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GAS CHROMATOGRAPHY-MASS SPECTROMETRY PROFILING AND MOLECULAR DOCKING ANALYSIS OF *Musa acuminata* BARK EXTRACT

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ABSTRACT

Physiological wound healing requires many biochemical processes, along with cellular functioning, to occur. The research investigates the restorative properties of *Musa acuminata* bark extract by conducting GC-MS profiling combined with molecular docking analysis. Between them, the GC-MS analysis detected multiple bioactive compounds, including flavonoids, tannins, terpenoids, and phenolic compounds that present antioxidant, anti-inflammatory, and antimicrobial properties. Active compounds in these substances help create conditions that support new tissue development while speeding up the wound healing process. Molecular docking software named AutoDock Vina helped scientists evaluate how the active extract compounds bind with essential proteins for wound healing, such as matrix metalloproteinases. Several phytochemicals from the extract showed strong interaction with matrix metalloproteinases in docking experiments, thus indicating their capacity to contribute to collagen synthesis and tissue remodeling while reducing inflammation. A Lipinski's Rule of Five analysis established both drug-likeness and pharmacokinetic readiness for the compounds. Wound healing applications demonstrate potential therapeutic value because findings show that *Musa acuminata* bark extract exhibits effectiveness as a natural therapeutic agent. Additional studies with living subjects and clinical trials need to happen to prove effectiveness, along with demonstration of safety, so *Musa acuminata* bark extract can be used as a modern wound care treatment.

Keywords: Wound Healing, *Musa Acuminate,* GC-MS Analysis, Molecular Docking, Lipinski's Rule of Five, And Matrix Metalloproteinases (MMPs).

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INTRODUCTION

The dynamic biochemical wound healing response begins to activate when the skin suffers acute or chronic damage to reach its original health state. The normal wound healing process occurs through four different yet interconnected stages that begin with hemostasis within the first few hours after damage, followed by inflammation, and then moves into proliferation and remodeling stages, which can take from days 21 to numerous years. Health and economic growth suffer negative consequences when wound healing processes fail to achieve proper regulation. A wound that needs more than six weeks to heal will convert into a condition that produces pathological inflammation. The sustained inflammatory process generates abundant proinflammatory cytokines together with highly proteolytic conditions through the continuous activity of neutrophils and macrophages in the wound area. A multitude of interrelated biochemical and cellular mechanisms make tissue rebuilding for damaged cutaneous and subcutaneous structures into a complex pathophysiological process.[1] The process of tissue healing enables multiple enzyme pathways to activate. Any stage of this involved physiological process can lead to limitations, especially bacterial infection. Healing becomes hindered by three types of physiological conditions, including rheumatoid arthritis, zinc deficiency, and diabetes. The main substances found in traditional herbal remedies derive from plant-based natural ingredients. Standards of extraction practice use minimal industrial processing to obtain these plant-derived chemicals. This medical center delivers the principal therapeutic services to patients worldwide.

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This medical field produces annual revenue that exceeds US$ 60 billion according to the WHO Traditional Medicine Strategy (2002). Scientists study these plants to determine how their multiple essential plant-derived substances affect potential wound-healing processes. The use of phytochemicals and plant extracts in wound healing treatments has increased because these treatments contain multiple active components and cause no adverse effects. Experiments have discovered healing properties of alkaloids along with carbohydrates, Flavonoids, terpenes, and other phytochemicals.[2,3] The *Musa acuminata* banana exists as an endangered species that grows only in Southeast Asia. The banana ranks as various types of different subspecies within the Musa genus and the Musaceae family. People often use different parts of M. acuminata subspecies to cover their scrapes and bruises, as well as wounds, according to traditional practice. Research indicates that very few of the banana subspecies have shown beneficial dressing properties and wound-calming properties, along with decreased pain feeling while accelerating wound healing. For several centuries, banana plants became a crucial part of traditional medicine practices. Multiple medical conditions, including ulcerative colitis, intestinal lesions and diarrhea and dysentery, and diabetes, are among the situations where this fruit receives medical application in addition to burn wound treatment. The organic ash of banana leaves treats eczema, while the plant flowers manage dysentery and menorrhagia. Medicinally speaking, Fruited plant stem juice serves as an effective remedy to treat gastrointestinal diseases. Laboratory examination of fresh *Musa acuminata* extract assessed its potential capabilities as a wound healer based on current research findings.[4] The tissue remodeling functions of both MMPs and zinc-dependent proteolytic enzymes encompass both extracellular matrix breakdown and rebuilding activities.[5,6] Small-molecule binding patterns undergo routine examination in molecular docking investigations to study continuous patterns in proteins. The binding potential of *Musa acuminata* fresh extract active molecules with their target receptors was examined through molecular docking procedures. Fresh extract demonstrates possible wound healing capabilities through docking tests of matrix metalloproteinase 2 crystals (PDB ID: 1GEN, 4DPE, 5H8X, Q5H[7,8]).

EXPERIMENTAL

GC-MS Analysis

An analysis of the fresh extract utilized GC-MS techniques. The GC-MS analysis results on wound healing prospects of the investigated compound are as follows.[9] To analyze liquid materials using GC-MS, researchers filter out solid impurities and choose optional derivatization for improved volatility. The GC accepts 1–2 µL of liquid sample, which runs in split mode when the solution contains low concentrations or splitless mode for strong concentration levels. The analytical system vaporizes the sample, which then travels through a capillary column by helium gas as a carrier, where separation occurs based on volatility strength. The mass spectrometer performs ionization of column-separated compounds, after which it identifies samples through their specific mass-to-charge ratios. Data analysis requires scientists to match chromatographic data with spectral data points from reference libraries for compound identification as well as quantity determination.[10, 11]

In-silico Molecular Docking Studies

The Auto DockVina V.1.2.7 software performed Molecular Docking analysis for the protein-ligand molecule interactions. The designed ligands relied on ChemDraw software before conducting binding affinity assessments for protein-ligand interactions. We built PDBQT models of docked proteins combined with their ligand molecules. The active site cavity of the protein molecule requires the grid to position correctly around specific active site residues. The docking process involved individual fittings of targets with their active compound elements. The strength between ligands and particular proteins is evaluated through free energy calculation methods. The binding data evaluation focused on kcal/mol strength measurements combined with binding position analysis.[12]

Lipinski's Rules

Lipinski's rule of five represents its other name as the Pfizer rule of five. Christopher independently created this rule in 1997. This traditional evaluation method helps determine drug likeness in compounds, while the pharmacokinetic drug properties are estimated without biological activity prediction.[13-16] A drug-like compound must satisfy all Lipinski rules unless it violates at most one of these criteria:

- No more than five hydrogen bond donors should exist in the molecule.
- Less than ten Hydrogen bond acceptors are recommended for the compound.
- A molecular weight below 500 Dalton defines the established drug likeness parameter.
- The partition coefficient, together with the log p value, must remain below 5.
- So there should be only a single rule violation.
- More than one rule violation in the parameters leads to reduced compound permeability and absorption potential.

RESULTS AND DISCUSSION

GC-MS Analysis

(+) - (S)-1-Bromo-2-methylbutane: Molecular weight 151.04, melting point 118°C, boiling point 121°C to 122°C.
1-Cyclopropyl-2-propen-1-one: C_6H_8O, Molecular weight: 96.13.
2-Isopropyl-5-methylphenyl isobutyrate: $C_{14}H_{20}O_2$, Molecular Weight: 220.31, melting point 18°C, boiling point 175°C.
3,5-Octadien-2-one: $C_8H_{12}O$ Molecular Weight: 124.18, boiling point 194-160°C.
3,7-Octadien-2-one: $C_3H_{12}O$, Molecular Weight: 124.18, boiling point 84-85°C.
3-Bromopentane: $C_5H_{11}Br$, Molecular Weight: 151.04, melting point 126°C, boiling point 118-119°C.
3-Buten-2-one: C_4H_6O, Molecular Weight: 70.09, melting point 7°C, boiling point 81.4°C.
3-Methyl-1-pentene: C_6H_{12}**,** Molecular Weight: 84.16, melting point 154°C, boiling point 54°C.
3-Methyl-3-buten-2-one: C_5H_8O, Molecular Weight: 84.12, melting point 54°C, boiling point 98°C.
3-Penten-2-one: C_5H_8O, Molecular Weight: 84.12, boiling point 122°C.
4,4-Dimethyl-1-hexene: C_8H_{16}, Molecular Weight 112.21, melting point 103.01°C, boiling point 107°C.
4-Hexen-2-one, 3-methyl: $C_7H_{12}O$, Molecular Weight 112.17, boiling point 90°C.
4-tert-Butylphenyl acetate: $C_{12}H_{16}O_2$, Molecular Weight 206.28.

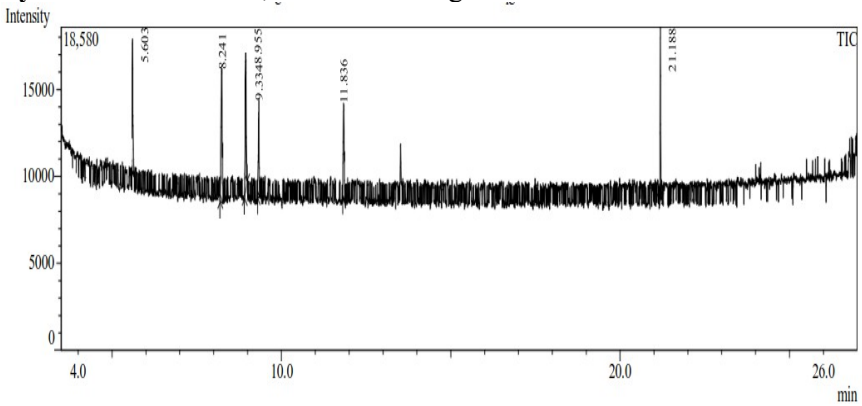


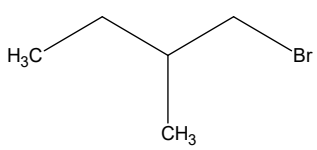
Fig.-1: GC-MS Analysis of Fresh Extract of *Musa acuminata*

5-Ethyl-3-nonen-6-one: $C_{11}H_{20}O$, Molecular Weight: 168.28.
Benzoic acid, 2-(isopropyl)oxy-, methyl ester: $C_{11}H_{14}O_3$, Molecular Weight 194.23.
Butanoic acid, 2-propenyl ester: $C_7H_{12}O_2$, Molecular Weight 128.169, melting point 44-45°C, boiling point -62.68°C.
Ethylene oxide: C_2H_4O, Molecular Weight: 44.05, melting point 104°C, boiling point -112.46°C.
Hydroxyurea: $CH_4N_2O_2$, Molecular Weight: 76.055, boiling point 141°C.
Isothymol isobutyrate: Molecular Weight: 220.31.
Methyl 2-(pentyloxy) benzoate: Molecular Weight: 222.28.
Methyl 2-butoxybenzoate: Molecular Weight: 208.25.
Octa-3, 5-dien-2-one: $C_8H_{12}O$, Molecular Weight 124.18, melting point 194-195°C.
Pentandioic acid, (p-t-butylphenyl) ester: $C_{15}H_{20}O_4$, Molecular Weight: 264.32.
Pentanoic acid, 5-hydroxy-, p-t-butylphenyl ester: Molecular Weight: 250.33.
Salicylic acid acetate, methyl ester: Molecular Weight: 194.18.

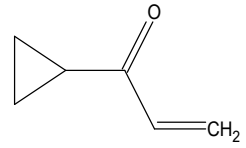
Semicarbazide: CH_5N_3O, Molecular Weight 75.07, melting point 175-177°C, boiling point 394.09°C. **Thymol acetate:** $C_{12}H_{16}O_2$, Molecular Weight: 192.25, melting point 28-30°C, boiling point 241-243°C. **(4E)-3-Methyl-4-hexen-2-one:** C7H12O Molecular Weight: 112.17, boiling point 207.2°C. **(+) - (S)-1-Bromo-2-methylbutane:** $C_5H_{11}Br$, Molecular Weight 151.04, melting point 105.4°C, boiling point 121-122°C. GC-MS Analysis of Fresh Extract of Musa acuminata were shown in Fig .1.

Structure of Ligands

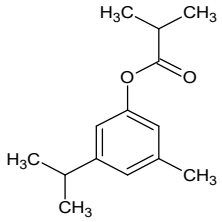
The identified ligands from the GC-MS structure were drawn by using ChemDraw.



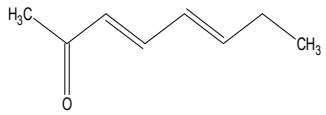
(S)-1-Bromo-2-methylbutane



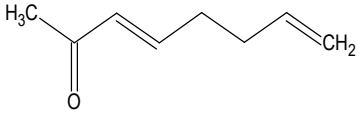
1-Cyclopropyl-2-propen-1-one



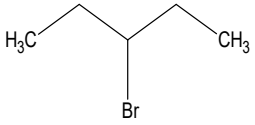
2-Isopropyl-5-methylphenyl isobutyrate



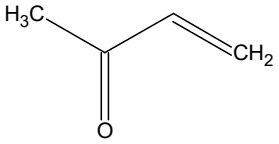
3,5-Octadien-2-one



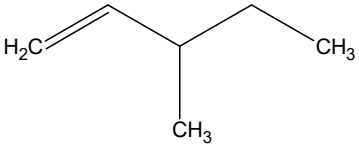
3,7-Octadien-2-one



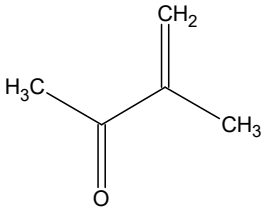
3-Bromopentane



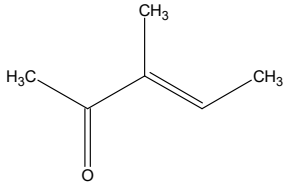
3-Buten-2-one



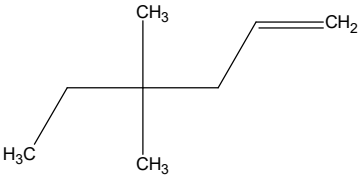
3-Methyl-1-pentene



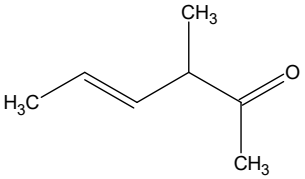
3-Methyl-3-buten-2-one



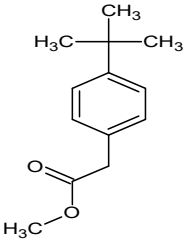
3-Penten-2-one



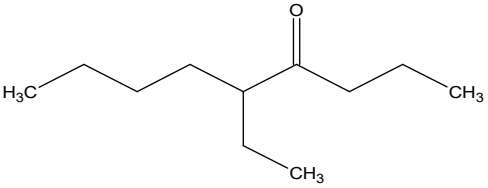
4,4-Dimethyl-1-hexene



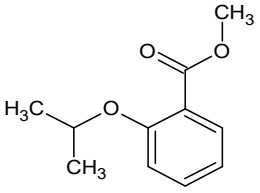
4-Hexen-2-one, 3-methyl



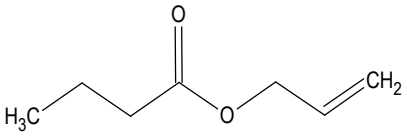
4-tert-Butylphenyl acetate



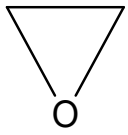
5-Ethyl-3-nonen-6-one



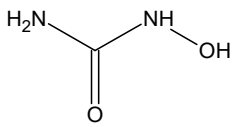
Benzoic acid, 2-(isopropyl)oxy-, methyl ester



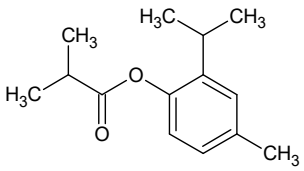
Butanoic acid, 2-propenyl ester



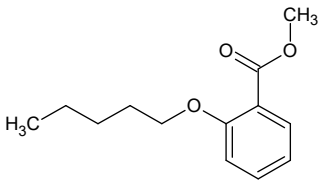
Ethylene oxide



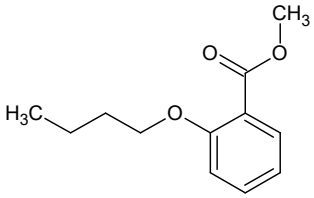
Hydroxyurea



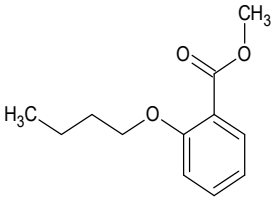
Isothymol isobutyrate



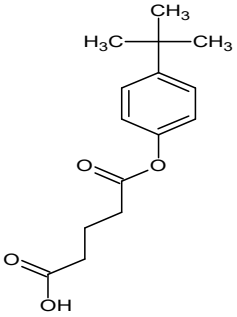
Methyl 2-(pentyloxy)benzoate



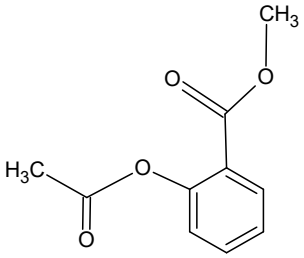
Methyl 2-butoxybenzoate



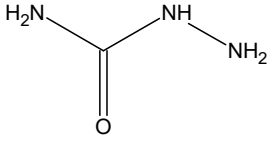
Octa-3,5-dien-2-one



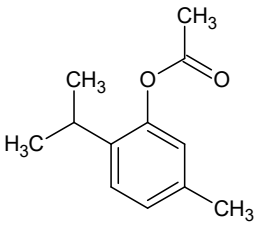
Pentandioic acid, (p-t-butylphenyl)ester



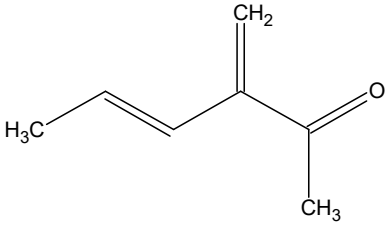
Salicylic acid acetate, methyl ester



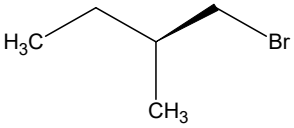
Semicarbazide



Thymol acetate



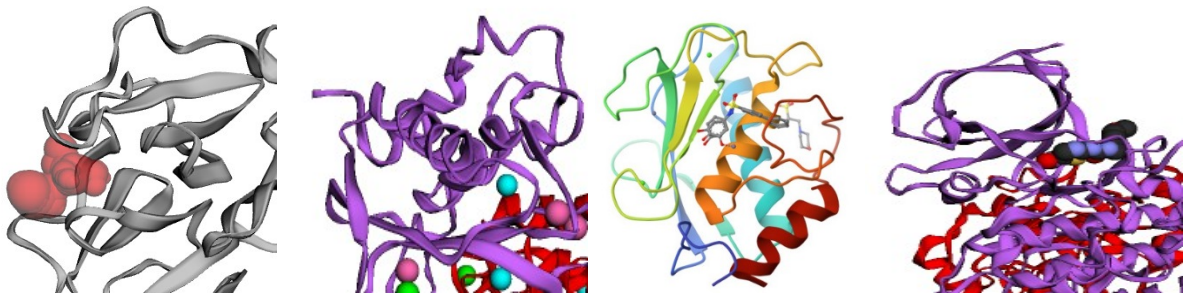
(4E)-3-Methyl-4-hexen-2-one



(+) - (S)-1-Bromo-2-methylbutane

Fig.-2: Structure of Ligands

Structure of Protein



1GEN 4DPE 5H8X 1Q5K

Fig.-3: Structures of Proteins

Molecular Docking Studies

The Auto Dock vina 2.0 software succeeded in docking all five target proteins to the designed ligands. The evaluation of binding affinities through molecular interactions led to identifying the best possible docked positions between proteins and ligands. The binding energy values for ligands appear in Table-3. A prediction of ligand features occurred through the application of Lipinski rules of five that included Molecular mass, hydrogen bond donor and hydrogen bond acceptor, and LOGP and Molar Refractivity data, which appear in Table-4.Structure of ligands and proteins were shown in Fig. 2 and 3.

The summary of amino acid residues that bind with ligands appears in Table-1. The protein-ligand bond occurs through hydrogen bonds and van der Waals interactions as observed in Table-2. 2-Dimensional Interaction of compounds bound to protein active site were shown in Fig.4. Interaction between Ligands with Proteins were shown in Fig.5.

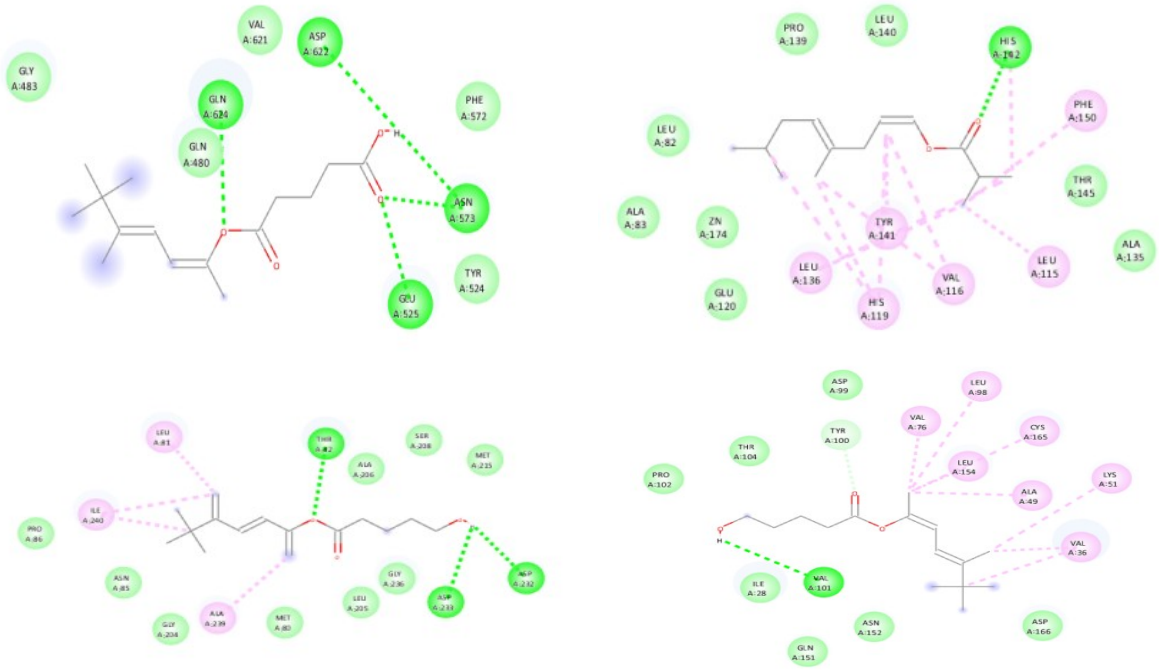


Fig.-4: Two-Dimensional Interaction of Compounds Bound to Protein Active Site (PDB ID: 1DF5)

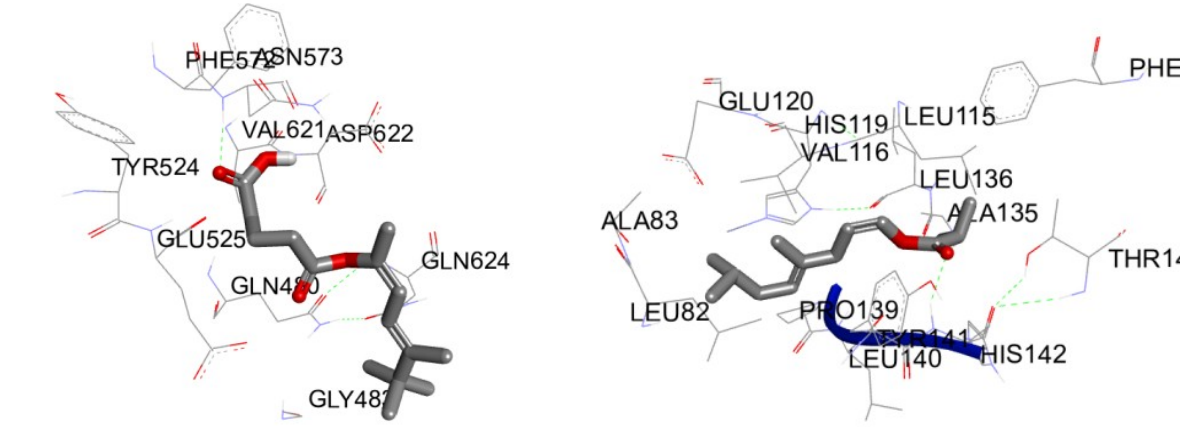
Table-1: Amino Acid Residues on the Protein Interact with Ligands

S. No.	Proteins	Amino acid residues
1	1GEN	Phe 572, Asn 573, Val625, Asp622, Tyr524, Glu525, Gln480, Gln624, Gly483
2	4DPE	Glu120, His119, Leu115, Val116, Ala83, Leu82, Pro139, Leu140, Tyr141, His142, Leu136, Ala136

3	5H8X	Met215, Asp233, Asp232, Gly204, Leu205, Ala206, Ala239, Ile240, Asn85, Leu81, Met 80, Thr82, Gly236, Pro86
4	1Q5K	Val76, Asp166, Cys165, Leu98, Asp 99, Lys 51, Asn151, Ala49, Val 36, Gln 151, Ile 28, Tyr 100, Leu 154, Val 101, Pro 102, Thr104

Table-2: Amino Acid Residues on the Protein that form Hydrogen and Van Der Waals Bonds with Ligands

S.No.	Proteins	Hydrogen bond	Van der walls bond
1	1GEN	Gln624, Asp622, Asn573, Glu525	Gly483, Gln480, Val621, Phe572, Tyr524
2	4DPE	His142, Ala83	Leu82, Ala83, Zn174, Glu120, Pro139, Leu140, Thr145, Ala135
3	5H8X	Thr82, Asp233, Asp232	Pro86, Asn85, Gly234, Met83, Leu205, Gly235, Ala206, Ser208, Met215
4	1Q5K	Val101	Asp99, Tyr100, Rhr104, Pro102, Ile28, Gln151, Asn152, Asp166



(A) (B)

(C) (D)

Fig.-5: Interaction between Ligands with Proteins
A-Ligands with 1GEN, **B**-Ligands with 4DPE, **C**-Ligands with 5H8X, **D**-Ligands with 1Q5K

Table-3: Binding Energies of Ligands Interacting with Proteins

Ligands	1GEN	4DPE	5H8X	1Q5K
	kcal/mol	kcal/mol	kcal/mol	kcal/mol
(S)-1-Bromo-2-methylbutane	-4.1	-4.1	-4.2	-3.6
1-Cyclopropyl-2-propen-1-one	-5.1	-5.3	-5.2	-4.6
2-Isopropyl-5-methylphenyl iso-butyrate	-4.3	-4.7	-4.4	-3.9
3,5-Octadien-2-one	-5.7	-6	-5.4	-5.8

3,7-Octadien-2-one	-5.1	-5.9	-5.7	-4.8
3-Bromopentane	-5.1	-5.6	-5.4	-4.5
3-Buten-2-one	-3.6	-4	-4.1	-3.7
3-Methyl-1-pentene	-3.8	-3.8	-3.7	-3.1
3-Methyl-3-buten-2-one	-4.2	-4.3	-4.5	-3.8
3-Penten-2-one	-4.2	-4.3	-4.3	-3.7
4,4-Dimethyl-1-hexene	-4.3	-4.4	-4.4	-3.6
4-Hexen-2-one, 3-methyl	-4.4	-4.7	-5	-4.3
4-tert-Butylphenyl acetate	-4.9	-5.3	-5.3	-4.6
5-Ethyl-3-nonen-6-one	-5.5	-6.3	-5.8	-5.9
Benzoic acid, 2-(isopropyl)oxy-, methyl ester	-5.7	-6	-6	-5.6
Butanoic acid, 2-propenyl ester	-5.7	-6.9	-5.8	-5.8
Ethylene oxide	-4.3	-5.2	-4.9	-4.1
Hydroxyurea	-2.6	-2.4	-2.3	-2.1
Isothymol isobutyrate	-4.2	-4.3	-4.5	-4.1
Methyl 2-(pentyloxy)benzoate	-5.7	-8	-5.9	-6.2
Methyl 2-butoxybenzoate	-4.1	-4.1	-3.9	-3.6
Octa-3,5-dien-2-one	-5.1	-6.7	-5.6	-5.6
Pentandioic acid, (p-t-butylphenyl)ester	-5.1	-5.9	-5.7	-4.8
Salicylic acid acetate, methyl ester	-6.1	-6.8	-4.9	-6.3
Semicarbazide	-5.7	-6.5	-6	-6.5
Thymol acetate	-6	-6.4	-5.3	-5.4
(4E)-3-Methyl-4-hexen-2-one	-4.4	-4.4	-4.5	-4
(+) - (S)-1-Bromo-2-methylbutane	-5.9	-8	-6	-6.2

Table-4: Lipinski's rules of ligands

S. No.	LIGANDS	Lipinski's rule				
		Molecular mass (<500)	Hydrogen bond donor(<5)	Hydrogen bond acceptor (<10)	High lipophilicity (<5)	Molar refractivity (40-130)
1	(S)-1-Bromo-2-methylbutane	151.04	0	0	2.7	1.445
2	1-Cyclopropyl-2-propen-1-one	96.13	0	1	1	
3	2-Isopropyl-5-methylphenyl iso-butyrate	220.31	1	1	3	1.39
4	3,5-Octadien-2-one	124.18	0	1	1.8	1.50
5	3,7-Octadien-2-one	124.18	0	1	1.8	1.50
6	3-Bromopentane	151.04	0	0	2.8	1.44
7	3-Buten-2-one	70.08	0	1	0.5	1.41
8	3-Methyl-1-pentene	84.16	0	0	2.7	1.38
9	3-Methyl-3-buten-2-one	84.11	0	1	0.9	1.42
10	3-Penten-2-one	84.11	0	1	0.5	1.42
11	4,4-Dimethyl-1-hexene	112.21	0	0	3.6	1.410
12	4-Hexen-2-one, 3-methyl	112.17	0	1	1.5	
13	4-tert-Butylphenyl acetate	206.28	0	2	3.4	1.50
14	5-Ethyl-3-nonen-6-one	168.28	0	1	3.1	
15	Benzoic acid, 2-(isopropyl)oxy-, methyl ester	194.22	0	3	2.8	1.51

16	Butanoic acid, 2-propenyl ester	128.16	0	2	1.6	1.41
17	Ethylene oxide	44.05	0	1	-0.1	1.35
18	Hydroxyurea	76.06	3	2	-1.8	1.45
19	Isothymol isobutyrate	220.30	0	2	4.2	1.49
20	Methyl 2-(pentyloxy)benzoate	222.28	0	3	3.8	1.5
21	Methyl 2-butoxybenzoate	208.25	0	3	3.3	1.5
22	Octa-3,5-dien-2-one	124.18	0	1	1.8	1.5
23	Pentandioic acid, (p-t-butylphenyl)ester	264.32	1	4	3.1	
24	Salicylic acid acetate, methyl ester	194.18	0	4	1.5	
25	Semicarbazide	75.07	3	2	-1.8	1.44
26	Thymol acetate	192.25	0	2	3.3	1.49
27	(4E)-3-Methyl-4-hexen-2-one	112.70	0	1	1.5	
28	(+) - (S)-1-Bromo-2-methylbutane	151.05	0	0	2.7	1.44

CONCLUSION

Research on *Musa acuminata* bark extract shows strong indications for its use as a natural healing agent through chemical profiling and docking analysis of major compounds. Bioactive compounds such as flavonoids, tannins, saponins, and phenolic compounds found in the extract enable antioxidant effects and antimicrobial action alongside anti-inflammatory activities that help wound healing processes. The tested extract compounds show high affinity to wound-healing proteins according to molecular docking analyses, which provides evidence for multisystemic repair mechanisms when used for tissue restoration and inflammatory reduction, and cell proliferation support. The therapeutic properties of *Musa acuminata* bark extract reveal its potential to become a valuable addition for wound care applications, according to these research findings. Proof of safety alongside effectiveness and usability for contemporary wound management practices requires extra in vivo studies alongside clinical trials.

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CONFLICT OF INTERESTS

The authors declare that there is no conflict of interest.

AUTHOR CONTRIBUTIONS

All the authors contributed significantly to this manuscript, participated in reviewing/editing and approved the final draft for publication. The research profile of the authors can be verified from their ORCID ids, given below:

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