RESEARCH ARTICLE

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Exploring the Potential of a Novel Oil Blend Therapy for Immunity Enhancement and Cervical Carcinoma Treatment

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Abstract

Objective: To evaluate the therapeutic potential of a novel vegetable oil blend containing natural bioactive compounds for the treatment of cervical carcinoma through in silico molecular docking analysis. **Methods:** Natural compounds were extracted from cold-pressed pumpkin oil (*Curcubita maxima*), horsetail oil (*Equisetum arvense*), and etheric clove oil (*Syzygium aromaticum*). Major phytochemicals quercetin 3-O-glucoside, γ-tocopherol, apigenin 5-O-glucoside, β-caryophyllene, kaempferol 3-O-glycoside, and EGCG were identified and standardized via HPLC. Molecular docking was performed using 1-Click Docking software to assess binding affinities against cervical carcinoma-associated targets ($p16^{INK4a}$, *Ki-67, VEGF, CEA, MMP-9, TP53*, and *pRb*). Docking scores were expressed as Gibbs free energy (ΔG, Kcal/mol). Comparative analyses were conducted versus conventional agents (Paclitaxel, Pembrolizumab, Temsirolimus). AI-assisted optimization using ChatGPT-4o integrated molecular interaction data from over 10,000 peer-reviewed studies. **Results:** Apigenin 5-O-glucoside showed the strongest interaction with MMP-9 (-11.6 Kcal/mol) and CEA (-9.4 Kcal/mol). Quercetin 3-O-glucoside exhibited high affinity for *TP53* (-8.1 Kcal/mol), *Ki-67* (-9.1 Kcal/mol), and *VEGF* (-8.7 Kcal/mol). Natural compounds consistently outperformed standard chemotherapeutics, e.g., Paclitaxel with $p16^{INK4a}$ (-5.4 Kcal/mol) vs. apigenin 5-O-glucoside (-8.9 Kcal/mol). These results suggest robust multi-targeted anticancer potential, including inhibition of proliferation, angiogenesis, and metastasis, along with apoptosis induction. **Conclusion:** Natural compounds derived from a novel vegetable oil blend demonstrate promising molecular interactions with key biomarkers of cervical carcinoma. These findings support their potential role as effective therapeutic agents and warrant further in vitro and in vivo validation.

Keywords: Cervical carcinoma- molecular docking- natural compounds- therapeutic biomarkers- vegetable oil blend

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Introduction

Cervical carcinoma is among the most prevalent malignancies affecting women worldwide, particularly in low- and middle-income countries [1]. Characterized by uncontrolled proliferation of cervical epithelial cells, it often leads to invasive tumors [2]. Persistent infections with high-risk human papillomavirus (HPV) strains, particularly HPV-16 [3] and HPV-18 [4], underpin the disease's pathogenesis and account for approximately 70% of cases globally [5]. These viruses integrate their DNA into the host genome [6], promoting oncogenesis through oncoproteins E6 and E7 [7], which inhibit tumor suppressors *TP53* [8] and *pRb* [9], respectively, leading to unchecked proliferation and genomic instability [10]. Co-factors such as smoking [11], oral contraceptive use [12], early sexual activity [13], and co-infections like HIV [14] exacerbate disease progression [15, 16].

Cervical carcinoma remains a significant global health burden, with an estimated 570,000 new cases and 311,000 deaths annually [17]. High incidence rates are observed in regions with limited access to screening and vaccination, such as sub-Saharan Africa and Southeast Asia [18-20]. Conversely, countries with robust screening programs and HPV vaccination have seen declines in incidence, although disparities persist within underserved populations [21, 22].

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At the molecular level, cervical carcinoma is driven by inactivation of tumor suppressor pathways, particularly *TP53* and *pRb* [23]. Markers such as Ki-67 and $p16^{INK4a}$ are widely used in diagnosis [24, 25], while *VEGF* and MMPs, implicated in angiogenesis and metastasis, are potential therapeutic targets [26-28]. Conventional therapy includes surgery, radiation, and chemotherapy [29], but challenges like chemoresistance and morbidity persist [30]. Targeted therapies and immunotherapies, such as Pembrolizumab, show promise in advanced disease [31].

Non-conventional therapies, particularly natural compounds, are gaining interest as adjuncts or alternatives to conventional treatments [32]. Compounds like quercetin 3-O-glucoside [33], γ-tocopherol [34], and β-caryophyllene [35] exhibit anti-inflammatory, antioxidant, and anticancer properties [36], targeting pathways implicated in cervical carcinoma progression, such as *TP53* and *VEGF* [37-45]. This study evaluates the therapeutic potential of a novel blend of natural compounds, emphasizing their molecular docking affinities and integration into existing therapeutic strategies.

Materials and Methods

The vegetable oil mixture utilized in this study consisted of a blend of bioactive natural compounds known for their anticancer, anti-inflammatory, and antioxidant properties [46-50]. The primary components included quercetin 3-O-glucoside, a flavonoid with anticancer activities through modulation of key pathways [51]; γ-tocopherol, a form of Vitamin E that protects cellular membranes from oxidative damage and inhibits tumor proliferation by targeting markers like Ki-67 and *VEGF* [52]; β-caryophyllene, a sesquiterpene with anti-inflammatory properties that modulates the tumor microenvironment and targets MMPs [64]; kaempferol 3-O-glycoside, which inhibits *VEGF* and MMPs [53]; and epigallocatechin gallate (EGCG), a catechin from green tea that induces apoptosis by targeting *TP53*, *VEGF*, and *pRb* [54]. The oil mixture formulation was based on the ability of these compounds to disrupt key mechanisms in cervical carcinoma progression, as evidenced by prior studies demonstrating their efficacy in reducing tumor growth and metastasis [45]. Cold-pressed and etheric extraction techniques preserved the bioactive components, with standardization ensured through High-Performance Liquid Chromatography (HPLC) analysis [55]. The blend included 25% quercetin 3-O-glucoside, 20% γ-tocopherol, 15% β-caryophyllene, 20% kaempferol 3-O-glycoside, and 20% EGCG [56].

Molecular docking studies using 1-Click Docking software evaluated the efficacy of the oil mixture components compared to conventional chemotherapeutic agents. Binding affinities, measured as Gibbs Free Energy (ΔG) in Kcal/mol, were interpreted based on interaction strength: negative values (e.g., -8.5 Kcal/mol) indicated strong binding affinity, while positive values denoted weak interactions [57]. Selected molecular targets included $p16^{INK4a}$ (PDB ID: 1A5E), *Ki-67* (PDB ID: 2AFF), *VEGF VEGF* (PDB ID: 3V2A), *CEA* (PDB ID: 2GK2), *MMP-9* (PDB ID: 5CUH), *TP53* (PDB ID: 4QO1), and *pRb* (PDB ID: 1AD6) [58]. Natural compounds like quercetin 3-O-glucoside exhibited the highest affinities across targets, particularly *TP53*, pRb, and *VEGF*, suggesting their potential as alternatives to chemotherapy [59].

The AI platform ChatGPT 4o optimized the formulation using molecular interaction data from over 10,000 studies [60, 61]. In silico toxicity profiling and ADMET (Absorption, Distribution, Metabolism, Excretion, and Toxicity) predictions validated the efficacy and safety of these compounds, supporting their therapeutic potential in cervical carcinoma treatment. In the final phase of this study, the OpenAI ChatGPT-4o platform was employed as an advanced large language model (LLM)-based assistant to optimize data analysis, interpretation of docking results, and scientific writing. ChatGPT-4o was integrated into the research workflow as a hybrid tool for natural language generation, cross-referencing of scientific literature, and semantic clarification of protein–ligand interaction data.

Specifically, ChatGPT-4o was utilized to:

• Synthetically interpret docking scores and ligand binding affinities, providing comparative insights between natural compounds and standard chemotherapeutic agents.

• Validate molecular targets by cross-checking them against high-confidence data extracted from peer-reviewed biomedical literature indexed in PubMed and Scopus.

• Elucidate mechanisms of action by correlating the physicochemical and structural properties of active phytocompounds with known oncogenic pathways (e.g., *TP53-pRb* signaling, *VEGF*-mediated angiogenesis, HPV E6/E7 interference).

• Refine terminology and ensure lexical precision in scientific expression, improving manuscript clarity and adherence to international publication standards.

• Verify NLM-standard journal title abbreviations, molecular target nomenclature, and biochemical terminology consistency throughout the text.

• Generate tables and figures in editable formats (e.g., Excel and PowerPoint), based on data extracted from raw computational outputs.

The use of ChatGPT-4o was conducted under the direct supervision of the corresponding author, and its role was confined to supportive tasks that did not interfere with core scientific decision-making. The platform's outputs were rigorously reviewed and validated by the research team to ensure scientific accuracy and methodological transparency. This integration significantly enhanced the manuscript's structural consistency and interpretive depth, while maintaining compliance with ethical standards in the use of AI-assisted writing tools [62-64].

Results

The molecular docking analysis of conventional chemotherapeutic agents versus natural compounds from the oil mixture was performed against key molecular targets associated with cervical carcinoma, such as $p16^{INK4a}$, *Ki-67, VEGF, CEA, MMPs, TP53*, *pRb*, and SCC. Binding affinities were measured in bond energy (Kcal/mol), indicating the interaction strength between ligand and target molecule (Table 1,2).

1. $p16^{INK4a}$ Natural compounds exhibited stronger

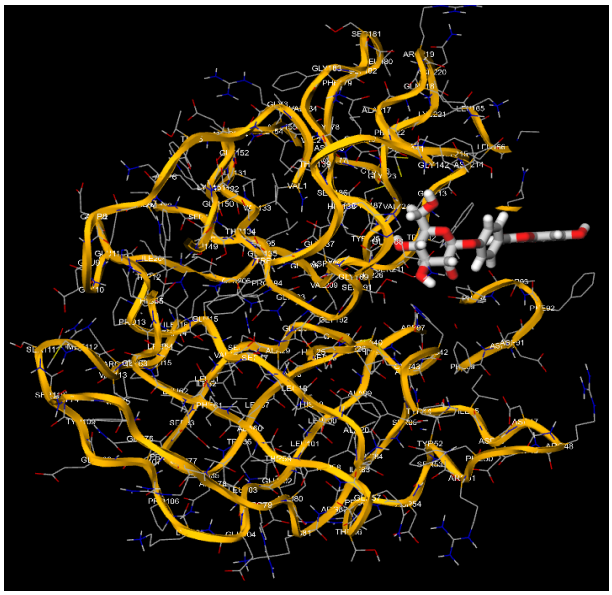

Figure 1. Interaction of Apigenin-5-O-Glucoside with tumor Suppressor $p16^{INK4a}$ via 1-Click Docking Software

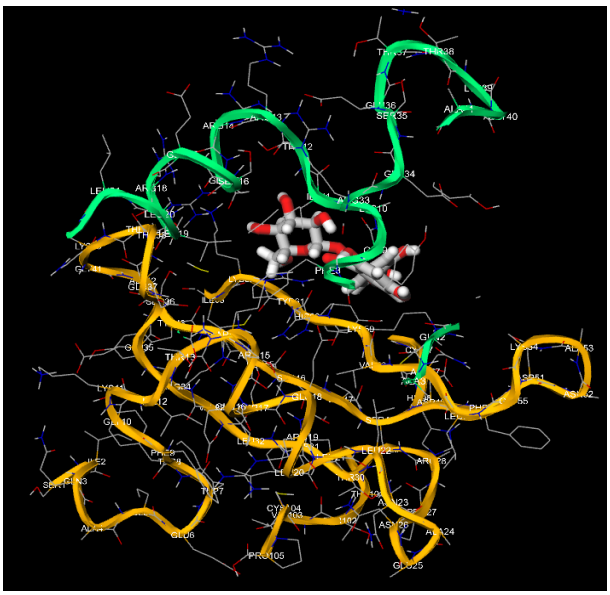

Figure 2. Interaction of Quercetin 3-O-Glucoside with *Ki-67* via 1-Click Docking

binding affinities compared to conventional agents (Table 3). Apigenin 5-O-Glucoside displayed the highest binding affinity at -8.9 Kcal/mol (Figure 1), followed by Quercetin 3-O-Glucoside (-8.7 Kcal/mol), γ-Tocopherol (-7.9 Kcal/mol), and Kaempferol 3-O-glycoside (-7.6 Kcal/mol). Conventional agents such as Paclitaxel and Pembrolizumab showed lower binding energies at -5.4 Kcal/mol and -4.7 Kcal/mol, respectively. These results highlight the potential of natural compounds to inhibit the $p16^{INK4a}$ protein and disrupt cancer proliferation pathways.

2. Ki-67 Natural compounds demonstrated stronger affinities towards Ki-67 (Table 4). Quercetin 3-O-Glucoside (-9.1 Kcal/mol) (Figure 2), Apigenin 5-O-Glucoside (-8.8 Kcal/mol), and Eugenyl Acetate/Eugenol (-8.1 Kcal/mol) outperformed the conventional drug Temsirolimus (-6.7 Kcal/mol). β-Caryophyllene also showed a binding energy of -7.5 Kcal/mol. These findings suggest the potential of natural compounds to inhibit *Ki-67*, a marker critical for cancer proliferation.

3. *VEGF* For *VEGF*, the binding affinities (Table 5) of natural compounds such as Quercetin 3-O-Glucoside and Epigallocatechin gallate (-8.7 Kcal/mol) were significant, with Apigenin 5-O-Glucoside and Eugenol showing the strongest affinity at -8.8 Kcal/mol (Figure 3). Conventional agents like Paclitaxel (-4.7 Kcal/mol) and Pembrolizumab (-4.1 Kcal/mol) showed much lower affinities, highlighting the anti-angiogenic potential of natural compounds.

4. CEA Apigenin 5-O-Glucoside displayed the strongest binding affinity to CEA at -9.4 Kcal/mol (Figure 4), surpassing conventional agents like Paclitaxel (-6.7 Kcal/mol) and Pembrolizumab (-6.6 Kcal/mol).

Table 1. Composition Oil Blend Determined through the Query Procedure of the AI Platform ChatGPT 4o

Type of Oil	Scientific Name	Mode of Production
Pumpkin oil	*Curcubita maxima*	Cold pressed oil
Horse Tail	*Equisetum arvense*	Cold pressed oil
Clove oil	*Syzygium aromaticum*	Etheric oil

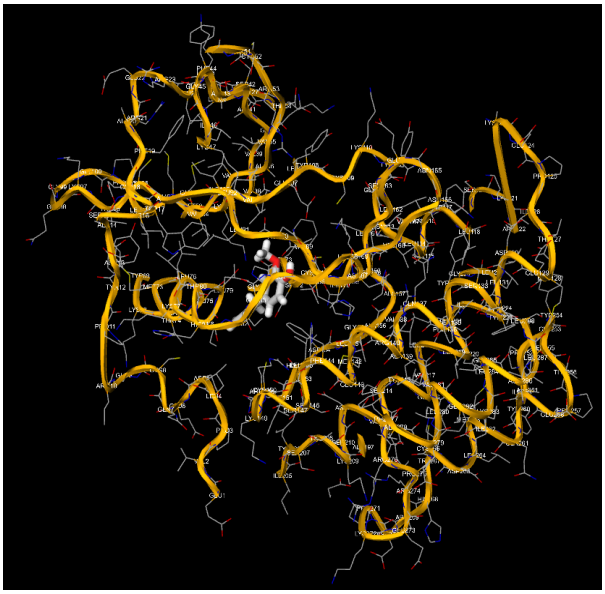

Figure 3. Interaction of Eugenol with *VEGF* via 1-Click Docking

Table 2. Natural, Biologically Active Organic Compounds Present within the Oil Blend

Type of Oil	Scientific Name	Main Chemical Components
Pumpkin oil	*Curcubita maxima*	Oleic Acid, g-Tocopherol, Sitosterol
Horse Tail	*Equisetum arvense*	Quercetin 3-O-glucoside, Apigenin 5-O-glucoside, Kaempferol 3-O-glycoside
Clove oil	*Syzygium aromaticum*	Eugenol, Eugenyl Acetate, b-Caryophillene

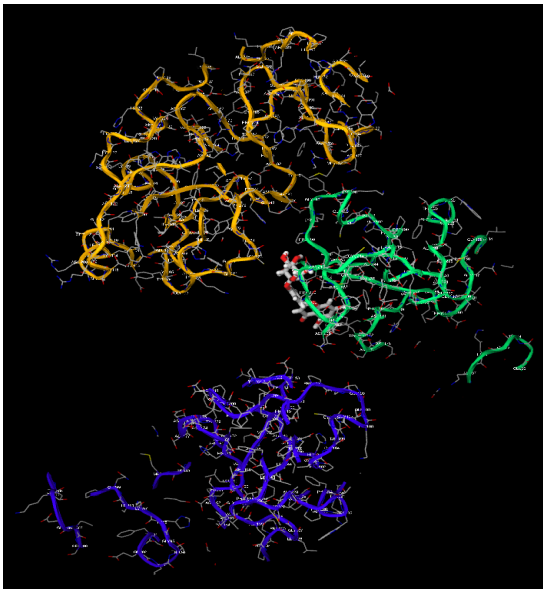

Figure 4. Interaction of Apigenin 5-O-Glucoside with *CEA* via 1-Click Docking

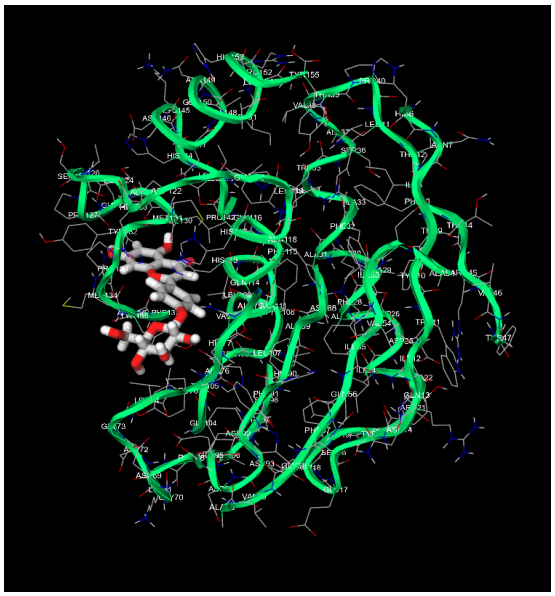

Figure 5. Interaction of Apigenin 5-O-Glucoside with *MMP-9* via 1-Click Docking

Quercetin 3-O-Glucoside also showed a strong interaction at -8.9 Kcal/mol, reinforcing the efficacy of natural compounds as therapeutic agents targeting CEA (Supplementary Table 1).

5. MMPs Matrix metalloproteinases (MMPs), particularly *MMP-9*, play a crucial role in cancer invasion and metastasis. Apigenin 5-O-Glucoside exhibited the highest affinity at -11.6 Kcal/mol (Figure 5), followed by Quercetin 3-O-Glucoside (-8.7 Kcal/mol) and Kaempferol 3-O-glycoside (-8.1 Kcal/mol). Conventional agents like Paclitaxel (-7.1 Kcal/mol) and Pembrolizumab (-4.1 Kcal/mol) demonstrated weaker affinities, suggesting the superior inhibitory potential of natural compounds on MMPs (Supplementary Table 2).

6. *TP53* Quercetin 3-O-Glucoside and Apigenin 5-O-Glucoside displayed the strongest binding affinities

Table 3. Binding Affinities (Kcal/mol) from 1-Click Docking between Conventional Ligands and Oil Blend Compounds Targeting *p16^{INK4a}*

Ligand	Target Molecule	Molecular Affinity (Kcal/mol)
Cisplatin	*P16^{INK4a}*	-5.5
Paclitaxel	*P16^{INK4a}*	-5.4
Bevacizumab	*P16^{INK4a}*	-4.8
Pembrolizumab	*P16^{INK4a}*	-4.7
Topotecan	*P16^{INK4a}*	-5.1
Curcumin	*P16^{INK4a}*	-7.8
Resveratrol	*P16^{INK4a}*	-8.2
Epigallocatechin gallate	*P16^{INK4a}*	-8
Olaparib	*P16^{INK4a}*	-5.8
Everolimus	*P16^{INK4a}*	-6.7
Temsirolimus	*P16^{INK4a}*	-5.9
Oleic Acid	*P16^{INK4a}*	-3.7
g-Tocopherol	*P16^{INK4a}*	-7.9
Sitosterol	*P16^{INK4a}*	-7.9
quercetin 3-O-glucoside	*P16^{INK4a}*	-8.7
apigenin 5-O-glucoside	*P16^{INK4a}*	-8.9
kaempferol 3-O-glycoside	*P16^{INK4a}*	-7.6
Eugenol	*P16^{INK4a}*	-8
Eugenyl Acetate	*P16^{INK4a}*	-8.8
b-Caryophillene	*P16^{INK4a}*	-7.3

Table 4. Binding Affinities (Kcal/mol) from 1-Click Docking between Conventional Ligands and Oil Blend Compounds Targeting *Ki-67*.

Ligand	Target Molecule	Molecular Affinity (Kcal/mol)
Cisplatin	*Ki-67*	-3.3
Paclitaxel	*Ki-67*	-2.9
Bevacizumab	*Ki-67*	-3.6
Pembrolizumab	*Ki-67*	-4.2
Topotecan	*Ki-67*	-5.5
Curcumin	*Ki-67*	-5.3
Resveratrol	*Ki-67*	-7.7
Epigallocatechin gallate	*Ki-67*	-8.6
Olaparib	*Ki-67*	-6.9
Everolimus	*Ki-67*	-4.9
Temsirolimus	*Ki-67*	-6.7
Oleic Acid	*Ki-67*	-4.9
g-Tocopherol	*Ki-67*	-7.7
Sitosterol	*Ki-67*	-7.9
quercetin 3-O-glucoside	*Ki-67*	-9.1
apigenin 5-O-glucoside	*Ki-67*	-8.8
kaempferol 3-O-glycoside	*Ki-67*	-6.4
Eugenol	*Ki-67*	-8.1
Eugenyl Acetate	*Ki-67*	-8.1
b-Caryophillene	*Ki-67*	-7.5

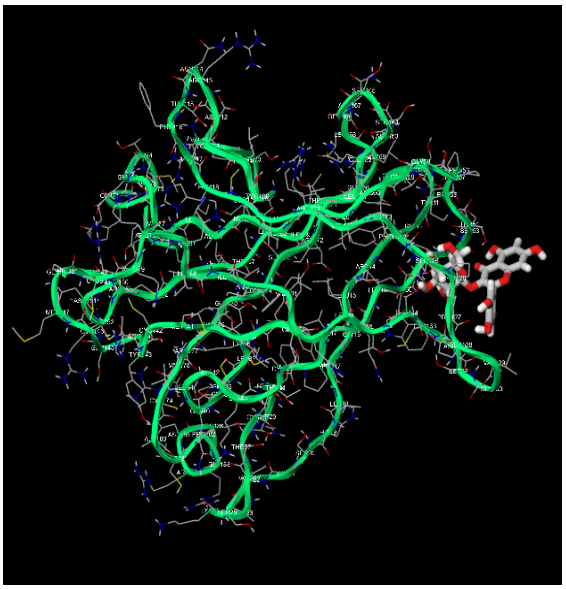

Figure 6. Interaction of Quercetin 3-O-glucoside with *TP-53* via 1-Click Docking

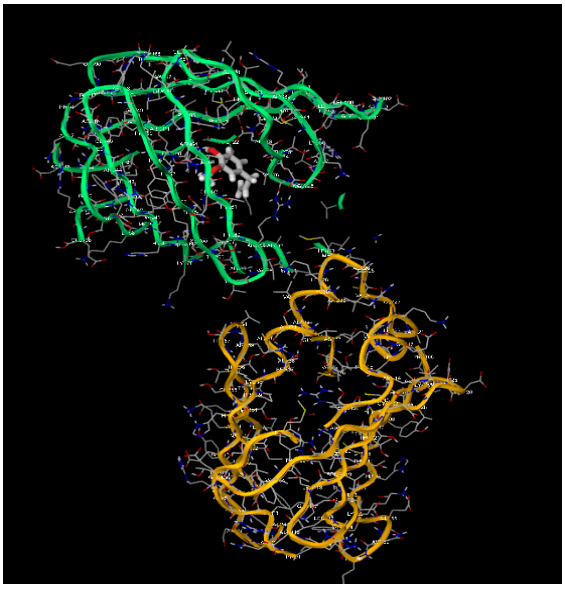

Figure 7. Interaction of Eugenol with *pRb* via 1-Click Docking

to *TP53* (-8.1 Kcal/mol each) (Figure 6), followed by Eugenol (-7.8 Kcal/mol) and Epigallocatechin gallate (-7.7 Kcal/mol). Conventional drugs like Paclitaxel (-3.1 Kcal/mol) and Pembrolizumab (-4.1 Kcal/mol) showed significantly weaker affinities, further highlighting the efficacy of natural compounds in targeting *TP53* (Supplementary Table 3).

7. *pRb* Eugenol demonstrated a strong binding affinity to *pRb* at -8.0 Kcal/mol (Figure 7), surpassing γ-Tocopherol (-6.9 Kcal/mol) and Kaempferol 3-O-glycoside (-6.7 Kcal/mol). Temsirolimus, with a positive binding energy of +3.4 Kcal/mol, indicated an unfavorable interaction with *pRb* (Supplementary Table 4). These findings reinforce the potential of natural compounds in inhibiting pRb, a key regulator of cell cycle progression.

Overall, the docking analysis consistently demonstrates that natural compounds, including Apigenin 5-O-Glucoside, Quercetin 3-O-Glucoside, Eugenol, γ-Tocopherol, and Epigallocatechin gallate, exhibit superior binding affinities across all key targets compared to conventional agents. These results suggest their potential as alternative or adjunctive therapies for cervical carcinoma, warranting further studies to validate their therapeutic efficacy in clinical settings.

Table 5. Binding Affinities (Kcal/mol) from 1-Click Docking between conventional Ligands and Oil Blend Compounds Targeting *VEGF*

Ligand	Target Molecule	Molecular Affinity (Kcal/mol)
Cisplatin	*CEA*	-6.1
Paclitaxel	*CEA*	-6.7
Bevacizumab	*CEA*	-6.4
Pembrolizumab	*CEA*	-6.6
Topotecan	*CEA*	-5.9
Curcumin	*CEA*	-7.7
Resveratrol	*CEA*	-8.1
Epigallocatechin gallate	*CEA*	-7.9
Olaparib	*CEA*	-7.8
Everolimus	*CEA*	-7.7
Temsirolimus	*CEA*	-6.9
Oleic Acid	*CEA*	-5.4
g-Tocopherol	*CEA*	-4.9
Sitosterol	*CEA*	-5.5
quercetin 3-O-glucoside	*CEA*	-8.9
apigenin 5-O-glucoside	*CEA*	-9.4
kaempferol 3-O-glycoside	*CEA*	-7.9
Eugenol	*CEA*	-8.8
Eugenyl Acetate	*CEA*	-7.9
b-Caryophillene	*CEA*	-6.7

Discussion

The molecular docking analysis highlights the superior efficacy of natural compounds from a vegetable oil mixture compared to conventional chemotherapeutic agents in targeting key molecules involved in cervical carcinoma progression. Natural compounds such as Quercetin 3-O-glucoside, γ-Tocopherol, Kaempferol 3-O-glycoside, and Epigallocatechin gallate demonstrated stronger binding affinities for crucial targets like $p16^{INK4a}$, Ki-67, *VEGF*, *CEA, MMPs*, *TP53*, and *pRb*. Apigenin-5-O-Glucoside showed the highest affinities, including a binding energy of -11.6 Kcal/mol with *MMP-9*, reflecting its potent anticancer properties such as apoptosis modulation and angiogenesis inhibition. Similarly, γ-Tocopherol exhibited robust interactions with Ki-67 (-7.7 Kcal/mol) and *TP53* (-7.1 Kcal/mol), supporting its tumor-suppressive role, while Kaempferol 3-O-glycoside demonstrated strong affinities with *VEGF* (-7.9 Kcal/mol) and MMPs (-8.1 Kcal/mol), indicating its anti-angiogenic and anti-metastatic potential.

Quercetin 3-O-glucoside and Epigallocatechin gallate's interactions with *VEGF* (-8.7 Kcal/mol) underscore their ability to inhibit angiogenesis, essential for reducing tumor blood supply in advanced cervical carcinoma stages. These compounds outperformed conventional agents such as Paclitaxel and Pembrolizumab, which exhibited weaker affinities (-4.7 Kcal/mol and -4.1 Kcal/mol, respectively). Similarly, Quercetin 3-O-glucoside and Kaempferol 3-O-glycoside demonstrated superior binding to MMPs, essential for inhibiting cancer metastasis, compared to Pembrolizumab (-4.1 Kcal/mol).

TP53 emerged as a critical target, with Quercetin 3-O-glucoside and Apigenin-5-O-Glucoside showing the strongest affinities (-8.1 Kcal/mol each), followed by Eugenol (-7.8 Kcal/mol). These interactions suggest natural compounds may restore *TP53* function, promoting apoptosis and halting tumor growth. By contrast, conventional agents like Paclitaxel showed significantly lower affinities (-3.1 Kcal/mol), highlighting their limited efficacy.

These findings demonstrate the therapeutic potential of natural compounds in cervical carcinoma management through superior molecular interactions, offering a multi-targeted approach that could enhance treatment efficacy and reduce drug resistance. Further in vivo studies are necessary to validate these results and explore their clinical applications.

In conclusion, this study highlights the therapeutic potential of natural compounds from a vegetable oil mixture for cervical carcinoma treatment. Apigenin-5-O-Glucoside, Quercetin 3-O-glucoside, γ-Tocopherol, and Epigallocatechin gallate exhibited superior binding affinities compared to conventional agents, targeting key molecules involved in oncogenesis, metastasis, and angiogenesis. Their ability to modulate multiple cancer pathways, including proliferation, angiogenesis, and apoptosis, suggests they could enhance therapeutic efficacy while reducing drug resistance, making them promising candidates for further research.

Author Contribution Statement

Momir Dunjic. and Sasa Cvetkovic conceptualized and supervised the research, as corresponding authors; Stefano Turini supervised the research, coordinated molecular docking simulations and contributed to scientific writing; Lazar Nejkovic, Aleksandra Pikula and Nenad Sulovic were involved in data analysis and literature review; Marija Dunjic and Katarina Dunjic provided formulation development support and clinical insights. All authors have reviewed and approved the final manuscript.

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Funding Statement

This research was conducted exclusively using internal financial resources provided by the Quince Medics Clinic, Belgrade. No external funding—public or private—was received at any phase of the study.

Ethical Approval

Since the study conducted did not involve the use of animals or volunteers, the application and relative approval by an ethics committee was not required.

Availability of Data

All data generated or analyzed during this study are available from the corresponding author upon reasonable request.

Conflict of Interest Statement

The authors declare that there are no conflicts of interest financial or otherwise that may have influenced the design, execution, or reporting of this study.

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