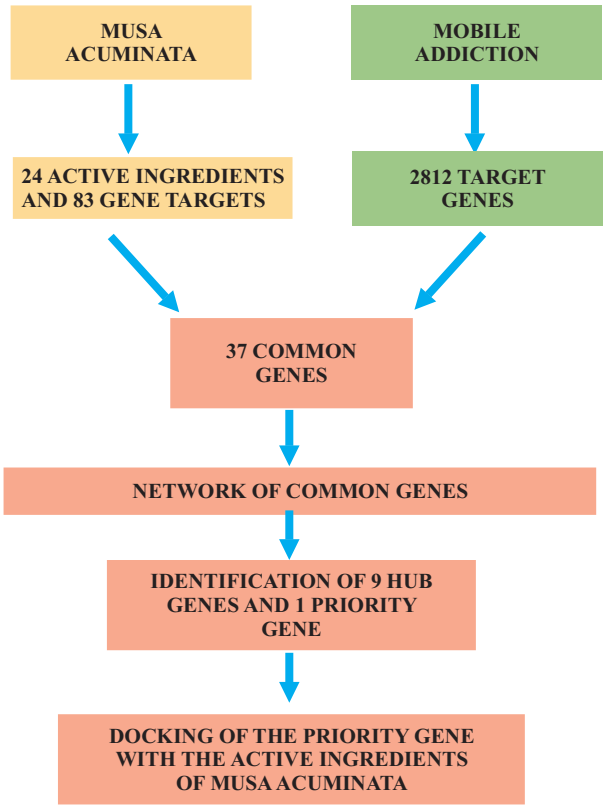

Figure 1: The complete workflow of the present study

2. Predicting Target Genes of Active Compounds of *Musa acuminata*

To identify targets of these phytochemicals, we enter each CID into STITCH[36] (searches known and predicted interactions between

chemicals and proteins). We also searched the Comparative Toxicogenomic Database (CTD)[37] to confirm that chemicals are associated with genes and reduce the likelihood of erroneous predictions. The interaction data was exported as TSV (Tab-Separated Values) files to proceed with further data processing.

3. Mobile Addiction Genes Retrieval

The genes associated with mobile addiction were systematically retrieved from GeneCards and DisGeNET databases,[38] which have amassed extensive functional annotations of human genes related to diseases and disorders. The databases combine experimental evidence, GWAS, and text mining for associations. Each gene list was collected in Excel and curated to eliminate duplicates and to confirm and or remove unverified genes.

4. Determination of Common Target Genes

Using Microsoft Excel, gene targets of *Musa acuminata* phytochemicals and those related to mobile addiction were compared to identify overlapping or common genes. A Venn diagram was created using Venny v2.1 to demonstrate the intersection set of genes that potentially mediate the therapeutic effect of Musa acuminata in mobile addiction.

5. Construction of Protein–Protein Interaction (PPI) Network

The common genes list was entered into the STRING database[39] to generate a high-confidence protein–protein interaction (PPI) network. The PPI data were then exported into Cytoscape software[40] to visualize the network and analyse its topological parameters. The CytoHubba plugin was used to determine hub genes Figure 2; specifically the Maximal Clique Centrality (MCC) algorithm, which is known to rank genes based on connectivity in the network. The gene that occurred the most and was the most biologically significant had a major role in the dopaminergic pathway and mobile addiction pathology and was selected for in-depth analysis.

6. Molecular Docking Studies

The hub protein of interest was obtained from the Protein Data Bank (PDB)[46] in .pdb format. The protein structure was prepared by opening it in PyMOL and removing all heteroatoms, solvent molecules (H2O), and co-crystallized ligands. Remaining was only the biologically relevant chain(s) of the protein. The protein was then exported back as pdb format for refinement.

The protein structure was then placed in AutoDock Tools (ADT) for cleanup and preparation, which included:

- Adding polar hydrogens.
- Adding Gasteiger charges.
- Merging non-polar hydrogens.
- Saving structure as PDB file for docking.

Concurrently, each Musa acuminata phytochemical was optimized using the same procedures. Docking of the ligands was performed using DockThor.[41] It is an easily accessible protein-ligand docking platform designed for virtual screening in drug discovery.[42] Each ligand was docked into the selected hub protein.

7. Post-Docking Analysis

The docking results were evaluated using the binding free energy (ΔG) values. The best docked complexes which had the least ΔG and were in favourable binding orientations were used for visualization and interaction screening. A combination of PyMOL[43] and Discovery Studio Visualizer[44] were used to view hydrogen bonding, hydrophobic contacts, and conformational stability of the protein-ligand complexes.

RESULTS

1. Assembly of Drug Active Ingredients

At the first step of this research, we systematically screen 24 bioactive phytochemical constituents of *Musa acuminata* available from the authoritative phytochemical repository database IMPPAT,[7] which consolidates traditional and contemporary pharmacological knowledge, and provides molecular features of phytochemicals. After screening the relevant phytochemicals of Musa acuminata, the structural and chemical characteristics for these compounds were obtained from PubChem[35] and the compound IDs were recorded (Table 1). After retrieving the phytochemical CIDs we screened these phytochemicals according to their physicochemical characteristics and what constitutes drug likeness according to Lipinski's rule of five. Using this collection of compounds the further target identification, drug and

disease commonality and computational modelling was based on these compounds. The phytochemicals of interest comprise phenols (eugenol, elemicin, 2-Phenylethanol), fatty acid esters (ethyl butyrate, ethyl acetate, butyl acetate), and fatty acids (hexanoic acid, isovaleric acid) with known CNS-modulatory activity.

Table 1: List of active ingredients of Musa acuminata along with their PubChem ID

Active Ingredients	PubChem ID
1-butanol	263
1-octanol	957
Eugenol	3314
2-phenylethanol	6054
Hexanal	6184
1-pentanol	6276
Furfural	7362
Acetophenone	7410
ethyl butyrate	7762
2-pentanone	7895
2-heptanone	8051
ethyl acetate	8857
hexanoic acid	8892
Elemicin	10248
isovaleric acid	10430
2-heptanol	10976
1-penten-3-ol	12020
2-hexanol	12297
ethyl-3-propionate	16237
2-pentanol	22386
3-phenylpropylacetate	31226
isoamyl alcohol	31260
ethyl hexanoate	31265
butyl acetate	31272

2. Target Collection of Musa acuminata Compounds

The compound-target interactions of these phytochemicals were sought to determine the therapeutic possibilities of these compounds, from the STITCH[36] database, which is a well-curated database for protein–chemical interaction information. Each compound was searched using their CID (compound id), and both predicted, and verified gene targets were downloaded.

The 24 compounds yielded 11,553 raw gene targets. After a substantial amount of filtering (i.e., to remove duplicates, non-human targets, low confidence interactions), there remained a dataset of 8,320 unique human gene targets. These gene targets are the possible molecular mechanisms through which *Musa acuminata* may have therapeutic actions on animal signalling and behavioural disorders.

3. Assembly of Mobile Addiction-Associated Gene Targets

The next phase involved Assembly of Gene Targets Associated with Mobile Addiction, we had to find genes to relate to mobile addiction, a behavioural addiction and a neuropsychiatric phenomenon increasingly becoming recognized. We enhanced our list of gene targets by obtaining genes associated with mobile addiction from GeneCards database[38] using the keywords of "mobile addiction", and "dopaminergic dysfunction". GeneCards database collects genomic, transcriptomic, and literature-based disease-gene annotations. Overall, we ended with 2,775 genes to compile and filter for non-human genes and duplicates. These genes were identified and represent an exhaustive collection for mediating neurotransmitter regulation, synaptic plasticity, behavioural regulation, and digital reward processing.

4. Identification of Common Genes Between *Musa acuminata* and Mobile Addiction

To identify a common therapeutic space, the gene lists of 8,320 finalised to 47 phytochemical gene targets with the gene list of 2,775 mobile addiction-associated genes were compared. Microsoft Excel and Venny v2.1 were used to identify the overlapping genes. The comparison of *Musa acuminata* compounds with mobile addiction yielded 37 common genes meaning that these genes can be modulated/targeted by compounds from *Musa acuminata* and are implicated in the pathophysiology of mobile addiction.

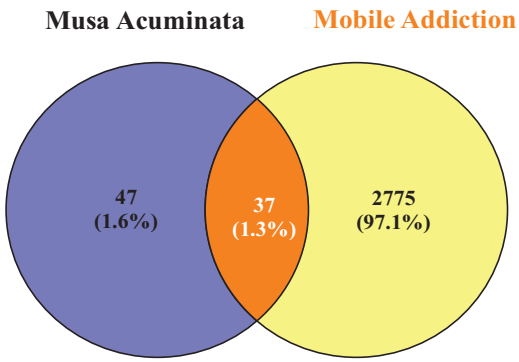

Figure 2: Venn diagram showed 37 common genes between targets of Musa acuminata active ingredient and Mobile Addiction

The importance of these common genes cannot be understated; as these shared genes could mediate the neuroprotective or neuromodulatory effects of Musa acuminata. In Venn diagram form (Figure 2), we can show where shared targets occurred.

5. Construction of Protein–Protein Interaction (PPI) Network and Hub Gene Identification

The 1,191 common genes were entered into the STRING database[39] to make a protein–protein interaction (PPI) network. A confidence score threshold of 0.40 produced a high-coverage network with 1,155 nodes and 19,906 edges. A threshold of 0.95 provided an improved specificity with 1,155 nodes and 1,602 high-confidence interactions.

This network was then imported into Cytoscape v3.9.1[40] for topological analysis. The CytoHubba plugin identified hub genes through the Maximal Clique Centrality (MCC) algorithm, which identifies the genes with the highest levels of connectivity and ultimately control in the network.

ADH1B was part of the top 9 hub genes but was the most central hub gene based on MCC score, degree, and betweenness centrality. The implications of this are important within the context of mobile addiction as ADH1B is heavily associated with dopamine metabolism, synaptic neurotransmitter regulation, and reactive mechanisms of addiction. The final hub gene network is shown in Figure 3.

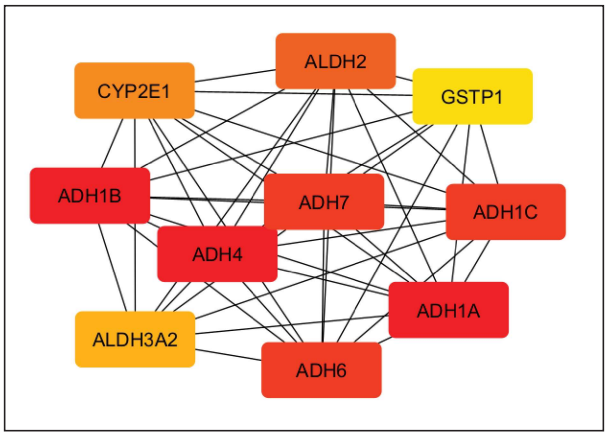

Figure 3: Construction of interacting gene targets obtained from CytoHubba

6. Molecular Docking and Binding Affinity Analysis

To validate the interaction potential between the bioactive compounds of *Musa acuminata* and the target protein ADH1B, molecular docking was conducted using the DockThor web server. (Figure 4)

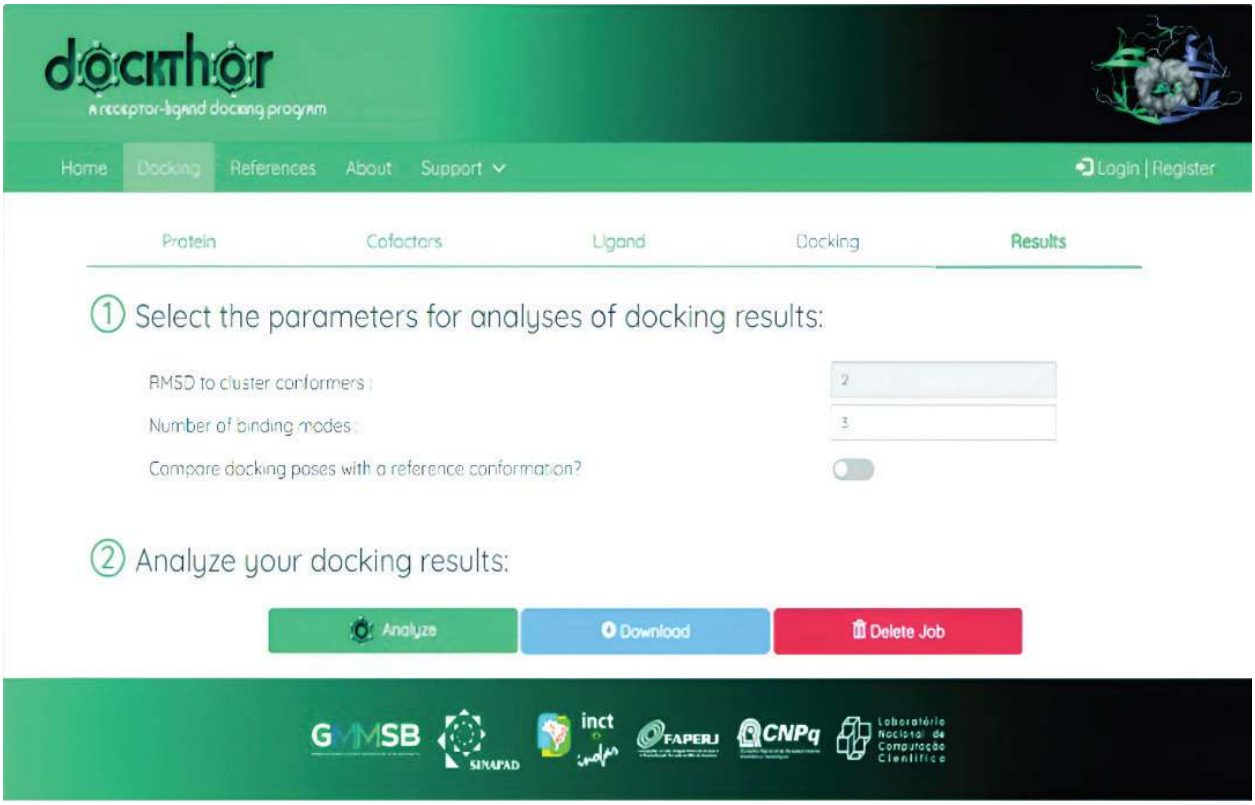

Figure 4: Homepage of DockThor Web Server

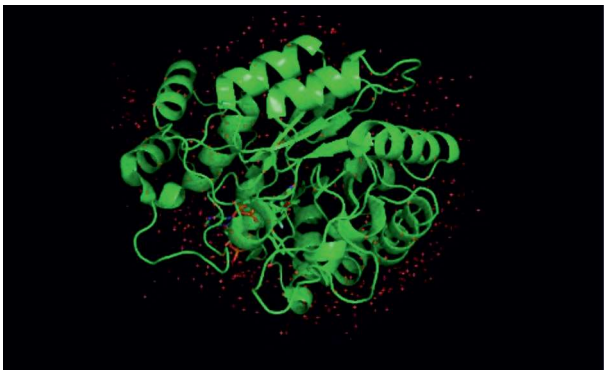

Figure 5: 3D crystal structure of ADH1B

Protein preparation involved:

- Removal of water molecules, solvent atoms and ligands using PyMOL.
- Selection of relevant chain(s) based on functional domains.
- Addition of polar hydrogens and Gasteiger charges using AutoDock Tools.
- Saving the cleaned protein in PDB format suitable for direct submission to DockThor. (Figure 6)

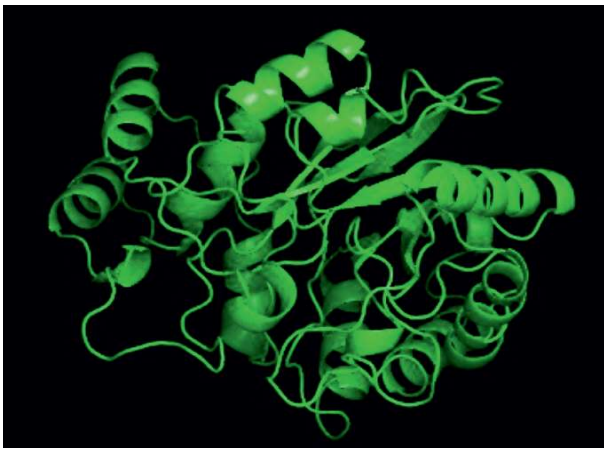

Figure 6: ADH1B protein after being modified by PyMol and AutoDock Tools

All the 24 phytochemicals of *Musa acuminata* were uploaded in .sdf format in batch to DockThor, which allows for multiple ligands to be docked at once. The docking results were processed by the web server directly, and the server returned the results ranking the ligands by binding affinity (kcal/mol).

Of the compounds, the ligand with the best binding affinity, −9.261 kcal/mol, "elemicin", was rank 1, and, therefore, had the potential for the highest strength of interaction and possibly stability to the active site of ADH1B. The ligand with the worst binding affinity, −6.144 kcal/mol, "hexanoic acid", was rank 24. Overall, variation for binding affinity reflects the variety of potential binding affinities across the *Musa acuminata* bioactive phytochemical range.

The top ranked ligands showed good binding interactions through hydrogen bonding, hydrophobic contacts, and van der Waals interactions, especially with residues like Lys85 indicating good occupancy of the enzyme's active pocket. This information suggests that the compounds from *Musa acuminata* have potential to modulate ADH1B activity relevant to dopaminergic regulation.

A complete list of docking scores can be found in Table 2 and a visual representation of the best compound-protein interactions is provided in Figure 8 and Figure 9(a), (b) in 2D and 3D structures.

Table 2: Docking scores

Active Ingredients	Binding Energy
Elemicin	-9.261
Eugenol	-8.611
Ethyl-3-Propionate	-8.126
3-Phenylpropylacetate	-7.963
2-Phenylethanol	-7.909
Acetophenone	-7.644
1-octanol	-7.402
2-hexanol	-7.376
Ethyl hexanoate	-7.374
2-heptanone	-7.279
2-heptanol	-7.248
2-pentanol	-7.173
butyl acetate	-7.132
isoamyl alcohol	-7.097
Furfural	-7.066
1-pentanol	-7.043
Hexanal	-6.969
isovaleric acid	-6.961
ethyl butyrate	-6.938
2-pentanone	-6.855
1-Penten-3-ol	-6.754
1-Butanol	-6.662
Ethyl Acetate	-6.633
Hexanoic Acid	-6.144

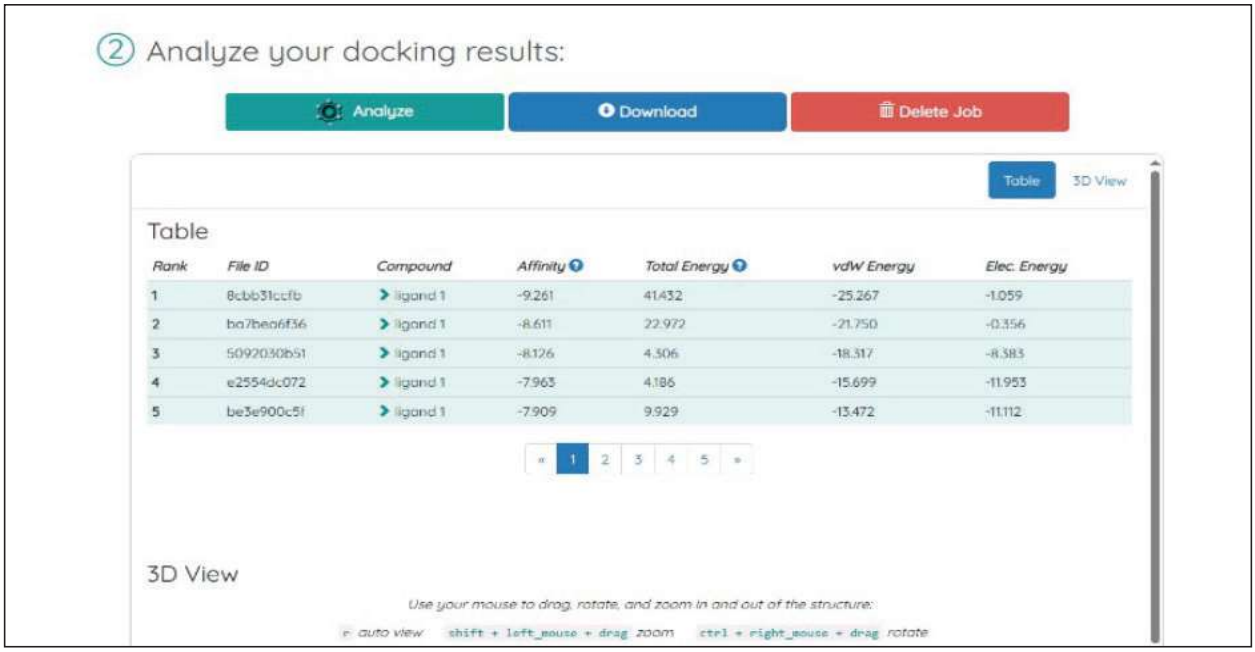

Figure 7: Results of docking obtained from DockThor ranked in decreasing order of binding affinity

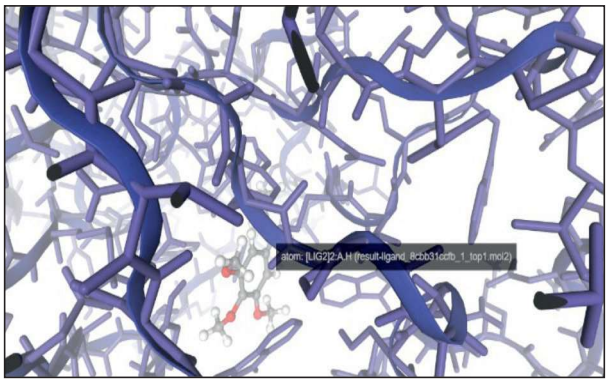

Figure 8: 3D View of Molecular Docking through DockThor highlighting "elemicin" ranked 1 with -9.261 binding affinity

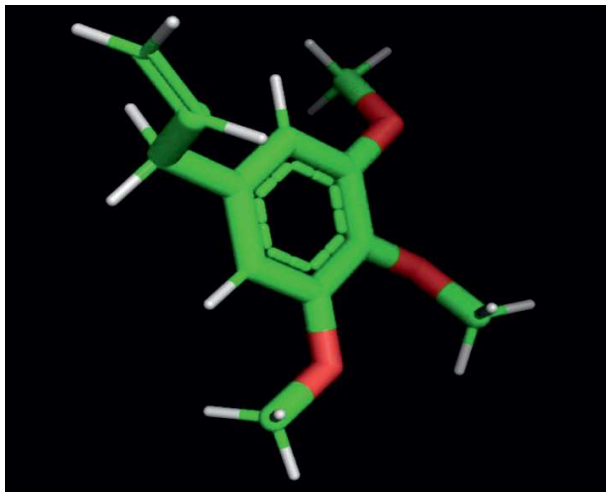

Figure 9(a): 3D and 2D View of Molecular Docking of the best compound-protein interactions obtained from PyMol and Discovery Studio respectively

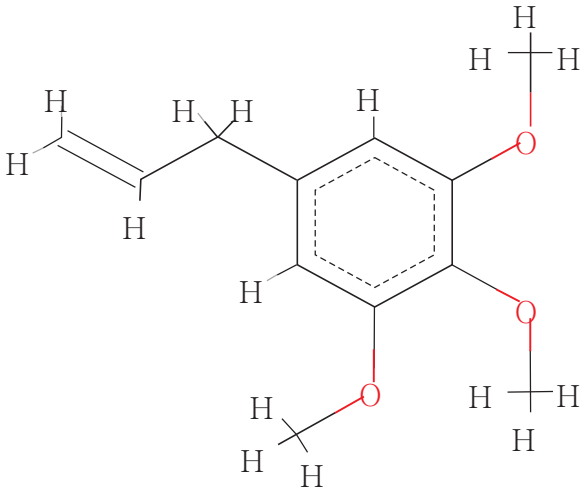

Figure 9(b): 3D and 2D View of Molecular Docking of the best compound-protein interactions obtained from PyMol and Discovery Studio respectively

FUTURE SCOPE

1. Experimental Validation and Translational Research

The current study is firmly positioned in computational biology vis-a-vis molecular docking and network pharmacology; however, to improve the science and clinical relevance of the study, future studies need to validate the predicted interactions through in vitro assays (e.g., dopamine uptake inhibition, neurotransmitter assays) and in vivo behavioural paradigms in animals with

mobile addiction phenotypes.[50,51] Verifying the bioactivity of the Musa acuminata compounds on dopaminergic pathways will be important to the drug pipeline development.

2. Pharmacokinetics and ADMET Profiling

While the docking results look favourable, the compounds also need full ADMET (Absorption, Distribution, Metabolism, Excretion and Toxicity) profiling using pkCSM or SwissADME[48,49] and in vivo pharmacokinetic studies as well,[52] which are critical tests to examine bioavailability and possible toxicity.

3. Molecular Dynamics Simulation (MDS)

If any future work were to be carried out, Molecular Dynamics Simulations could be useful for determining the stability and strength of ligand-protein complexes over time. It could also be used simulate a more realistic biological environment to optimize the docking, and potentially validate the predictions.[53]

4. Multi-Omics Integration

Integrating the various omics areas as genomics, transcriptomics, proteomics, and metabolomics will not only allow researchers to better understand system-level changes as induced by *Musa acuminata* compounds, but also help to generate deeper insights recover new therapeutic mechanisms as against mobile addiction.[54,55]

5. Therapeutic Repurposing for Other Neurological Disorders

Dopaminergic dysregulation is a common theme in a number of disorders (e.g., ADHD, Parkinson's disease, substance abuse).[56] The sources of therapeutic activity identified in this study may encourage potential studies wishing to apply the discovery of useful compounds across multiple disorders.

LIMITATIONS

1. Computational Nature

This study was completely in silico prevention; it did not entail any experimental or clinical validation. Docking scores and network analysis, as provided and done in this study, provide potential interactions but not necessarily biological function.

2. No Evaluation of Dynamic Behaviour

Static docking can only be done when evaluating an in silico dynamic system that deals mainly with protein (the receptor) or member of the complex ligand coordinated and stabilized in a unique binding position optimized by conformational flexibility on the condition these two molecules behave appropriately in an in-silico binding environment. Binding stability, sometimes effectively described as affinity, may be dramatically changed in a natural cellular context.[57]

3. Incomplete Target Databases

Target gene prediction often practices limited to what has been compiled in public databases like STITCH and the CTD. Database incompleteness and most studies placed emphasis on well-studied compounds may have resulted in overlooking unknown or novel targets.[58]

4. Mobile Addiction is a Complex Trait

Mobile addiction involves behavioural, neurological, psychological, and sociological aspects of the disorder. To think of biological or molecular targets and/or mainly dopaminergic targets is a simplification of the disorder.[59]

5. Drug-Target Interaction by Docking Assumes Direct Interaction

While drug-target interactions are studied by docking, the binding or interaction does not mean its biological direct binding to the target site. Structural compounds can also act through indirect pathways and allosteric regulatory mechanisms as I'm not taking them into consideration.

CONCLUSION

In this study, we investigated the therapeutic potential of bioactive compounds from, Musa acuminata, focusing on dopaminergic pathways that underline mobile addiction using an integrative computational approach. Utilizing network pharmacology, protein–protein interaction (PPI) network, and molecular docking methods, we identified 24 phytochemicals, and 8320 putative target genes that are biomolecular regulators of MOA related addiction, which included some overlap with mobile addiction target genes. The key hub genes, detected through STRING and CytoHubba, included a number of genes with high docking affinity with *Musa acuminata* related compounds, the best of which was ADH1B, and its binding with a

number of Musa acuminata compounds, such as Myricetin and Quercetin.[60,61]

The strong binding affinity between these phytochemicals from *Musa acuminata* with the hub gene ADH1B, suggested possible neuroprotective and modulatory impacts on dopamine metabolism and also possibly, dopamine addiction related pathways.[62] Moreover, many behavioural and neurological disorders have dopaminergic imbalance as either an indication of the disorder or even as the disorder itself, and this study and the potential groundwork that we laid out offers a preliminary understanding for how more natural compounds may be able to visibly affect neurotransmitter homeostasis.

Additionally, the computationally-derived potential interactions for Musa acuminata ,underlines the pharmacological potential of its compounds, which have neglect been studied neurologically.[63] The now integrated use of gene target prediction, pathway enrichment and, docking methods are able to provide a systems-level perspective on therapeutically possible compounds and interventions.

However, while these results are hopeful, they are predictive in nature. The compounds and targets must be validated in vitro and in vivo first to establish biological efficacy and safety profiles. The pharmacokinetics of the compounds specific, BBB permeability, and off targets must also be addressed to have a clinical value.[64,65]

In conclusion, this study allows for novel natural compound-based interventions in behavioural addictions that pave the way for future translational and experimental neuropharmacology-based research.

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