Investigating the anti-cancer compounds from *Calliandra harrisi* for precision medicine in pancreatic cancer via *in-silico* drug design and GC-MS analysis

Abstract: Pancreatic cancer is a fatal illness caused by mutations in multiple genes. Pancreatic cancer damages the organ that helps in digestion, resulting in symptoms including fatigue, bloating, and nausea. The use of medicinal plants has been crucial in the treatment of numerous disorders. The medicinal plant *Calliandra Harrisi* has been widely exploited for its possibilities in biology and medicine. The current study aimed to assess the biopotential of biologically active substances against pancreatic cancer. The GC-MS data of these phytochemicals from *Calliandra Harrisi* were further subjected to computational approaches with pancreatic cancer genes to evaluate their potential as therapeutic candidates. Molecular docking analysis revealed that N-[Carboxymethyl] maleamic acid is the leading molecule responsible for protein denaturation inhibition, having the highest binding affinity of 6.8 kJ/mol among all other compounds with KRAS inflammatory proteins. Furthermore, ADMET analysis and Lipinski’s rule validation were also performed revealing its higher absorption in the gastrointestinal tract. The results of the hepatotoxicity test demonstrated that phytochemicals are non-toxic, safe to use, and do not cause necrosis, fibrosis, or vacuolar degeneration even at excessive levels. *Calliandra Harrisi* has phytoconstituents that have a variety of pharmacological uses in consideration.

1 Introduction

Humans have used plants for a wide variety of purposes throughout history [1] because of their therapeutic effectiveness. Medicinal plants have been the subject of intensive research around the world. These plants provide a promising supply of primary chemicals for the creation of novel medications with desirable properties such as high efficacy, lack of adverse effects, and commercial feasibility [2]. More than 80% of the world’s population uses medicinal herbs to treat a wide variety of health ailments, according to surveys conducted by the World Health Organization. Incredible as it may seem, there is proof from fossil fuel records that humans have been using plants as medicine for nearly 60,000 years [3]. Many studies have shown that medicinal plants include phytoconstituents with a wide range of biological activity, including those that are anti-inflammatory, antibacterial, antifungal, antimalarial, anticancer, and antioxidant [4].

The general prognosis for pancreatic cancer has remained dismal for several decades with little progress, making it a major contributor to cancer-related deaths. Preventing or diagnosing the disease at an early, treatable stage is quite difficult at present due to unidentified tumor symptoms [5]. With a 5-year survival rate of just 12% across all stages, pancreatic cancer has the lowest chance of survival of any major malignancy [6]. The 5-year survival rate is only 44% in the subset of cases (15%) where the disease is identified locally [7]. Family history, being overweight, having type 2 diabetes, and smoking increase the likelihood of developing pancreatic cancer. Patients often present with advanced-stage disease even when the cancer is still localized because of the absence or vagueness of symptoms. The American Cancer Society reports that there were around 56,000 newly diagnosed cases of pancreatic cancer in the United States in 2019, with an estimated 45,000 fatalities [8]. After lung cancer and colon cancer,
Pancreatic cancer is now the third leading cause of cancer-related death in the United States. In 2018, GLOBOCAN estimated 459,000 new cases and 432,000 fatalities worldwide, placing it as the seventh largest cause of cancer-related deaths in both men and women [9]. Pancreatic cancer is expected to overtake breast cancer in mortality rates in the European Union in the near future [9].

Inherited factors are thought to be responsible for about 5–10% of all cases of pancreatic cancer [10]. There are several known family cancer disorders that raise the risk of acquiring pancreatic cancer. In the case of Peutz–Jeghers syndrome, a 35% increased risk of pancreatic cancer is caused by a mutation in the tumor suppressor gene STK11 (also known as LKB1) [11]. Hereditary breast and ovarian cancer syndrome typically connected to BRCA1 or BRCA2 mutations, is also associated with an increased risk of pancreatic cancer. BRCA2 mutations are the most common genetic risk factor for pancreatic cancer, with a relative risk of 3.5 for acquiring the disease, although the elevated risk for patients with a BRCA1 mutation is relatively small (2.8% compared to 1.3% in the normal population) [12]. Having a mutation in BRCA2, BRCA1, CDKN2A, ATM, STK11, PRSSI, MLH1, or PALB2 increases your risk of developing pancreatic cancer, while the risk varies depending on the specific mutation.

Pancreatic cancer is difficult to treat because of its multifaceted complexity at the genomic, epigenetic, and metabolic levels. Tumor microenvironment complexity increases due to interaction between neoplastic and stromal cells. Patient outcomes have improved only slightly despite developments in diagnosis, surgical care, radiation therapy, and systemic treatment [13]. The development of novel screening technologies for the early diagnosis of pancreatic cancers is urgently required. Adjuvant chemotherapy with gemcitabine or S-1 has shown improved long-term outcomes, and surgical excision is now the only possibly curative treatment [14]. However, there is a chance that some tumor cells will survive surgery, and surgery may not be an option if the disease has spread or is in a difficult location, such as near blood vessels. Surgery, radiotherapy, chemotherapy, and immunotherapy are all viable options for treating pancreatic cancer. But all these surgical treatments are costly and painful for patients [15].

The Fabaceae family includes the medicinally important plant Calliandra Harrisii. It is native to moist and semiarid areas of Central America and Mexico. Its numerous biological functions can be attributed to its abundance of phytoconstituents (secondary metabolites). The objective of this study was to analyze the phytochemical composition of two fractions, ethyl acetate and n-butanol, derived from the methanolic extract of Calliandra Harrisii, using GC-MS analysis. The KRAS gene is linked to pancreatic cancer, thus the researchers focused on measuring the phytochemicals and performing computer analysis on the gene [16]. The results of this study provide new information about the potentially useful phytochemicals found in Calliandra Harrisii for the treatment of a wide range of medical conditions.

2 Materials and methods

2.1 Collection and preparation of plant extract

The leaves of Calliandra Harrisii were obtained from Botanical garden of Punjab University, Lahore and the University of Central Punjab’s Botany Department verified its authenticity. The leaves were cleaned with clean water and allowed to air dry for three days. An amount of 500 g of the entire plant was ground into a fine powder after drying. Until they were extracted, the powder was stored in airtight plastic bottles.

2.2 Solvent extraction method

Dried leaves plant powder (500 g) was macerated in methanol (1500 mL) for seven days to produce the methanolic extract. Amorphous solid masses were created during the extraction and evaporating process using rotary evaporators. In order to overcome the crude extract (49.12 g), water (75 mL) was utilised. Using a separatory funnel, fractions were transferred to two separate solvents, chloroform, n-butanol and ethyl acetate, respectively.

2.3 Mass spectrometry using gas chromatography

The leaf extract of Calliandra Harrisii was analysed using gas chromatography-mass spectrometry (GC-MS) in accordance with the optimized procedures. Using a GC-MS model 7890B, 5977A operating at 75 eV of the ionisation energy, the methanolic extract was seen using a DB-5MS column with a 0.26 m film thickness, 0.35 mm diameter, and 40 m in length. One millilitre per minute of helium was used as the carrier gas. The columns were first heated for 1 min to 50 °C. It was then controlled for a temperature increase of 8 °C every minute to reach 290 °C over a consistent period of time. Helium was employed as a carrier gas to carry 1 mL of sample extract down the column at a flow rate of 1 mL/min. After the components had been separated in a 75 eV column, FID spectrosopy was used to identify and further analyze the components. NIST MS 2.0 libraries were used to determine the molecular weight, name, and chemical make-up of these substances.

2.4 Gene enrichment analysis

A functional enrichment study was performed by using FunRich using training databases that have been combined from diverse genomic and proteomic resources (>1.5 million annotations) [17]. The unique database enables the tool to be applied with genomes, lipidomics, and metabolomics datasets in along with proteomics datasets. It also enables adjustable font, scale, and colour for the data’s graphical representation (Venn, pie charts, bar graphs, columns, and heatmaps). In order to predict the enrichment analysis of pancreatic genes, this tool was assessed with target genes and heat map was generated for graphical representation of results [18].
2.5 Network pathway study

SIGNOR 2.0 is an online platform that is utilized to represent each related gene or protein interaction pathways and connection as a source entity that influences by up-regulation and down-regulation of a target entity. It is annotated with the regulatory mechanism that underlies the regulation like transcriptional regulation and epigenetic regulation etc. [19]. The representation of linkages is a dynamic, customizable graph, where the nodes are the entities and the edges are the causal connections between them. The pathway and interaction analysis in between the pancreatic cancer genes were studied with the aid of this tool.

2.6 Retrieval of gastric cancer genes

The Human Gene Database, accessible at https://www.genecards.org/, was utilized to identify genes associated with pancreatic cancer. This valuable resource offers a user-friendly and extensive collection of information on annotated and predicted human genes, all integrated into a searchable database [20]. 13 genes related to pancreatic cancer were obtained from the Protein Data Bank and visualized using Discovery Studio.

2.7 Structural retrieval of bioactive compounds

The structures of the compounds were retrieved from PubChem which is available at https://pubchem.ncbi.nlm.nih.gov/. PubChem, a chemical resource under the National Institutes of Health (NIH), serves as an easily accessible database [21]. It offers comprehensive information on chemical structures, physical and chemical properties, toxicity, health effects, biological activities, as well as patentability and safety assessments for both small molecules and chemically modified macromolecules [22].

2.8 Analysis of Venn diagrams (bioinformatics and evolutionary genomics system)

Bioinformatics and evolutionary genomics methodologies are employed to identify common targets associated with drugs and diseases [23]. These shared targets can be visualized using a Venn diagram, which can be accessed at the following URL: https://bioinformatics.psb.ugent.be/webtools/Venn/. This diagram effectively depicts the overlapping regions between disease and drug targets.

2.9 Protein–protein interaction

STRING is a bioinformatics based biological database that is used to evaluate the protein–protein interaction which can lead to better interaction analysis. STRING (https://string-db.org/) was accessed on May 23, 2023) was utilized to analyze the protein–protein interaction of pancreatic cancer genes. STRING predicted the number of nodes, number of edges, average node degree and functional partners as well.

2.10 Molecular docking

All the retrieved phytochemicals were screened through multiple ligands docking by PyRx. It is software to screen library of phytochemicals against target protein. The KRAS protein was screened against retrieved phytochemicals. The compound with highest binding affinity was further evaluated for binding energy through Autodock Vina. Firstly, protein was purified by utilizing Discovery Studio and ligand was prepared for active site identification and grid box was set. Docking was performed between KRAS and bioactive compounds. After docking the docked complex was visualized through Discovery studio which depicted bond length, and bond types between interesting molecules.

2.11 ADMET analysis

A molecule’s water solubility, blood–brain permeability, hepatotoxicity, physiochemical, pharmacokinetic, and medicinal chemistry were all determined using the free online tool Swiss ADME (http://www.swissadme.ch/). Swiss ADME of N-[Carboxymethyl]maleamic acid was employed to characterize compounds’ toxicity, solubility and drug likeness properties.

2.12 Molecular dynamic simulation (iMoDs)

It is a computer-aided simulation method for analyzing atoms or molecules’ physical motions (https://bio.tools/iM0ds). A few significant interactions can be identified using molecular dynamics (MD) simulation of hydrogen bond interactions. MD simulations make virtual screening and protein docking possible. The iMoDs server was used to run molecular dynamics simulations of KRAS docked complex with N-[Carboxymethyl]maleamic acid. This server offers details on routes involving macromolecules or homology that can be searched using normal mode analyses.

3 Results

3.1 GS-MS analysis of leaf extract of Calliandra Harrisi

A GCMS analysis was used to evaluate the chemical makeup of leave extract of Calliandra Harrisi. The identified compounds were seven in numbers and the repeated compounds were substituted by single ones. The principal compounds belonged to alkanes and these alkanes have major contribution with tetratetracontane. Likewise aromatic hydrocarbons, carboxylic acid and benzoic acid compounds were also detected and their molecular weight, % area and retention time are depicted in the Table 1 with their respective compound family names. The chromatogram in Figure 1 portrayed the peaks (x-axis) with their retention time (y-axis) of different compounds detected in leave extract of Calliandra Harrisi analyzed through GC-MS analysis.

3.2 Gene enrichment analysis

Pancreatic cancer genes including KRAS, TP53, CDKN2A, SMAD4, ATM, BRCA1, and BRCA2 and STK11 were analyzed
for their molecular functions. Taking the p value as $-\log_{10}$ and reference p value as 0.05 the genes portrayed 12.5% GTPase activity and kinase regulator activity. Transcription factor activity, serine/threonine kinase activity, and transcription regulator activity were predicted as 25% as shown in the graph (Figure 2).

### Table 1: Identified compounds present in leaf extract of Calliandra Harrisii through GC-MS analysis.

<table>
<thead>
<tr>
<th>Sr. No</th>
<th>Compound name</th>
<th>Molecular weight</th>
<th>% area</th>
<th>Retention time</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1,4-Dioxaspiro[4.5]decan-8-one, 7-(hydroxymethyl)-</td>
<td>186</td>
<td>1.88</td>
<td>26.526</td>
</tr>
<tr>
<td>2</td>
<td>2,3-Di-T-Butoxy-1,4-dioxane</td>
<td>232</td>
<td>23.06</td>
<td>9.592</td>
</tr>
<tr>
<td>3</td>
<td>2-Azacyclooctanone</td>
<td>127</td>
<td>2.28</td>
<td>18.882</td>
</tr>
<tr>
<td>4</td>
<td>2-Heptenoic acid</td>
<td>156</td>
<td>2.28</td>
<td>18.882</td>
</tr>
<tr>
<td>5</td>
<td>N-[Carboxylmethyl]maleamic acid</td>
<td>173</td>
<td>6.63</td>
<td>18.882</td>
</tr>
<tr>
<td>6</td>
<td>Oxazine</td>
<td>173</td>
<td>2.28</td>
<td>18.882</td>
</tr>
<tr>
<td>7</td>
<td>Spiro[1,3-dioxole-2,2’-[6,7]diazabicyclo[3.2.2]non-6-ene]</td>
<td>182</td>
<td>2.74</td>
<td>26.609</td>
</tr>
</tbody>
</table>

**Figure 1:** Chromatogram with peaks of identified compounds on x-axis and retention time on y-axis.

**Figure 2:** Prediction of GTPase activity, transcription factor activity, transcription regulator activity, kinase regulator activity and protein serine.
The heat map for pancreatic cancer genes predicts highest activity for *ATM* gene in human proteome for adult heart, B cells, CD4 cells, CD8 cells, and NK cells. Whereas, *KRAS* gene has been predicted with highest activity in maximum human proteome cells as shown in Figure 3.

### 3.3 Pathway analysis

The pathway and interaction analysis of pancreatic cancer genes *BRCA1, BRCA2, CDKN2A,* and *ATM* were performed with SIGNOR 2.0. The red lines depict down regulation, blue lines depict up regulation, green nodes represent the proteins, blue nodes represent complexes, yellow line is the cell membrane, and purple area is the nucleus respectively as shown in the Figure 4.

### 3.4 Potential disease target genes

GeneCards was utilized to search for target genes associated with pancreatic cancer. A total of eight genes strongly

![Figure 3: Heat map for pancreatic cancer genes (ATM, KRAS), KRAS gene have highest activity in maximum human proteome cells.](image)

![Figure 4: The pathway and interaction analysis of pancreatic cancer genes.](image)
implicated in causing pancreatic cancer were identified from GeneCards. These genes were selected based on previous studies, considering their significance in drug design. The complete gene sequences of these eight pancreatic cancer genes were retrieved from the Protein Data Bank (PDB), with the corresponding PDB IDs as follows: ATM (2lym), BRCA1 (1t15), BRCA2 (1iyj), CDKN2A (1a5e), KRAS (4obe), SMAD4 (1ygs), STK11 (2wtk), and TP53 (7vou). The visualization of these genes was performed using Discovery Studio Visualizer.

3.5 Structural retrieval of phytochemicals

The structures of the phytochemicals which identified through GCMS analysis were retrieved from PubChem. There were 16 compounds in the methanolic extract of Calliandra Harrisii which identified through GCMS analysis but seven compounds retrieved because they have anticancerous capability. The structures were saved in SDF format and then converted into PDB form using Discovery studio. The retrieved structures of phytochemicals are shown in given Table 2.

3.6 Analysis of Venn diagrams (bioinformatics and evolutionary genomics system)

The Venn diagram displays the overlap between recognized targets of identified chemical compounds and pancreatic cancer. A total of eight genes associated with pancreatic cancer were obtained, and the top four genes, namely BRCA2, KRAS, SMAD4, and STK11, were specifically utilized to generate the Venn diagram (Figure 5).

3.7 Protein–protein interaction

STRING was used to predict the protein–protein interaction of genes identified against pancreatic cancer. There was 13 numbers of nodes, 71 numbers of edges, 10.9 average node degrees and PPI enrichment p-value was 2.46e-13 predicted through STRING as shown in Figure 6.

3.8 Molecular docking

Pyrx was used to screen the library of phytochemicals against KRAS protein. It was noted that N-[Carboxymethyl] maleamic acid have highest binding affinity with target protein that is −6.3 kcal/mol and Spiro[1,3-dioxolane-2,2′-[6,7]diazabicyclo[3.2.2]non-6-ene] (−5.5). Lowest binding affinity was shown by oxazine that is −4.1 kcal/mol (Table 3). The docked complex is shown in Figure 7. Furthermore, Autodock vina was utilized to elaborate the binding energy of interacting molecules of KRAS protein and N-[Carboxymethyl] maleamic acid which showed −6.8 kcal/mol binding energy. Moreover, the molecular interaction visualized through Discovery Studio is shown in Figures 8 and 9.

3.9 ADMET analysis

ADMET analysis was performed and result shows that N-[Carboxymethyl] maleamic acid has lipophilicity iLOGP is 0.1, with high water solubility, high GI absorption and follow all Lipinski rule of five. The drug was effectively absorbed in the GI tract, according to the pharmacokinetic analysis and it did not break Lipinski’s rule (Table 4).

<table>
<thead>
<tr>
<th>No.</th>
<th>Names</th>
<th>Structures</th>
<th>PubChem ID</th>
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</thead>
<tbody>
<tr>
<td>1</td>
<td>2-Heptenoic acid</td>
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<td>5282709</td>
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<td>2</td>
<td>1,4-Dioxaspiro[4.5]decan-8-one, 7-(hydroxymethyl)</td>
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<td>3</td>
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<tr>
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<td>2-Azacyclooctanone</td>
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<td>5</td>
<td>Oxazine</td>
<td></td>
<td>12313776</td>
</tr>
<tr>
<td>6</td>
<td>2,3-DI-T-Butoxy-1,4-dioxane</td>
<td></td>
<td>545346</td>
</tr>
<tr>
<td>7</td>
<td>N-[Carboxymethyl]maleamic acid</td>
<td></td>
<td>1880137</td>
</tr>
</tbody>
</table>
The boiled egg model provided an easy, quick, readily repeatable, but novel and robust technique for analyzing small molecule brain access and passive gastrointestinal absorption that may be used for drug discovery and development. If the molecule is in the white region of the boiled egg model, it represents gastrointestinal absorption; if the molecule is in the yellow area of the boiled egg model, it represents access to the blood–brain barrier. According to the boiled egg model, the drug will be well absorbed in the blood–brain barrier (Figure 10).

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**Table 3**: The molecular docking analysis of the compounds with KRAS protein.

<table>
<thead>
<tr>
<th>Sr.No</th>
<th>Compounds</th>
<th>Docking energies</th>
</tr>
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<tbody>
<tr>
<td>1</td>
<td>N-[Carboxymethyl]maleamic acid</td>
<td>−6.3</td>
</tr>
<tr>
<td>2</td>
<td>Spiro[1.3-dioxidolane-2.2′:6,7]diazabicyclo[3.2.2]non-6-ene</td>
<td>−5.5</td>
</tr>
<tr>
<td>3</td>
<td>1,4-Dioxaspiro[4.5]decane-8-one, 7-(hydroxymethyl)</td>
<td>−5.2</td>
</tr>
<tr>
<td>4</td>
<td>2-Heptenoic acid</td>
<td>−5.2</td>
</tr>
<tr>
<td>5</td>
<td>2-Azacyclocloctanone</td>
<td>−4.6</td>
</tr>
<tr>
<td>6</td>
<td>2,3-Di-O-t-Butoxy-1,4-dioxane</td>
<td>−4.5</td>
</tr>
<tr>
<td>7</td>
<td>Oxazine</td>
<td>−4.1</td>
</tr>
</tbody>
</table>
3.10 Molecular dynamic simulation (by IMODs)

Based on field force, the molecular simulation done with IMODs predicted the stability of the docked complexes, as shown in Figure. This prediction was validated by the predicted B-factor, and the eigenvalues demonstrated how much energy was required to deform the complex with little variance. The eigenvalue of the docked complex structure of KRAS was predicted as 2.935744e06. The covariance and elastic maps of the docked complex were predicted to have few to no perplexing interactions. As shown in the Figure 11.

![Figure 7: Molecular interaction between KRAS and N-[Carboxymethyl] maleamic acid](image)

![Figure 8: 2D diagram of molecular interactions, conventional hydrogen bond (green) and carbon hydrogen bond (light green).](image)

![Figure 9: Visualization of interactions between KRAS and N-[Carboxymethyl] maleamic acid.](image)

<table>
<thead>
<tr>
<th>Physiochemical properties</th>
<th>ADMET analysis of the N-[Carboxymethyl] maleamic acid.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molecular formula</td>
<td>C(_6)H(_9)NO(_5)</td>
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<tr>
<td>Molecular weight</td>
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<tr>
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</tr>
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<tr>
<td>Num. H-bond acceptors</td>
<td>5</td>
</tr>
<tr>
<td>Num. H-bond donors</td>
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</tr>
<tr>
<td>Lipophilicity (iLogp)</td>
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</tr>
<tr>
<td>Water solubility log S (ESOL)</td>
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<tr>
<td>GI absorption</td>
<td>High</td>
</tr>
<tr>
<td>Log Kp (skin permeation)</td>
<td>−8.38 cm/s</td>
</tr>
<tr>
<td>Bioavailability score</td>
<td>0.56</td>
</tr>
<tr>
<td>Lipinski’s rule of 5</td>
<td>Accepted</td>
</tr>
</tbody>
</table>

Table 4: ADMET analysis of the N-[Carboxymethyl] maleamic acid.
4 Discussion

Although the obvious benefits of plants as food and shelter, their therapeutic value is frequently overlooked. Phytochemicals and their by-products are found in the bark, stems, leaves, flowers, and roots of plants and have a wide range of pharmacological effects. Alkaloids, flavonoids, phenolics, tannins, glycosides, gums, resins, and oils are all examples of these crucial compounds. In addition to killing rapidly dividing cells, they minimize oxidative stress, regulate cell growth factors, prevent blood vessel formation in malignant tissues, and cause apoptosis. Some flavonoids and polyphenols have shown anticancer effects via encouraging apoptosis [24], including methoxy licorflavanone and alpinumisoflavone. The methanolic extract of *Calliandra Harrisi* was fractionated into ethyl acetate and n-butanol, where flavonoids and other beneficial phytochemicals were identified through phytochemical analysis. The presence of specific phytoconstituents in *Calliandra Harrisi* fractions may increase their medicinal potential. Additionally, the identification of chemical components with biological activity was determined through the use of GC-MS analysis [25].

According to Robatel and Schenk pancreatic cancer, known for its aggressive nature, is among the most lethal forms of cancer worldwide [26]. As a result, treatment options primarily focus on providing palliative care, as only a small fraction of patients have tumors that can potentially be cured. Currently, the sole treatment approach with curative intent involves surgery followed by [27]. However, it is crucial to acknowledge that this treatment is not a permanent solution for pancreatic cancer and can have profound effects on the human body. Since the goal of chemotherapy is to kill cancer cells, the medications can have serious side effects like nausea, vomiting, hair loss, exhaustion, and damage to healthy organs and cells [28]. The severity of chemotherapy-related toxicity varies based on the specific drugs administered and an individual's tolerance, but it can substantially impact a patient's overall well-being. Moreover, chemotherapy may have lasting consequences, including organ damage, the development of secondary cancers, and fertility issues [29]. Consequently, there is an urgent necessity to discover novel therapeutic regimens to address these limitations and improve outcomes for pancreatic cancer patients.

Kostro and Sledzinski reported that in recent decades, there have been notable advancements in pancreatic surgery [30]. In specialized centers that handle a high volume of cases, the safety of pancreatic cancer surgery is comparable to major surgeries for other gastrointestinal cancers, with similar rates of morbidity and mortality. Although this treatment has the potential to be effective, it is highly painful for patients. Many cases of pancreatic cancer are diagnosed at advanced stages, where the tumor has spread beyond the pancreas or involves critical blood vessels. In such situations, surgical removal of the tumor may not be possible due to the extensive nature of the disease. Moreover, certain patients may have pre-existing health conditions that render them unsuitable for surgery.

According to (Kamisawa, Wood, Itoi, and Takaori) pancreatic cancer remains a significant health challenge that has yet to be effectively addressed, as traditional cancer treatments have limited impact on the progression of the disease [31]. The smoking, age, and certain genetic disorders are
the main risk factors, although the exact underlying causes are not well understood. However, advances in molecular biology have significantly enhanced our understanding of the development of pancreatic cancer. Approximately 15–20% of patients have resectable (able to be surgically removed) tumors, but only a small fraction of them, around 20%, survive beyond 5 years. For patients with locally advanced, unresectable, or metastatic disease, treatment focuses on palliative care.

Figure 11: Molecular dynamics docking simulations of KRAS docked complex with N-[Carboxymethyl]maleamic acid (a) indicates a low level of deformation at all residues (b) the B-factor (c) Eigen values (d) the variance explained in both purple and green are depicted. The complex’s covariance and elastic network are shown in (e) and (f), respectively.
Chemo-radiation with fluorouracil is used for locally advanced cases, while gemcitabine chemotherapy provides palliative benefits for metastatic disease [32]. Despite the resistance of pancreatic cancer to currently available treatments, there is ongoing research into new approaches. Preoperative chemo-radiation is being increasingly recommended, supported by logical reasoning, and there is a growing exploration of the expanded use of gemcitabine. However, the most promising prospects lie in developing new therapeutic strategies based on the molecular biology of pancreatic cancer. These innovative approaches hold the potential for significant advancements in the management of the disease [33].

Several studies have demonstrated the diverse biological activities of the flavonoid group, including antimicrobial, antioxidant, anti-inflammatory, anticancer, and anti-allergic effects. In this study, the chemical composition of the Calliandra Harrisi leaf extract was evaluated using a GC-MS technique, leading to the identification of seven phytochemicals present in Calliandra Harrisi. To assess their potential as drug candidates, the GC-MS results of these phytochemicals from Calliandra Harrisi were subjected to molecular docking with pancreatic cancer genes. Among the seven ligands tested against eight genes, N-[Carboxymethyl]maleamic acid exhibited the highest binding affinity with KRAS protein. Evaluating the efficacy and safety of these novel treatment approaches requires more study and clinical trials. In conclusion, there is promising evidence that compounds including phenolics and flavonoids isolated from the Calliandra Harrisi plant could be used to develop pancreatic cancer treatments. However, additional investigation is required to determine their efficacy, safety, and the most suitable formulation. If successfully developed as therapeutic agents, these compounds could offer a natural and alternative approach to treating pancreatic cancer, complementing the currently available treatment options.

5 Conclusion

The pharmaceutical research based on medicinal plants continues producing promising new novel possibilities for a wide range of pharmacological targets. The GC-MS testing of the methanolic extract identified the putative phytoconstituents, 1,4-Dioxaspiro[4,5]decane-8-one, 7-(hydroxymethyl), 2,3-DI-T-Butoxy-1,4-dioxane, 2-Azacyclooctanone, 2-Heptenoic acid, and N-[Carboxymethyl]maleamic acid, oxazine and Spiro[1,3-dioxolane-2,2'-[6,7]diazabicyclo[3.2.2]non-6-ene all of which had powerful biological effects. According to this study N-[Carboxymethyl]maleamic acid is the most effective lead chemical due to its greater binding affinity with target compound. The N-[Carboxymethyl]maleamic acid showed effectiveness against pancreatic cancer with no toxicity and high doses were safe for oral administrations, according to hepatotoxicity data. These results imply that Calliandra Harrisi is a top option for the treatment of inflammation and other conditions that affect humans. The pharmacological and therapeutic properties of Calliandra Harrisi revealed that it is a promising and adaptable medicinal plant that merits further study.

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References
