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Breast cancer Properties of Extract of *Artemisia absinthium*

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Abstract – Plants have been used for the treatment of various cancers since ancient times. Breast cancer is the second commonest global deadly menace. Natural plant extracts, herbal medicines, are generally accepted as safer drug substances than their synthetic counterparts. Artemisia absinthium, a perennial bushy plant, has traditionally been beneficial in diverse maladies, including hepatocyte overgrowth, hepatitis, gastritis, jaundice, wound healing, splenomegaly, dyspepsia, indigestion, bloating, stomach pain, anaemia and anorexia. It has also been known for its antioxidant, antifungal, antimicrobial, anthelmintic, anti-ulcer, anticarcinogenic, hepatoprotective, neuroprotective, antidepressant, analgesic, immunomodulatory, and cytotoxic properties. In this study, methanol extracts of powdered leaves of Artemisia absinthium was tried on breast cancer cells. The molecular content of the extract was determined by GC-MS. Chemical components were determinated for the *Artemisia absinthium* extract, and the inhibitory activities of these chemicals against the Crystal structure of breast cancer protein (PDB ID: 1A52 and 1JNX) downloaded from the Protein Data Bank site were compared.

Keywords – Artemisia Absinthium, Breast Cancer, GC-MS, Medicinal Plants, Molecular Modelling

I. INTRODUCTION

Herbal medicine sources often include edible plant species. Their traditional use as medicine involves up to 85% of the population in some of the Asian countries, including Japan [1,2].

Most synthetic drugs are derivatives of phytochemicals, which are known as alkaloids, flavonoids, terpenoids, saponins, and tannins, and during the last quarter of the twentieth century, 78% of FDA-approved drugs were of plant origin [3,4]. Plant sources are generally economical to obtain, and they are somewhat immune to drug resistance [5]. As medicines they modulate the action of cellular enzymes and hormones, strengthen immunity, and protect cells against the adhesion of pathogens [6]. Medicines of plant origin, thus, inherently have antimicrobial, anticancer, antioxidant, anti-inflammatory, and other therapeutic activities [7].

Artemisia is a species of Asteraceae, living especially in Europe, then in Asia and North Africa. Asteraceae is represented by almost 500 species, most of which produce compounds with antioxidant, antimicrobial, anti-ulcer, anthelmintic, antidepressant, anticancer, analgesic, hepatoprotective, neuroprotective and immunomodulatory activities [2,8].

Mass spectrometry, like GC-MS and LC-MS, provides the analytical means for the molecular characterisation of plant extracts [9]. This approach allows the identification of organic acids, alcohols, steroids, amino acids, alkaloids, esters, nitro compounds, and long-chain hydrocarbons [10]. Beside thujon and transsabinyl acetate, monoterpenes are among the constituents of the Artemisia absinthium oil [2,11].

The use of plant extracts as safer cancer drugs has been gaining a global momentum [12]. In the initiation and progression steps of breast cancer, the receptors of oestrogen and progesterone appear to play important roles [13]. These sex hormones go into cell nucleus through their cytoplasmic

receptors. In the nucleus they directly interact with specific DNA consensus, response elements, residing in target gene promoters, and thereby they can increase cell growth [14]. This activity could be proven by coadministering oestrogen blockers, and their overexpression is closely associated with the development of breast cancer [15]. This example reinstates that discovery of novel hormone inhibitors would be very helpful. For example, a methanol extract of A. absinthium has been shown to inhibit the growth of breast cancer cell line (MCF-7), and activate the mitochondrial apoptotic pathway in HCT-11, a colorectal cancer cell line [16]. This extract also seems to have killed another colon cancer cell line (DLD-1) [17]. These findings have prompted us to investigate the molecular activities of Artemisia absinthium extracts [2].

Chemotherapy, beside its beneficial features, often result in detrimental consequences because it generally does not discriminate normal cells. Methotrexate, cisplatin, and doxorubicin, are among the best known chemotherapeutic agents that cause many adverse outcomes such as bone marrow suppression, cardiac toxicity, neurological dysfunction. Unfortunately, many cancer cell lines can develop resistance to these therapeutic agents and especially this latter problem necessitates their alternatives [2,18].

Artemisia absinthium leaves appeared to be very rich in bioactive components. Costunolide (11.8%) and thujone (5.0%) were found in high amounts (Table 1) [19].

II. Materials and Method

1. Plant Material and Extraction Method

Collect the Artemisia absinthium plant. Generally, the flowering upper parts of the plant are preferred. Wash the herbs and dry thoroughly. Water can weaken the alcohol extraction process, so it is important that the herbs are completely dry. Add the dried herbs to the glass jar. Add enough alcohol to cover the herbs. It is generally preferred to add enough alcohol to completely cover the herbs. Close the jar tightly and shake well so that the herbs are thoroughly mixed with the alcohol. Store the mixture in a cool, dark place. Letting it sit for at least a few weeks allows the alcohol to draw the essences from the plant. After the waiting period is over, strain the mixture. This is done to separate plant debris and other unwanted particles. Pour the resulting liquid into a clean bottle or other storage container. This is the liquid to use to store your Artemisia absinthium extract.

Table 1. Chemical composition of Artemisia absinthium methanol extract

Molecule	Percentage
o-Cymene	0.4
Camazulene	0.6
Ehrysanthone	0.1
Einecs 228-063-1	14.6
Tau-Cadinol	1.2
Galactonic phenylhydrazide	0.6
Methoxyeugenol	1.4
Isothujol	0.8
Chiapin b	0.9
Thujone	5.0
beta-Eudesmene	1.1
Costunolide	11.8
Germacrene D	0.3
Germacrene D-4-ol	0.2
Tetraneurin d	1.8
dtxsid50880718	1.3
2,3-pinanediol	0.6
Arachidonic acid methyl ester	20.8
beta-linalool	0.3
Propylene	10.4

cis-sabinol	1.0

2. Molecular docking

Molecular docking calculations were conducted to compare the activities of molecules against antioxidant proteins and discover novel and potent compounds for their antioxidant properties. The Maestro Molecular modeling platform (version 12.8) by Schrödinger [20] was used for these calculations. Several modules, including protein preparation [21,22], LigPrep [23,24], and Glide ligand docking [25,26] were employed in the molecular docking calculations. The OPLS4 method was used for all calculations. This comprehensive approach allows for the investigation of potential interactions between the examined molecules and antioxidant proteins [27].

III. RESULTS

The outcomes from the GC-MS analysis have unveiled a diverse array of chemical compounds within the Artemisia absinthium. Each of these compounds has been identified, and their names are meticulously presented in Table 1, offering comprehensive details for each.

Molecular docking is a computer simulation method that models the interaction of a target molecule (usually a protein) and a small molecule (ligand) [28,29]. This method is used in many areas such as drug design, understanding biological interactions, and the discovery of biochemical processes [30].

Essentially, molecular docking attempts to predict how a ligand binds to a target protein and how stable that binding is [31]. This is used to identify potential drug candidates or understand biological interaction mechanisms [32].

In this investigation, the effectiveness of the compounds enumerated in Table 1 was individually appraised against breast cancer proteins via molecular docking computations [33,34]. These computations generated a multitude of parameters alongside their associated numerical values, playing a pivotal role in appraising the interactions and potential effectiveness of these compounds against breast cancer proteins [35-37].

Table 2. Numerical values of the docking parameters of molecule against proteins

1A52	Docking Score	Glide ligand efficiency	Glide hbond	Glide evdw	Glide ecoul	Glide emodel	Glide energy	Glide einternal	Glide posenum
o-Cymene	-6.63	-0.66	0.00	-20.42	-0.84	-29.39	-21.26	0.52	30
Camazulene	-8.02	-0.57	0.00	-26.89	0.10	-39.56	-26.78	0.23	50
Ehrysanthone	-6.50	-0.59	0.00	-18.39	-0.39	-26.42	-18.78	0.02	161
Einecs 228-063-1	-7.84	-0.41	-0.32	-22.61	-3.95	-37.60	-26.57	4.73	76
Tau-Cadinol	-8.21	-0.51	0.00	-27.00	-0.91	-39.51	-27.91	0.41	120
Galactonic phenylhydrazide	-5.56	-0.28	0.00	-8.56	-20.90	-24.68	-29.45	24.04	8
Methoxyeugenol	-5.91	-0.42	0.00	-27.13	-0.88	-37.29	-28.01	1.92	129
Isothujol	-6.71	-0.61	-0.32	-16.96	-1.90	-26.03	-18.86	0.82	377
Chiapin b	-8.09	-0.32	-0.32	-35.48	-4.35	-53.90	-39.84	3.04	93
Thujone	-6.50	-0.59	0.00	-18.39	-0.39	-26.42	-18.78	0.02	161
beta-Eudesmene	-7.81	-0.52	0.00	-24.20	-0.12	-35.41	-24.33	0.59	98
Costunolide	-8.42	-0.50	0.00	-29.20	-1.62	-46.29	-30.82	0.00	89
Germacrene D	-8.20	-0.55	0.00	-27.70	-0.13	-40.55	-27.83	1.44	14
Germacrene D-4-ol	-8.17	-0.51	0.00	-29.30	-0.72	-42.96	-30.02	1.12	210
Tetraneurin d	-8.41	-0.37	0.00	-41.23	-1.91	-55.97	-43.14	2.08	299
dtxsid50880718	-8.06	-0.45	0.00	-23.68	-0.73	-25.34	-24.41	0.08	341
2,3-pinanediol	-6.89	-0.57	0.00	-23.98	-3.02	-38.11	-26.99	0.34	206
Arachidonic acid methyl ester	-6.27	-0.27	0.00	-37.49	-0.93	-44.99	-38.43	8.48	154
beta-linalool	-3.77	-0.34	-0.16	-17.43	-4.83	-25.49	-22.26	4.67	16
Propylene	-3.64	-1.21	0.00	-7.76	-0.29	-9.82	-8.06	0.00	357
cis-sabinol	-7.11	-0.65	-0.16	-15.24	-3.94	-28.26	-19.18	0.77	218
1JNX	Docking Score	Glide ligand efficiency	Glide hbond	Glide evdw	Glide ecoul	Glide emodel	Glide energy	Glide einternal	Glide posenum
o-Cymene	-3.74	-0.37	0.00	-13.04	-1.60	-18.06	-14.63	0.01	187

Camazulene	-3.79	-0.27	0.00	-16.84	-0.64	-21.29	-17.49	0.34	74
Ehrysanthone	-4.36	-0.40	-0.15	-12.58	-2.82	-19.45	-15.40	0.01	53
Einecs 228-063-1	-5.17	-0.27	-0.79	-17.24	-9.99	-36.41	-27.24	3.05	147
Tau-Cadinol	-4.57	-0.29	-0.32	-13.80	-4.66	-24.22	-18.45	0.25	226
Galactonic phenylhydrazide	-3.77	-0.19	-0.16	-13.50	-25.88	-45.21	-39.38	13.77	105
Methoxyeugenol	-3.48	-0.25	-0.28	-12.79	-6.72	-24.21	-19.51	0.84	254
Isothujol	-4.67	-0.42	-0.32	-12.26	-4.02	-20.13	-16.28	2.74	156
Chiapin b	-4.34	-0.17	-0.45	-23.71	-9.51	-40.72	-33.22	3.37	362
Thujone	-4.36	-0.40	-0.15	-12.58	-2.82	-19.45	-15.40	0.01	53
beta-Eudesmene	-3.56	-0.24	0.00	-14.50	-0.69	-18.38	-15.19	0.09	254
Costunolide	-4.33	-0.25	-0.37	-14.51	-4.20	-23.54	-18.71	0.00	244
Germacrene D	-3.67	-0.24	0.00	-15.97	-0.23	-19.67	-16.20	0.49	178
Germacrene D-4-ol	-4.21	-0.26	-0.32	-15.27	-4.42	-24.16	-19.69	0.11	327
Tetraneurin d	-4.51	-0.20	-0.61	-22.73	-7.87	-37.51	-30.59	2.94	273
dtxsid50880718	-3.92	-0.22	0.00	-18.16	-1.63	-24.55	-19.79	0.00	274
2,3-pinanediol	-4.67	-0.39	-0.30	-14.09	-5.34	-25.66	-19.42	1.23	185
Arachidonic acid methyl ester	-2.11	-0.09	-0.11	-28.76	-3.62	-35.55	-32.38	2.27	396
beta-linalool	-2.12	-0.19	-0.32	-13.07	-3.95	-18.29	-17.02	1.99	355
Propylene	-3.21	-1.07	0.00	-6.84	-0.28	-8.48	-7.11	0.00	154
cis-sabinol	-4.71	-0.43	-0.32	-12.19	-5.13	-22.10	-17.33	2.49	257

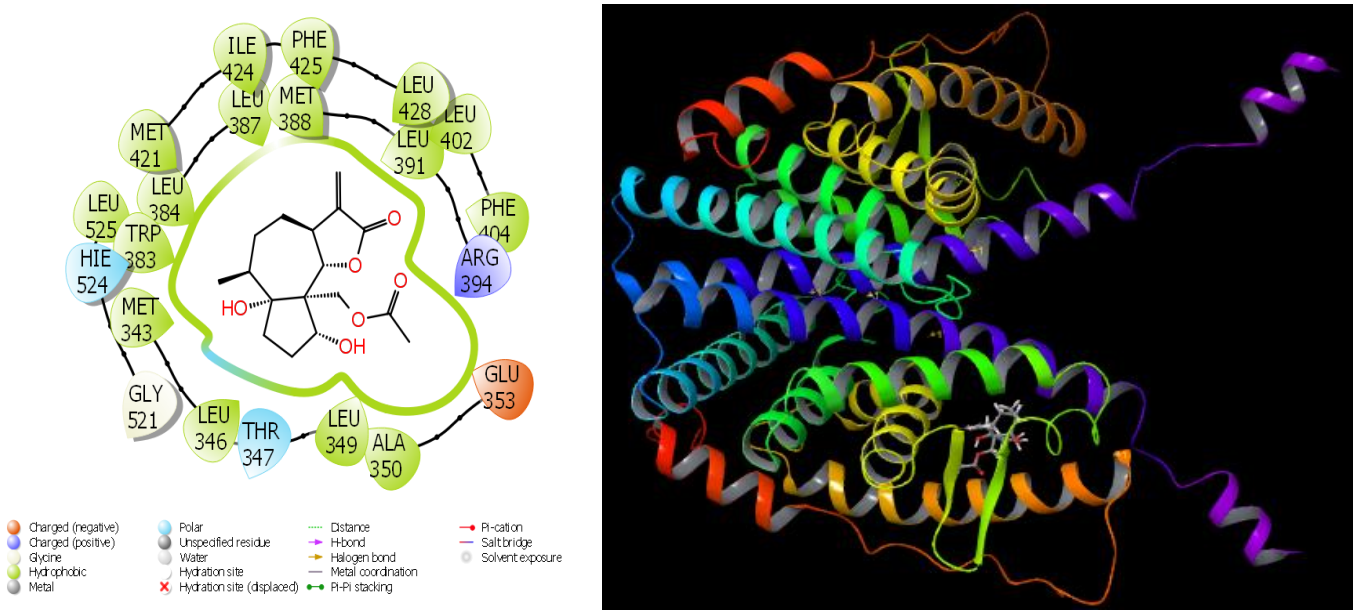

Figure 1. Tetraneurin D's Interactions with Proteins Related to breast Cancer (PDB ID: 1A52)

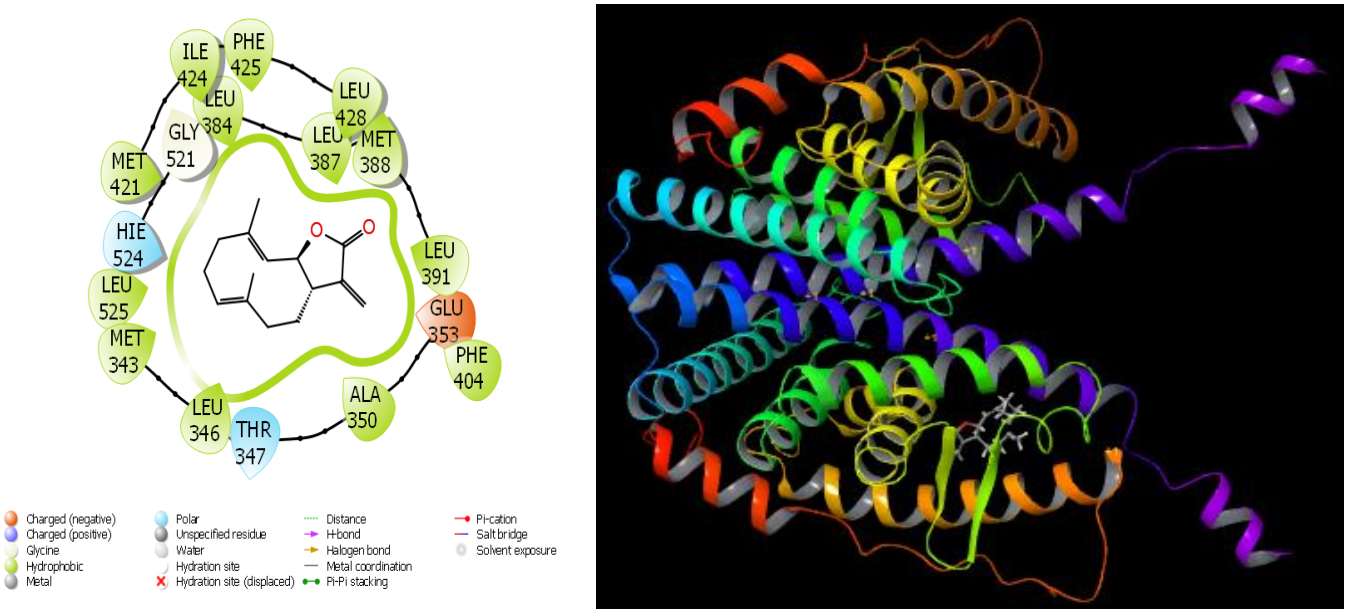

Figure 2. Costunolide's Interactions with Proteins Related to breast Cancer (PDB ID: 1A52)

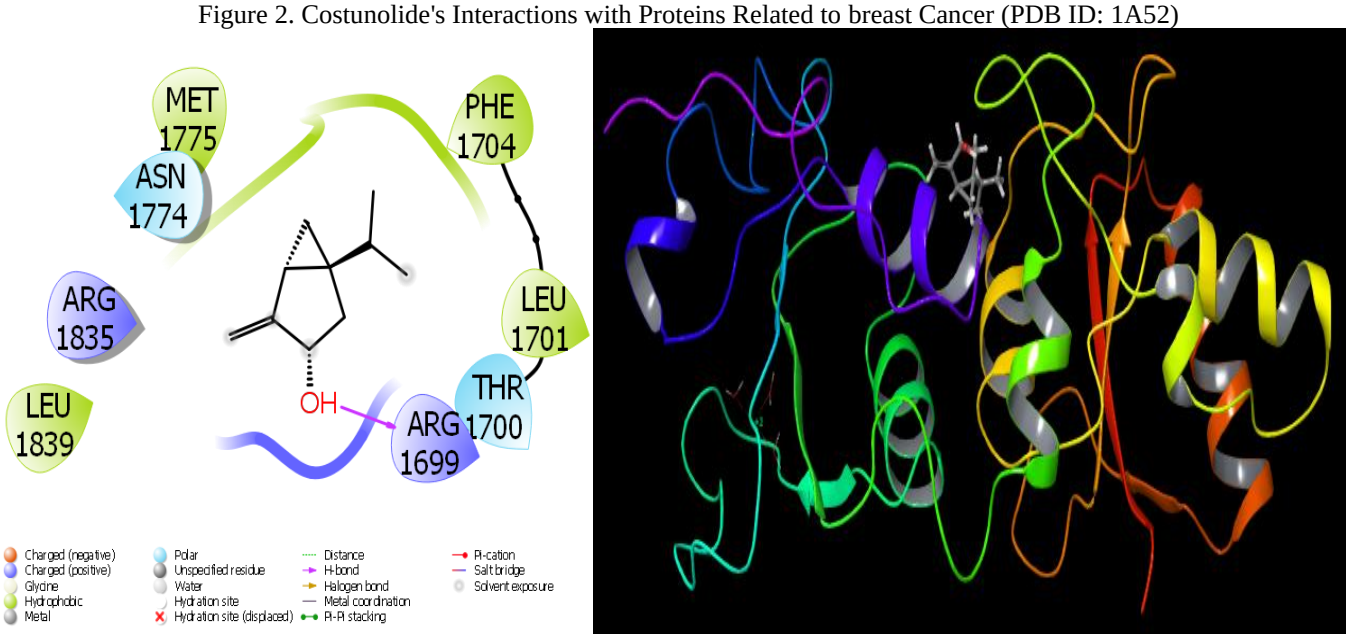

Figure 3. Cis-sabinol's Interactions with Proteins Related to breast Cancer (PDB ID: 1JNX)

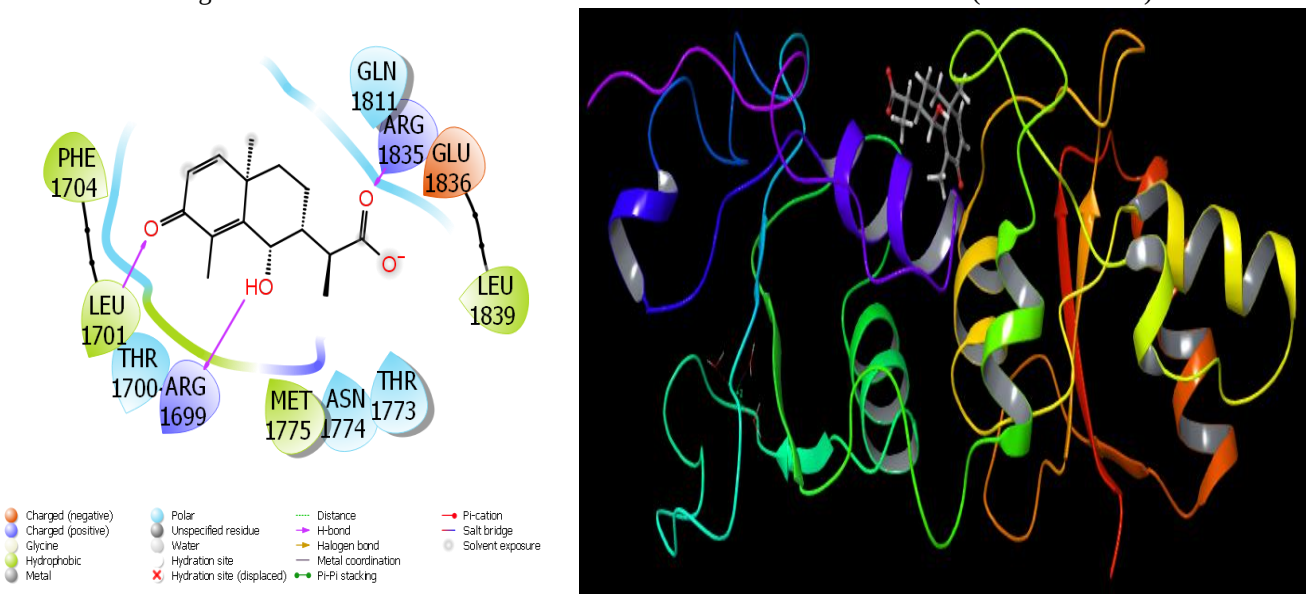

Figure 4. Einecs 228-063-1's Interactions with Proteins Related to breast Cancer (PDB ID: 1JNX)

The docking score, a vital metric derived from the calculations, holds a pivotal role in the comparative analysis of the activities of the molecules examined in your research [38,39]. It is noteworthy that the molecule exhibiting the most negative numerical value for the docking score is regarded as having the highest activity among the tested compounds [40,41]. This parameter serves as a key tool in evaluating the potential effectiveness of these molecules in their designated roles, such as inhibiting breast cancer proteins [42,43].

IV. CONCLUSION

The observation that Einecs 228-063-1, Cis-sabinol, Costunolide, and Tetraneurin D both present in the plant extract of Artemisia absinthium, demonstrated elevated activity against breast cancer proteins in your study implies potential applications for these specific compounds in targeting breast cancer proteins for therapeutic purposes. This finding underscores the significance of delving deeper into the mechanisms of action and exploring the potential of Einecs 228-063-1, Cis-sabinol, Costunolide, and Tetraneurin D as treatments for breast cancer. Further investigations in this direction could contribute valuable insights to the development of therapeutic strategies for breast cancer.

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