IJHSR
ijhighschoolresearch.org
RESEARCH ARTICLE

Exploration of the Medicinal Origin and Clinical Anti-Cancer Value of Wumei (*Mume fructus*)

Mengjia Li

Queenwood School for Girls, 47 Mandolong Road, Sydney, NSW, 2088, Maggie_li2006@outlook.com

ABSTRACT: Wumei is the nearly mature fruit of *Prunus mume (Sieb.) Sieb. Et Zucc.*, a deciduous tree of the Rosaceae family. It possesses unique advantages and characteristics in anti-cancer properties. Thus, the study aims to examine the historical origins and evolution of traditional Chinese medicine Wumei (*Mume fructus*) and to investigate its potential anti-cancer effects using network pharmacology research techniques. This study uses network pharmacology techniques to examine the historical origins and evolution of Wumei (*Mume fructus*) and its potential anti-cancer effects. Initially, a comprehensive review of the plant's distribution, medicinal properties, and processing techniques was conducted. Active compounds of Wumei were identified using the TCMSP database, and the SwissTargetPrediction database was used to predict their potential targets. A protein-protein interaction network was established to investigate the primary targets and pathways involved in Wumei's anti-tumor mechanism. Eight effective components of Wumei were identified, predicting 282 potential targets. The PPI network includes key proteins such as VEGFA, SRC, AKT1, ESR1, and BCL2L1. Biological enrichment analysis indicates potential interactions with cancer-related pathways, including the PI3K Akt, Rap1, Ras, and MAPK signaling pathways. Wumei targets various tumors, including medulloblastomas, astrocytomas, lymphomas, mesothelioma, prostate cancer, breast cancer, and head and neck cancers. Wumei is a traditional Chinese medicine with both medicinal and edible properties, offering diverse clinical health benefits.

KEYWORDS: Robotics and Intelligent machines, C, Anti-Cancer, TCM, Wumei.

Introduction

Wumei is a dry, nearly mature fruit of *Prunus mume (Sieb.) Sieb.et Zucc*, a deciduous tree of Rosaceae. It is native to China and is commonly found in Yunnan, Fujian, Sichuan, Anhui, and Guizhou.[1] Statistics show that there are 50-60 different artificially cultivated varieties in China, and all of them can be used for Wumei processing.[2] Wumei is a traditional Chinese medicine with the effects of astringing lung qi, astringent intestines, relieving diarrhea, promoting fluid production, quenching thirst, relieving vexation, and relieving ascariasis, it has a long history of medication, which is flat in nature, sour and astringent in taste, and belongs to liver, spleen, lung and large intestine meridians.[3] Modern pharmaceutical studies have confirmed that the effective components of Wumei include citric acid, ursolic acid, stickers, sterols, flavonoids, alkaloids, and so on.[4] Wumei is a product with homology of medicine and food. As early as 2002, the National Health and Health Commission of China listed Wumei in the catalog of homology of medicine and food, which not only has good edible value but also has good medicinal value. Especially, it has unique advantages and characteristics in anti-cancer. In recent years, the emerging network pharmacology research method has found widespread application in traditional Chinese medicine research, facilitating in-depth exploration of drug-biological system interactions through computer technology and informatics methods.[5] Network pharmacology holds promise for systematically elucidating the potential anti-cancer mechanism of Wumei. Thus, this study utilizes a combination of literature review and network pharmacology research to investigate the anti-cancer properties of Wumei preliminarily. Based on the study of ancient and modern literature, this paper systematically summarizes the medicinal value of Wumei from the resource distribution, historical origin, and traditional Chinese medicine understanding, combined with modern network pharmacology research, and puts forward the clinical value of Wumei against cancer.

1. Medicinal origin of Wumei:

1.1 Distribution of plant resources of Wumei:

The cultivation history of Wumei, also known as smoked plum, black plum, plum seed, and orange plum meat, dates back to ancient times as documented in the Notes on Materia Medica Classic. The plum originated in China and is cultivated and found in both wild and cultivated forms across a wide geographic area encompassing the Qinling Mountains, south of the Huaihe River, and between latitudes 23-33 degrees north.[6] The provinces of Taiwan, Guangdong, Jiangsu, and Zhejiang are primarily engaged in the introduction and cultivation of plum fruit. The cultivation of fruit plums predominantly consists of original variety plums, while wild plums are primarily found in the western and southwestern regions of Sichuan, Yunnan, and Guizhou provinces. According to the "Southern Cooperative Group for Variety Arrangement and Quality Research of Commonly Used Chinese Herbal Medicines" and "Chinese Medicinal Materials Science," Wumei is primarily cultivated in Fujian, Sichuan, Zhejiang, Hunan, and Guangdong provinces.[7,8] Among the different regions where Wumei is produced, the quality of Wumei from Zhejiang is notable, while the largest output comes from Sichuan. There

DOI: 10.36838/v7i7.1

are three prevalent processing methods for Wumei: drying, smoking, and baking, with the primary method being the cultivation of variant plums. The drying method includes hot drying and steaming drying, while the smoking method can be categorized into pine smoking and miscellaneous wood smoking, each utilizing distinct fuels. The predominant method of consumption for this clinical medicinal product is smoking, and due to the superior quality of the product from Zhejiang Changxing, it is colloquially referred to as "black plum smoked by green fruit," highlighting the company's dominant position in the market.

1.2 Tracing back to the medicinal value of Wumei:

Shennong's classic of materia medica records the medicinal use of Wumei for the first time, which is listed as a medium product, flat in nature, sour and astringent in taste, and belongs to the lung, liver, spleen, kidney, stomach, and large intestine meridians.[9] Its functions mainly include astringent lung qi, astringent intestine to stop diarrhea, promoting fluid production to quench thirst, relieving vexation, etc. It is used for chronic cough due to lung deficiency, asthenia, heat to quench thirst, chronic diarrhea, and constipation. The Materia Medica of past dynasties has described the efficacy of Wumei in detail, and *Shennong's classic of materia medica* puts forward "governing qi, removing heat and annoyance, reassuring, limb pain, being dry and heartless, killing muscles, removing green moles and evil meat." It is pointed out that Wumei can remove green moles and evil meat, which should be the earliest anti-tumor record of Wumei. *LiuJuanZi Ghost* left a prescription that also records the efficacy of Wumei in removing evil meat. In the book, Wumei meat is used to burn and preserve, and it can be eliminated overnight. Meng Shen's *Dietetic Materia Medica* records that Wumei can relieve constipation for external use, and its description of symptoms is similar to intestinal obstruction. It says, "The stool is impassable, and the qi is running to death. Ten Wumeis are placed in soup, and the nucleus must be removed. The pestle is as big as a jujube, and the lower part is accepted, which can be passed when it is young." *Compendium of Materia Medica* points out that Wumei can be used to treat gastric cancer and esophageal cancer, saying: "Converging lungs and astringing intestines, treating chronic cough, diarrhea, nausea and choking diaphragm, vomiting, detumescence, phlegm, killing insects, relieving fish poison, horse sweat poison and sulfur poison." Symptoms such as joint pain, skin paralysis, boredom, and diarrhea are also common clinical problems of cancer, and Wumei also has very good effects. As pointed out in the List of Famous Doctors, Wumei has the functions of stopping dysentery, quenching thirst, and dredging tendons. *Rihuazi Materia Medica* also said: "Eliminate labor, treat bone steaming, relieve boredom, astringent intestines, stop dysentery, eliminate alcohol toxicity, treat paralysis of dry skin, remove black spots, and make people sleep." When *Materia Medica Jingshu* talks about the treatment of limb pain and hemiplegia with Wumei, it thinks that its mechanism lies in "because moisture is immersed in meridians, the tendons are relaxed or painful; Liver is the main tendons, acid enters the liver and nourishes the tendons, and the liver is nourished, so the bones are soft and the organs are beneficial." In addition, *Materia Medica Qiuyuan* talks about how Wumei can be used for blood syndrome, which has good curative effect on hematuria, hematochezia, and various blood diseases. The use method of Wumei emphasizes that it should be dipped in salt when it is used raw, which can warm gallbladder and promote fluid production, and has better effect. At the same time, it also points out that pregnant women can eat more, especially the Wumei, before Xiaoman has the best effect. Wumei, as a traditional Chinese medicine with the homology of medicine and food, has been widely concerned at home and abroad. It contains a large number of organic acids, sugars, and vitamins, and has the effects of helping to lower blood sugar, clearing the throat and moistening the throat, improving skin moisture, stimulating appetite, regulating mood, relieving headaches after drinking, and resisting tumors. Because it has the effects of relieving cough (chronic cough, dry cough), relieving deficiency sweating (spontaneous sweating due to qi deficiency, night sweating due to yin deficiency), stopping metrorrhagia (Wumei charcoal), stopping diarrhea (both deficiency and excess, cold and heat), stopping leukorrhagia (yellow leukorrhagia, thin white matter, red and white), etc., Chinese medicine calls it a good medicine for "five stops."[10]

1.3 Processing and application of Wumei:

As shown in Figure 2, Wumei has different processed products with different effects, such as clean Wumei, Wumei meat, vinegar Wumei, Wumei charcoal, and so on. The records of Wumei, Wumei meat, Wumei charcoal, steamed Wumei, and vinegar Wumei are included in the 1963 edition of I*ntegration of Traditional Chinese Medicine Processing Experience*.[11] The Pharmacopoeia of the Chinese pharmacopeia in different periods has different records on processed products of Wumei, and the 1963 edition contains Wumei, Wumei meat, and Wumei charcoal.[12] The 1977 edition did not contain Wumei meat, and the 1985 edition added Wumei meat: "Take clean Wumei, moisten it to make it soft or steam it to remove the core."[13,14] At present, the processing methods (Code for Processing Chinese Herbal Medicine), Chinese Pharmacopoeia (2000 edition), and Integration of Traditional Chinese Medicine Processing Experience are vinegar, charcoal frying, and steaming.[11,15,16] The four common methods for preparing black plums are shown in Figure 1. According to comprehensive data analysis, the processing methods of Wumei include frying, baking, steaming, boiling, roasting, and charcoal making without auxiliary materials, and vinegar making, wine making, salt making, and honey making with auxiliary materials. In the Han Dynasty, *Jin Kui Yu Han Jing* was recorded as the earliest processing method of Wumei. "Soak Wumei in bitter wine for one night, remove the core, steam it under five buckets of rice, and pound it into mud when the rice is cooked."[17]

In various regions of China, two types of Wumei decoction pieces are utilized: pure Wumei meat and nuclear combination. Currently, they are commonly employed without nuclear removal for several reasons. Firstly, the clinical efficacy of Wumei remains unaffected by the removal of the nucleus, and the process of removal is deemed laborious and time-consuming. Additionally, the inclusion of the nucleus in Wumei facilitates its storage, transportation, preservation, and processing, there

by extending its shelf life and reducing the likelihood of decay. Furthermore, the presence of the kernel in Chinese medicine Wumei aids in distinguishing authentic from counterfeit Wumei, thus justifying the retention of the kernel.[18]

Various processed products of Wumei exhibit distinct clinical applications, including the preservation of acidity in their raw form and the promotion of salivation, alleviation of vexation, and enhancement of astringency and hemostasis following charcoal preparation. Wumei is abundant in organic acids, notably malic acid and citric acid, which are considered the most significant. It has been observed that the organic acids present in Wumei products predominantly exist in diverse salt forms. Following vinegar treatment, these acids are converted into salt organic acids, subsequently reverting to a free state, thereby enabling them to exert a distinct pharmacological effect.[18]

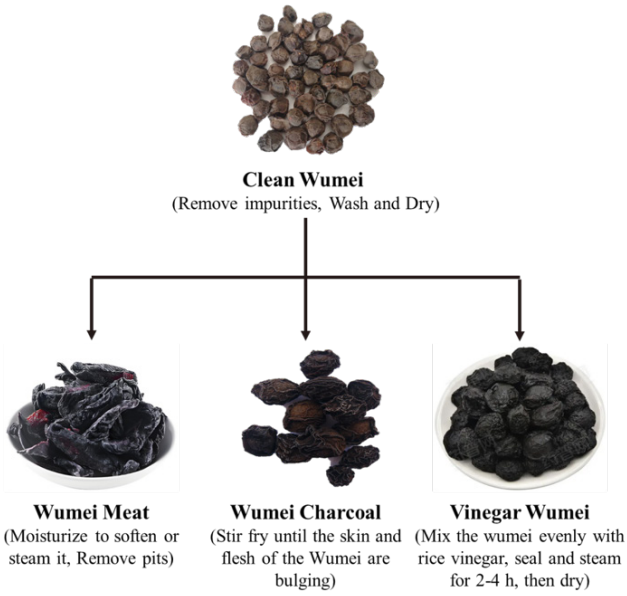


Figure 1: Four common Wumei processed products. This picture mainly shows four common processed products of Wumei: Clean Wumei, Wumei Meat, Wumei Charcoal, and Vinegar Wumei.

1.4 Clinical value of Wumei against cancer:

The prevention and treatment of cancer through the lens of both Chinese and Western medicine is a topic of significant interest. Extensive clinical observations, in conjunction with traditional Chinese medicine's perspective on malignant tumors, suggest that cancer can be viewed as a manifestation of a yin-yang imbalance. Central to the pathogenesis of cancer transformation is the interplay between healthy qi and cancer toxins. One aspect of disease development involves the healthy dissipation of qi and positive deficiency loss in solid absorption. In contrast, another aspect involves the consumption of healthy qi by cancer toxins, which promote cancer diffusion and metastasis. In light of this characteristic, a fixation-based treatment method has been proposed for clinical cancer treatment. This approach aims to strengthen body resistance and fixation to prevent the outward dispersion of healthy qi, correct deficiencies, and prevent or reduce cancer spread and metastasis.

Contemporary research has validated that Wumei contains various chemical compounds such as organic acids, flavonoids, terpenoids, and polysaccharides. Specifically, the organic acids and volatile components exhibit notable antioxidant properties, while flavonoids, terpenoids, and sterols demonstrate significant anti-tumor effects. The terpenoids ursolic acid and oleanolic acid, found in the pulp of Wumei, are identified as natural anticancer agents. Oleanolic acid demonstrates potent inhibitory properties against the proliferation and progression of malignant tumors, leading to the restoration of serum protein levels in tumor-bearing mice and suppression of DS-PAGE protein component expression.[19] Oleanolic acid has been shown to upregulate the expression of the P21 protein and downregulate the expression of the Ki-67 protein in lymphoma-bearing mice, thereby exerting control over the proliferation of tumor cells in mice.[20] Ursolic acid, a naturally occurring compound, exhibits anti-tumor properties by effectively inhibiting the growth of A172 glioma cells, SGC7901 gastric cancer cells, and A-549 lung cancer cells.[21] Research conducted by Xu Chao has demonstrated the efficacy of Wumei extract in inhibiting colon cancer and cervical cancer. Additionally, Chao's research indicates that Wumei extract can effectively impede the migration of colon cancer HT29 cells.[22] Furthermore, the extract has been found to alleviate hematochezia and physical deterioration in patients with colon cancer, potentially preventing the progression from colitis to cancer. The extract of Wumei pulp demonstrates promising preventive properties against various types of cancer, including liver cancer, gastric cancer, renal cancer, melanoma, leukemia, endometrial adenocarcinoma, and ovarian cancer. Several traditional Chinese medicine formulations incorporating Wumei exhibit notable anti-cancer efficacy, such as Wumei pills, Wumei-Siwu decoction, and allergic decoction. The traditional Chinese medicine prescription known as the Wumei Pill consists of various herbs such as Wumei, asarum, dried ginger, Coptis chinensis, Angelica sinensis, Heishun tablets, Chuanjiao, cassia twig, ginseng, and Phellodendron amurense exhibit therapeutic properties including wind-calming and astringent effects, yang-supporting and yin-strengthening actions, as well as warming and tonifying properties. This prescription is commonly used in clinical practice for the treatment of pancreatic cancer, lung cancer, cervical cancer, and liver cancer, among others, and has demonstrated positive clinical outcomes. In a study conducted by Huang Jinchang *et al.*, [21] patients diagnosed with advanced pancreatic cancer were administered the Wumei Pill.[23] Following a 3-month treatment period, the findings indicated an appetite improvement rate of 80.00%, an abdominal pain relief rate of 52.63%, and a clinical effective rate of 71.43%. Chu Shirong clinically selected 45 patients with gastric cancer and treated them with the Wumei Pill.[24] The results showed that it had the best curative effect on stage II patients, which could improve the quality of life, hemogram, and T cell subsets of patients. Contemporary pharmacological research has demonstrated that Wumei and its associated compounds exhibit anti-tumor properties through various mechanisms, including the inhibition of precancerous lesions, modulation of gene expression, alteration of protein activity

DOI: 10.36838/v7i7.1

and signal pathway expression, suppression of tumor cell proliferation and metastasis, and facilitation of tumor cell apoptosis.

Methods

Table 1: Research on anti-cancer effects of Wumei in the PubMed database.

By searching the PubMed database for relevant experimental research literature, the anti-cancer mechanism of Wumei formula preparation was summarized.

References	Single herb/Formula	Study type	Cancer type	Mechanism
[25]	Formula (Wumei pill)	*in vivo and in vitro*	Colon Cancer	AHCY-mediated hedgehog signaling pathway
[26]	Formula (Wumei pill)	*in vivo*	Colon Cancer	PI3K/Akt signaling pathway
[27]	Formula (Compound Wumei Powder)	*in vivo*	Gastric Cancer	Cox-2/PGE2-PI3K/AKT/GSK3 β/ β-Catenin Signaling Pathway

1. Network pharmacological analysis of Wumei against cancer:

Traditional Chinese medicine emphasizes the importance of a holistic approach to disease treatment. Modern pharmacological research has demonstrated that traditional Chinese medicine can effectively address diseases through the manipulation of multiple targets and pathways. The development of a network action mode based on multiple targets and pathways further exemplifies the holistic perspective inherent in traditional Chinese medicine. In recent years, the network pharmacology research approach has been commonly employed to investigate the mechanism of action of traditional Chinese medicine. Following the principles of network pharmacology research, this study conducts an initial investigation into the principal bioactive compounds of Wumei and their potential anticancer mechanisms.

1.1 Data and Methodology:

1.1.1 Determination of Active Components in Fructus Mume:

In this study, the TCMSP platform (http://tcmspw.com/tcmsp.php) was utilized to identify the constituents of Wumei. Subsequently, the drug components were filtered based on their bioavailability (OB) ≥ 30% and drug-likeness (DL) ≥ 0.18.[28]

1.1.2 Target analysis of bioactive components in Wumei:

According to the screening results, the active components of Wumei were imported into the PubChem database (https://pubchem.ncbi.nlm.nih.gov/) to obtain the SMILES structure of each active component. The SMILES structure was used to detect the targets on the SwissTargetPrediction platform (http://www.swisstargetprediction.ch/), and the predicted targets were screened according to Probability > 0.

1.1.3 Construction of the target protein interaction (PPI) network of efficacious substances in Wumei:

The target of active components of Wumei was imported into the STRING database (https://string-db.org/), and the mapping relationship of the protein interaction network (PPI) was obtained, which was also visualized by the Cytoscape software. In addition, through the Cytoscape plug-in MCODE topology analysis of the PPI network, we can get the key sub-modules in the network, and the targets in the key modules are the key targets of Wumei.

1.1.4 Biological enrichment analysis:

In this study, biological enrichment analysis was carried out on the targets of efficacious substances in Wumei, including KEGG pathway enrichment analysis, DisGENET disease enrichment analysis, and PaGenBase cell and tissue enrichment analysis. Biologic enrichment analysis was performed by the online tool Metascape (http://metascape.org/), and the screening threshold of enrichment results was $P < 0.05$.

Results and Discussion

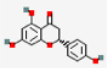
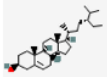
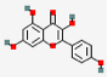
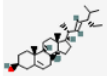
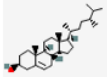
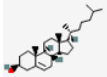
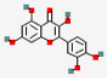
1. Result

1.1 Screening of effective substances in Wumei:

Forty compounds of Wumei were retrieved by the TCMSP data platform. According to oral bioavailability (OB) ≥ 30% and drug-like (DL) ≥ 0.18, eight effective substances were screened. See Table 1 for specific molecular structures and parameters.

1.2 Prediction of the action target of effective substances in Wumei:

Table 2: Efficacious Substances of Fructus Mume. The data is sourced from the TCMSP database and PubChem database, summarizing the main active ingredients of Wumei, including molecule name, 2D structure, oral bioavailability, etc.

Mol ID	Molecule Name	2D Structure	OB (%)	DL
MOL001040	(2R)-5, 7-dihydroxy-2-(4-hydroxyphenyl) chroman-4-one		42.36	0.21
MOL000358	Beta-sitosterol		36.91	0.75
MOL000422	Kaempferol		41.88	0.24
MOL000449	Stigmasterol		43.83	0.76
MOL005043	campest-5-en-3beta-ol		37.58	0.71
MOL008601	Methyl arachidonate		46.9	0.23
MOL000953	CLR		37.87	0.68
MOL000098	Quercetin		46.43	0.28

The SwissTarget platform was used to predict the action targets of 8 pharmacodynamic substances in Wumei. After screening out repeated targets, a total of 282 were obtained. Further, a network of "Wumei-pharmacodynamic substances

-action targets" with 291 nodes and 568 edges was constructed by Cytoscape (Figure 3).

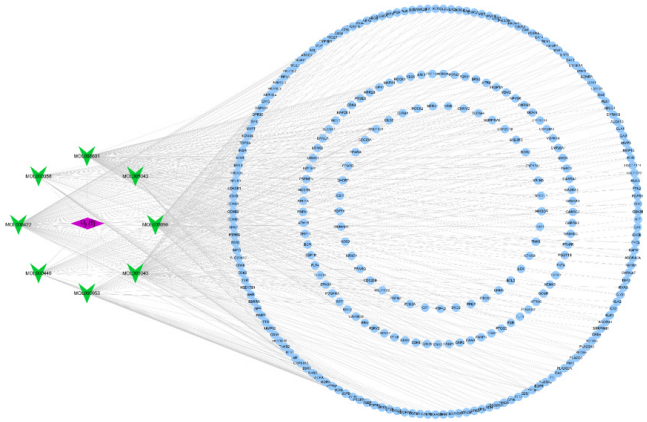


Figure 2: Wumei-pharmacodynamic substances-target network. The red diamond-shaped nodes represent Wumei, the green arrow nodes represent medicinal substances, and the blue circular nodes represent targets.

1.3 PPI network of action targets of Wumei pharmacodynamic substances:

The potential targets of Wumei obtained above are introduced into the STRING platform to build the PPI network, which contains 277 nodes and 2548 edges (Figure 4). The network topology analysis is carried out by the CytoHubba plug-in. The 20 most critical targets in the network (from high to low according to MCC value) are screened out: VEGFA, SRC, AKT1, ESR1, BCL2L1, IGF1R, MAPK1, PTGS2, EGFR, MDM2, MAP2K1, MCL1, CCNB1, MMP9, PIK3CA, AR, GSK3B, MAPK14, MMP2 and KDR. (Figure 5, Table 2)

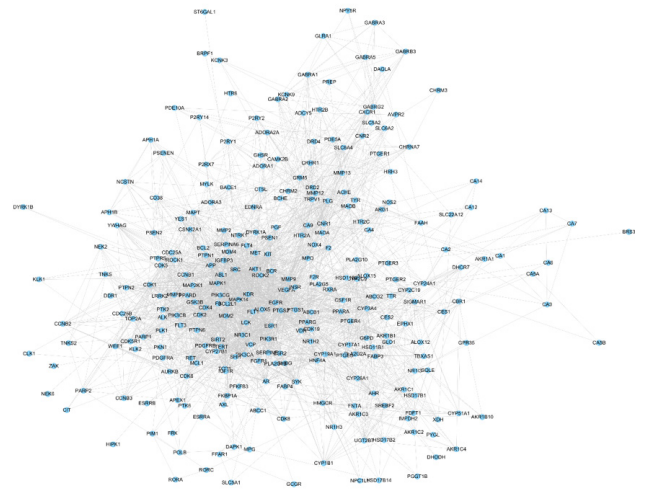


Figure 3: PPI Network of Wumei's potential targets. The blue nodes in the PPI network represent potential targets of Wumei, and the mapping relationships between targets were obtained through the STRING database.

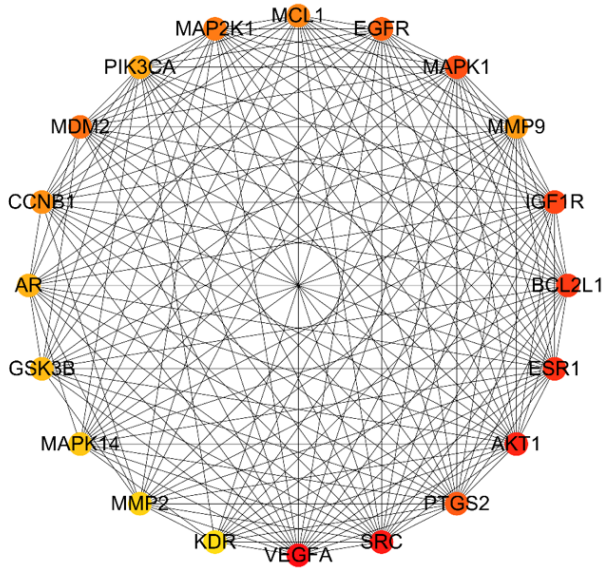


Figure 4: Key targets of the PPI network. Screen key targets in the PPI network through the CytoHubba plugin and associate the color of the target with the MCC value. The closer the color is to red, the higher the MCC value of the node.

Table 3: Ranking of key targets. This table displays the names of the 20 most critical targets in the PPI network, and ranks the top 20 targets based on MCC values.

Rank	Name
1	VEGFA
2	SRC
3	AKT1
4	ESR1
5	BCL2L1
6	IGF1R
7	MAPK1
8	PTGS2
9	EGFR
10	MDM2
11	MAP2K1
12	MCL1
13	CCNB1
14	MMP9
15	PIK3CA
16	AR
17	GSK3B
18	MAPK14
19	MMP2
20	KDR

1.4 Prediction of the anticancer mechanism of Wumei Enrichment analysis of the KEGG pathway:

KEGG pathway enrichment analysis showed that there were thirteen signaling pathways: pathways in cancer, PI3K-Akt signaling pathway, Rap1 signaling pathway, Ras signaling pathway, Central carbon metabolism in cancer, MAPK signaling pathway, Steroid biosynthesis, Neuroactive ligand-receptor interaction, Arachidonic acid metabolism, Nitrogen metabolism, Calcium signaling pathway, Steroid hormone b-Steroid

DOI: 10.36838/v7i7.1

biosynthesis, Neuroactive ligand-receptor interaction, Arachidonic acid metabolism, Nitrogen metabolism, Calcium signaling path, Steroid hormone biosynthesis and Ovarian steroidogenesis.

Table 4: KEGG Signal Pathway. According to the KEGG pathway enrichment analysis results, the table displays the top 13 pathways closely related to cancer, sorted by P-value.

HSA05200	**Pathways in cancer**	-41.27604898	-37.62417411	56/531
HSA04151	**PI3K-Akt signaling path**	-28.09546047	-25.22451062	38/354
HSA04015	Rap1 signaling path	-23.35571358	-20.72364582	28/210
HSA04014	Ras signaling path	-22.14156524	-19.59967412	28/232
HSA05230	**Central carbon metabolism in cancer**	-17.46310856	-15.26425657	16/70
HSA04010	**MAPK signaling path**	-14.07898933	-12.12536991	23/294
hsa00100	Steroid biosynthesis	-7.660813539	-6.23129697	6/20
HSA04080	Neuroactive ligand-receptor interaction	-36.17845309	-32.87177467	45/362
HSA00590	Arachidonic acid metabolism	-16.92690069	-14.77195419	15/61
HSA00910	Nitrogen metabolism	-20.68530566	-18.25104841	12/17
HSA04020	Calcium signaling path	-24.16113838	-21.4662798	30/240
hsa00140	Steroid hormone biosynthesis	-13.86315093	-11.9233198	13/61
HSA04913	Ovarian steroidogenesis	-11.87762713	-10.07733073	11/51

1.5 DisGENET disease enrichment analysis:

The findings of the DisGENET disease enrichment analysis indicate that Wumei drug targets have the potential to impact a range of diseases, including but not limited to adult medulloblastoma, childhood medulloblastoma, diabetes, memory disorder, neuralgia, childhood astrocytoma, non-Hodgkin's lymphoma, cognitive impairment, amyloidosis, mesothelioma, benign prostatic hyperplasia, endothelial dysfunction, hormone-resistant prostate cancer, pre-senile dementia, secondary bone malignant tumor, enzyme inhibition disorder, fatty liver, breast cancer stage IV, meningioma, and head and neck cancer (Figure 6). It can be seen from the above that tumor diseases account for 50% of the top 20 diseases.

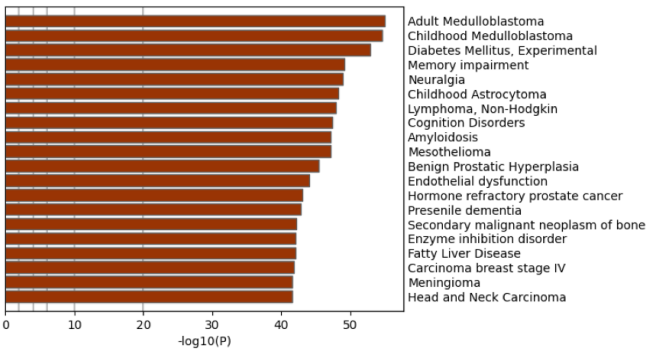


Figure 5: DisGENET enrichment analysis. This figure shows the enrichment analysis results of DisGENET disease, with the x-axis representing - logP. The larger the value, the higher the correlation between Wumei's targets and the disease.

1.6 Analysis of cell and tissue enrichment of PaGenBase:

The findings from the PaGenBase enrichment analysis indicate that the effective components of Mume plum primarily target various tissues, including the liver, placenta, uterus, kidney, caudate nucleus, breast, small intestine, lung, and others. At the cellular level, Wumei appears to affect dorsal root ganglion cells, adipocytes, prostate cells, liver cancer cells, hepatocytes, ovarian cancer cells, brain cells, Burkitt's lymphoma cells, human umbilical vein endothelial cells, bronchial epithelial cells, and myocardial cells (Figure 7).

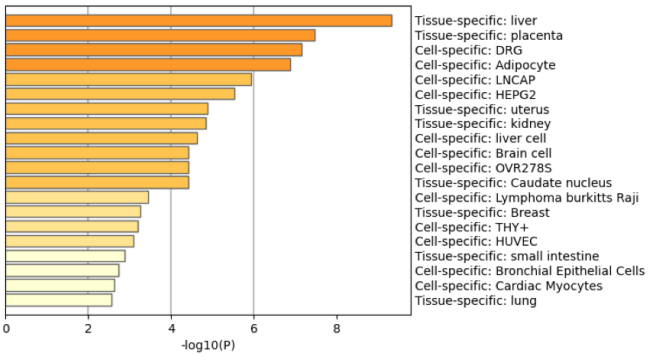


Figure 6: PaGenBase enrichment analysis reflects the tissues and organs involved in the target of Wumei's targets. This figure shows the results of PaGenBase disease enrichment analysis, with the x-axis representing - logP. The larger the value, the higher the correlation between Wumei's targets and the tissue or organ.

2. Discussion:

Wumei, a traditional Chinese medicine derived from the same source as food and medicine, is recognized for its safety and reliability, as well as its diverse clinical health and therapeutic benefits. Originating in China, Wumei is particularly renowned for its superior quality when produced in Zhejiang, although the most significant production of Wumei occurs in Sichuan. Various processed forms of Wumei, including purified Wumei, Wumei meat, vinegar Wumei, and Wumei charcoal, offer distinct therapeutic effects. The historical significance of Wumei in traditional Chinese medicine dates back to ancient texts such as *Shennong's Classic of Materia Medica*, which highlights its medicinal properties, including astringent lung qi, astringent intestines to stop diarrhea, generating fluids to quench thirst, relieving roundworms, and alleviating restlessness. Wumei's diverse clinical effects, particularly in the realm of cancer prevention and treatment, have garnered significant attention within the traditional Chinese medicine community. Currently, there is a growing body of research on the anti-tumor properties of Wumei. However, the majority of findings are constrained. This study aims to employ network pharmacology techniques to comprehensively investigate its anti-tumor mechanism.

However, this study has some limitations. This study primarily utilizes literature reviews and database analysis to ascertain the active components and potential targets of Ume. The reliability and precision of these databases may be constrained by the current state of research and data gathering, potentially leading to the exclusion or misinterpretation of specific active ingredients or targets. Furthermore, while network pharmacology techniques offer valuable insights into predicting drug mechanisms, this study lacks direct experimental verification to substantiate its predictive findings. Without experimental support, the proposed mechanisms remain hypothetical, highlighting the necessity for experimental studies to validate the computational predictions and bridge the gap between theoretical models and biological reality. Experimental validation plays a critical role in confirming the mechanism of drug

action and therapeutic potential and is imperative for the advancement of drug development.

Conclusion

This study conducted a preliminary analysis to predict 282 drug action targets of *Prunus mume*. The protein-protein interaction network topology analysis results identified key targets such as VEGFA, SRC, and AKT1. Among these targets, VEGFA, a vascular endothelial growth factor, was found to be involved in the pathogenesis of lung cancer, colon cancer, breast cancer, and other tumors, making it a significant drug target for anti-tumor therapy.[29,30] The SRC family of non-receptor tyrosine kinases plays a crucial role in the interplay between inflammation and cancer by facilitating communication and signaling between immune cells and tissue cells, thereby contributing to the initiation and advancement of cancer.[31] AKT1 has been identified as a carcinogen and is a critical component of the PI3K pathway, playing a significant role in developing and advancing diverse tumor types.[32,33] Pathway enrichment analysis reveals that Wumei is implicated in pathways associated with tumorigenesis, including *Pathways in cancer*, *PI3K Akt signaling pathway*, *Central carbon metabolism in cancer*, and *MAPK signaling pathway, et al*. However, this study still has certain limitations. Firstly, network pharmacology only relies on database mining and prediction, which may miss some components and targets. At the same time, the results of related mechanism research need to be further verified through experiments.

In conclusion, Wumei, a widely used traditional Chinese medicine in clinical settings, demonstrates notable medicinal properties, particularly in the realm of anti-tumor activity. Wumei has the potential to modulate various pathways and targets associated with tumors, thereby exerting therapeutic effects on diverse types of malignancies. Nevertheless, additional investigation and clinical trials are imperative to validate the anticancer efficacy and clinical utility of Wumei.

Future research should prioritize experimental validation of key compounds identified through network pharmacology, such as ursolic acid, which has shown pro-apoptotic and anti-proliferative effects in cancer models.[34] For instance, studies have demonstrated that ursolic acid inhibits NF-κB signaling and induces apoptosis in human cancer cells, supporting its predicted role in tumor suppression pathways. Similarly, oleanolic acid has been reported to exhibit anti-inflammatory and anti-cancer properties, which align with the bioinformatics-based findings.[35] These existing experimental results provide the foundation for designing targeted experimental studies to confirm the predicted molecular mechanisms and therapeutic roles of Wumei's active constituents.

Acknowledgment

The completion of the thesis is attributed to the support and encouragement of many people. I would like to express my sincere gratitude to my mentor, Professor Li, for his helpful guidance, valuable suggestions, and constant encouragement. He gave me much help and advice during the whole writing process, making my accomplishments possible.

References

1. National Pharmacopoeia Commission. Pharmacopoeia of the Peo ple's Republic of China: Part I. Beijing: China Medical Science a nd Technology Press; 2015.
2. Liu Youping, Chen Hongping, Wan Deguang. Research progress on Wumei. Journal of Chinese Medicinal Materials 2004;06:459-462. https://10.13863/j.issn1001-4454.2004.06.033
3. Zhong Gansheng. Traditional Chinese Medicine. Beijing: China Traditional Chinese Medicine Press; 2016,p 718-719.
4. Ye Jing, Fu Jing, Yu Han. Comparison of characteristic spectra of Wumei raw and its charcoal products. Journal of Hubei University of Traditional Chinese Medicine 2017;19 (06): 42-45.
5. Zhao L, Zhang H, Li N. Network pharmacology, a promising app roach to reveal the pharmacological mechanism of Chinese medic ine formula. J Ethnopharmacol. 2023 Jun 12;309:116306. https://doi.org/10.1016/j.jep.2023.116306
6. Xie Zongwan. Theory and application of traditional Chinese medi cine varieties. Beijing: People's Health Publishing House; 2008, p 754-755.
7. Xu Guojun. Science of Chinese Medicinal Materials. Beijing: Chi na Medical Science and Technology Press; 1996, p 1053-1055.
8. Xu Guojun. Study on Variety Arrangement and Quality of Comm only Used Chinese Herbal Medicines Southern Collaboration Gr oup: Volume IV. Fuzhou: Fujian Science and Technology Press; 2 001, p 357-404.
9. Cui Ling. Shennong Materia Medica, Volume I. Tianjin: Tianjin Ancient Books Publishing House; 2009,p 176.
10. Zhang Suoqing, Gui Fengyun. Clinical application of the "Wuzh i" effect of Wumei. Gansu Traditional Chinese Medicine, 2003;10 : 42.
11. Institute of Traditional Chinese Medicine, Institute of Tradition al Chinese Medicine, Beijing Institute of Pharmaceutical Bioassa y. Integration of the processing experience of traditional Chinese medicine. Beijing: People's Health Publishing House; 1963, p 165.
12. Pharmacopoeia Committee of the Ministry of Health of the PR C. Pharmacopoeia of the People's Republic of China (Part I). Beiji ng: People's Health Publishing House; 1963, p 56.
13. Pharmacopoeia Committee of the Ministry of Health of the PR C. Pharmacopoeia of the People's Republic of China. Beijing: Peo ple's Health Publishing House; 1977, p 118.
14. Pharmacopoeia Committee of the Ministry of Health of the PR C. Pharmacopoeia of the People's Republic of China (Part I). Beij ing: People's Health Publishing House; 1985, p 57.
15. Health Bureau of Hubei Revolutionary Committee. Specificatio n for processing Chinese herbal medicines. Wuhan: Hubei People' s Publishing House; 1979, p 108.
16. Pharmacopoeia Committee of the Ministry of Health of the PR C. Pharmacopoeia of the People's Republic of China (Part I). Beij ing: People's Health Publishing House; 2000, p 59.
17. Han Zhang Zhongjing. Synopsis of Golden Chamber. Beijing: P hotocopy of People's Health Publishing House; 2000, p 644.
18. Xu Laying, Liu Fen, Mao Weilun, Yu Peng. Discussion on the ev olution of Wumei processing in ancient and modern times. Hubei Journal of Traditional Chinese Medicine 2003;25 (5): 51-54.
19. Shen Hongmei, Qiao Weizhuo, Su Zhongwu. Advances in Chem istry, Pharmacology, and Clinical Research of Fructus Mume. Chi nese Patent Medicine 1993; 7: 35-36.
20. Zeng Wenbin, Li Mingjie, Zhu Qiuhua, etc. Inhibitory effect of oleanolic acid on lymphoma-bearing mice. Chinese Journal of Cli nical Pharmacology 2020; 36 (18): 2865-2868.
21. Chen Weiyan, Liu Chunying. Regulation of ursolic acid on apopt osis and autophagy of gastric cancer cell line MGC-803 and its m echanism. Chinese Journal of Cancer Biotherapy 2019;26 (6): 638 -643.

DOI: 10.36838/v7i7.1

22. Xu Chao. Experimental study on preventing the occurrence and development of colorectal cancer with Wumei extract. Nanjing: N anjing University of Traditional Chinese Medicine, 2016.
23. Huang Jinchang and Xu Lin. Clinical observation on 21 cases of pancreatic cancer treated with modified Wumei Pill. Chinese Cli nician 2012;40 (11): 52-55.
24. Chu Shirong. Observation on the therapeutic effect of modified Wumei Pill on 45 cases of gastric cancer. Clinical Research of Tra ditional Chinese Medicine 2018; 10 (34): 5-9.
25. Wang J, Ding K, Wang Y, Yan T, Xv Y. Wumei Pill Amelio rates AOM/DSS-Induced Colitis-Associated Colon Cancer through I nhibition of Inflammation and Oxidative Stress by Regulating S-Adenosylhomocysteine Hydrolase- (AHCY-) Mediated Hedgeh og Signaling in Mice. Oxid Med Cell Longev. 2022;26;2022:4061 713. https:// doi.org/10.1155/2022/4061713
26. Lu ZH, Ding Y, Wang YJ. Early administration of Wumei Wan inhibits myeloid-derived suppressor cells via the PI3K/Akt pathw ay and amino acid metabolism to prevent Colitis-associated Colo rectal Cancer. J Ethnopharmacol. 2024;27:118260. https:// doi.or g/10.1016/j.jep.2024.118260
27. Ma NX, Sun W, Wu J. Compound Wumei Powder Inhibits the I nvasion and Metastasis of Gastric Cancer via Cox-2/PGE2-PI3K /AKT/GSK3β/β-Catenin Signaling Pathway. Evid Based Compl ement Alternat Med. 2017;2017:3039450. https:// doi.org/10.11 55/2017/3039450
28. Jinlong Ru; Peng Li; Jinan Wang; Wei Zhou; Bohui Li; Chao H uang; Pidong Li; Zihu Guo; Weiyang Tao; Yinfeng Yang; Xue Xu ; Yan Li; Yonghua Wang; Ling Yang. TCMSP: a database of syste ms pharmacology for drug discovery from herbal medicines. J Ch eminformatics2014;6(1):13.https://doi.org/10.1186/1758-2946-6-13
29. Liu X, He H, Zhang F, Hu X, Bi F, Li K, Yu H, Zhao Y, Teng X, Li J, Wang L, Zhang Y, Wu Q. m6A methylated EphA2 and VE GFA through IGF2BP2/3 regulation promotes vasculogenic mi micry in colorectal cancer via PI3K/AKT and ERK1/2 signalling. Cell Death Dis 2022;13(5):483. https:// doi.org/10.1038/s41419-022-04950-2
30. Zhang H, Zhou J, Li J, Wang Z, Chen Z, Lv Z, Ge L, Xie G, De ng G, Rui Y, Huang H, Chen L, Wang H. N6-Methyladenosine Promotes Translation of VEGFA to Accelerate Angiogenesis in Lung Cancer. Cancer Res 2023;83(13):2208-2225. https://doi.or g/10.1158/0008-5472.CAN-22-2449
31. Liu ST, Pham H, Pandol SJ, Ptasznik A. Src as the link between inflammation and cancer. Front Physiol. 2014;4:416. https:// doi. org/10.3389/fphys.2013.00416
32. Deng L, Zhu X, Sun Y, Wang J, Zhong X, Li J, Hu M, Zheng H. Prevalence and Prognostic Role of PIK3CA/AKT1 Mutations in Chinese Breast Cancer Patients. Cancer Res Treat 2019; 51(1):128 -140. https:// doi.org/10.4143/crt.2017.598
33. Niu M, Zhang B, Li L, Su Z, Pu W, Zhao C, Wei L, Lian P, Lu R, Wang R, Wazir J, Gao Q, Song S, Wang H. Targeting HSP90 Inhibits Proliferation and Induces Apoptosis Through AKT1/E RK Pathway in Lung Cancer. Front Pharmacol 2022;14;12:724192. https:// doi.org/10.3389/fphar.2021.724192
34. Shanmugam, M.K., Dai, X., Kumar, A.P., Tan, B.K.H., Sethi, G. and Bishayee, A. Ursolic acid in cancer prevention and treatment: Molecular targets, pharmacokinetics and clinical studies. Bioche mical Pharmacology. 2013 [online] 85(11), pp.1579–1587. doi:htt ps://doi.org/10.1016/j.bcp.2013.03.006
35. Lee, W., Yang, E.-J., Ku, S.-K., Song, K.-S., and Bae, J.-S. Anti-i nflammatory Effects of Oleanolic Acid on LPS-Induced Inflamat ion In Vitro and In Vivo. Inflammation. 2012, 36(1), pp.94–102. doi:https://doi.org/10.1007/s10753-012-9523-9.

Author

Mengjia is currently a high school student in Australia. Through diverse courses and hands-on experience in the bio-lab, she has developed a strong interest in biomedical science, particularly in the mechanisms of Traditional Chinese Medicine. She is eager to explore the possible cross-application of Chinese herbs and modern treatments for diseases.