JETIR.ORG ISSN: 2349-5162 | ESTD Year : 2014 | Monthly Issue
JOURNAL OF EMERGING TECHNOLOGIES AND INNOVATIVE RESEARCH (JETIR)
An International Scholarly Open Access, Peer-reviewed, Refereed Journal

Using in-silico screening analysis, Leea indica is evaluated as a medicinal plant with phytoconstituents 3-O-alpha-L-Arabinoside as new potential inhibitors for cancer cells.

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Abstract
A group of illnesses known as cancers are defined by the unchecked development and division of aberrant cells. Metastasis, the term for the spread of cancer cells at this stage, if unchecked, can be fatal. Tobacco, chemicals, radiation, infectious agents, and other environmental elements, in addition to some internal ones, all contribute to the development of cancer (inherited mutations, hormones, immune conditions and random mutations). According to the World Health Organization, the number of cancer cases globally is expected to rise by 70% during the following two decades. The current work used molecular docking techniques to evaluate several physiologically active chemicals found in medicinal plants as possible inhibitors. The Maestro 12.8 did the Docking study contrasting the anti-cancer medication Erdafitinib with the phytoconstituents found in Leea indica leaf 3-O-alpha-L-Arabinoside. The outcomes show the potency of this screening approach, which can hasten the development of novel drugs to treat emerging infectious diseases and disorders. When compared to the anti-cancer medicine Erdafitinib, whose docking score was 6.559, the phytoconstituents screening chemicals extracted from the medicinal plant Leea indica, such as 3-O-alpha-L-Arabinoside (-6.559), were more effective (-5.572). The docking results reveal that phytoconstituents found in Leea inidica plants have a great deal of potency against malignant cells and can be utilised to stop the growth of cancerous cells, making them an essential source for new antineoplastic medications in the future that target carcinoma.
Keywords: Erdafitinib, Leea indica, molecular docking, anti-cancer.

1. Introduction

A group of illnesses known as cancers are defined by the unchecked development and division of aberrant cells. Metastasis, the term for the spread of cancer cells at this stage, if unchecked, can be fatal. Tobacco, chemicals, radiation, infectious agents, and other environmental elements, in addition to some internal ones, all contribute to the development of cancer (inherited mutations, hormones, immune conditions and random mutations). Cancer has a wide variety of complex, poorly understood causes. Numerous factors, such as dietary elements, specific illnesses, a lack of physical exercise, obesity, and environmental contaminants are known to raise the risk of cancer [1]. These elements may interact to start or encourage carcinogenesis in humans, making cancer the major cause of mortality. In India, cancer is become one of the leading causes of mortality. There are thought to be between 2 and 2.5 million cancer cases worldwide at any given moment. Annually, there are more than 7 lakh new instances of cancer and 3 lakh fatalities from it. At any given time, about 15 lakh patients need access to facilities for diagnosis, treatment, and follow-up [2]. With an estimated 14.1 million new cases and 8.2 million fatalities directly attributable to cancer in 2012, compared to 12.7 million infections in 2008, cancer remained the biggest cause of mortality in the globe. According to the World Health Organization [3], the number of cancer cases globally is expected to rise by 70% during the following 20 years. The leading causes of cancer mortality are breast and cervical cancer. In 140 of 184 nations throughout the world, breast cancer is the most common cancer diagnosed in women, and incidence has climbed by more than 20% since the 2008 estimates, while mortality has increased by 14%. After breast, colorectal, and lung cancers, cervical cancer is the fourth most frequent cancer in women worldwide; it is especially prevalent in sub-Saharan African nations with limited resources. Chemotherapy is used to treat recurrent cancers throughout the body using traditional anticancer medications, which can have substantial clinical adverse effects [4]. The development of multidrug resistance, large doses, non-specific distribution, severe toxicity to normal cells, insufficient drug concentrations at tumours, and malignant cells are the main causes of side effects. As a result, ongoing research is being done to develop new anti-cancer medicines that can target tumour cells specifically while having little adverse effects on normal organs [5].

Leea indica

Leea indica (Burm.f.) Merr, belonging to the family Vitaceae, is commonly known as Bandicoot berry in English, Chhatri in Sanskrit, and Hastipalash in Hindi. The plant is distributed in various parts of the world such as India, Malaysia, China, and Thailand. The plant is distributed in forests of tropical and subtropical India, from Himalayas to southward to the Peninsula. The plant is medicinally important

and is widely used in indigenous systems of medicine. The root is antidiarrheal, antidysenteric, antispasmodic, cooling, and sudorific. The juice of young leaves is digestive. An ointment prepared from roasted leaves relieves vertigo [6,7]. The plant L. indica is a large perennial shrub with stout, soft-wooded stems, alternate leaves (2-3 pinnate, sometimes 1-pinnate), leaflets ovate or oblong-lanceolate, 25 cm × 10 cm, apex acuminate, margin irregularly serrate, base truncate, pinnately veined. Flowers are pale-green/greenish-white, bisexual, in large terminal compound corymbose cymes, bracts minute, calyx 5-lobed, petals 5, and spreading. Stamens 5 in number, stamina tube white in color, anthers are united in buds. Fruit is a berry, 8 mm across, globose, often 2–6 lobed, to 0.5 cm in diameter, purplish–black when ripe. Flowering occurs more or less throughout the year [8,9]. The plant L. indica has ethnomedicinal importance worldwide. Various parts of the plants, namely, leaves, roots, stem bark, inflorescence, and flowers in certain formulations such as paste and decoction are being in use for treating several ailments. Roots and leaves are predominantly used. The plant is used medicinally in several formulations to treat ailments such as fever, bone fracture, diarrhea, dysentery, body ache, head ache, malaria, rheumatism, asthma, and gastric ulcer. A brief detail on some of the uses of L. indica to treat diseases and disorders in India and in other parts of the world (namely, Nepal, Bangladesh, Malaysia, Indonesia, and Thailand) [10] is presented in Table 1.

Table 1: Reported ethnobotanical uses of different parts *of L. indica* geographically distributed in India

Region	Part	Uses	References
Jalpaiguri district, West Bengal, India	Root	Bone fracture	Bose *et al*.[11]
Hassan district, Karnataka, India	Root	Sudorific, diarrhea, dysentery, colic	Kumar and Shiddamallayya[12]
Thrissur district, Kerala, India	Root	Diarrhoea, dysentery, hyperdipsia, ulcer, skin diseases	Deepa *et al*.[13]
Golaghat district, Assam, India	Fruit	Extracts used for purple dye	Barukial and Sarmah[14]
Visakhapatnam district, Andhra Pradesh, India	Tuber	Liver enlargement	Rao *et al*.[15]
Rajasthan, India	Inflorescence, tuber	Chest pain in children (inflorescence extract), allergy (tuber paste)	Swarnkar and Katewa[16]
Shimoga district, Karnataka, India	Leaf	Diarrhea and dysentery in cattle	Rajakumar and Shivanna[17]
Car Nicobar island, Nicobar, India	Leaf	Cuts and wounds	Verma *et al*.[18]
Kalakad Mundanthurai Tiger Reserve, Tamil Nadu, India	Leaf, flower	Rheumatism	Sutha *et al*.[19]
Kanyakumari district, Tamil Nadu, India	Root	Diarrhea	Sukumaran and Raj[20]

More than 80% of existing anticancer drugs were derived from plants. Likewise, in our study we choose the mollic acid α-L-arabinoside a phytochemical present in the leaves of Leea indica showed cytotoxic effect on CaSki (cervical cancer) cells [21].

2. Research and Methodology

2.1 Molecular docking:

The molecular docking method allows us to characterize how small molecules behave in the binding site of target proteins and to better understand basic biological processes by simulating the interaction between a small molecule and a protein at the atomic level [22]. There are more and more new therapeutic targets available for drug discovery as a result of the completion of the human genome project. The development of nuclear magnetic resonance spectroscopy, crystallography, and high-throughput protein purification methods has also led to the understanding of several structural features of proteins and protein-ligand complexes. These developments now make it possible for computational methods to be used in all phases of drug discovery [23-27]. Prediction of the ligand structure as well as its placement and orientation within these sites (often referred to as pose) and evaluation of the binding affinity are the two fundamental processes in the docking process. These two actions have an impact on sample techniques and scoring systems, which will be covered in the theory section.

The efficiency of docking procedures is greatly improved by knowing the location of the binding site prior to docking actions. Before docking ligands into the binding site, the binding site is frequently known; the efficiency of docking procedures is greatly improved by knowing the location of the binding site prior to docking actions. Before docking ligands into the binding site, the binding site is frequently known. Additionally, by contrasting the target protein with a family of proteins that perform a comparable function or with proteins that have been co-crystallized with different ligands, one can learn more about the sites. Additionally, by contrasting the target protein with a family of proteins that perform a comparable function or with proteins that have been co-crystallized with different ligands, one can learn more about the sites. Without knowing the binding sites, cavity detecting software or internet services, such GRID [28-29], POCKET [30], Surf Net [31-32], PASS [33] and MMC [34].

2.2 Examples of how molecular docking is used in drug discovery

The method that has been used the most frequently is molecular docking. Though its primary use is in structure-based virtual screening to find new compounds that are active against a specific target protein, there have been some notable successes in this area [35].

2.2 Docking studies using Maestro 12.8

The method that has been used the most frequently is molecular docking. Though its primary use is in structure-based virtual screening to find new compounds that are active against a specific target protein, there have been some notable successes in this area [36]. In reality, it is not a stand-alone procedure but is typically incorporated into a workflow comprising several *in silico* and experimental techniques [37].

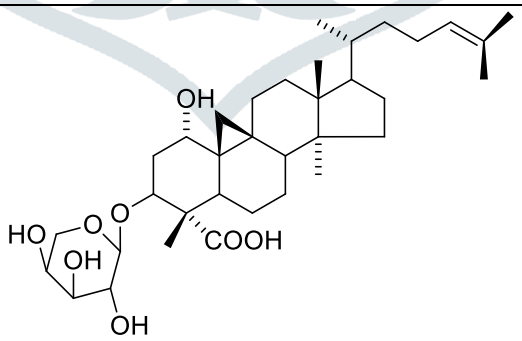
2.3 Docking preparation of predicted TPP and 5 ligands

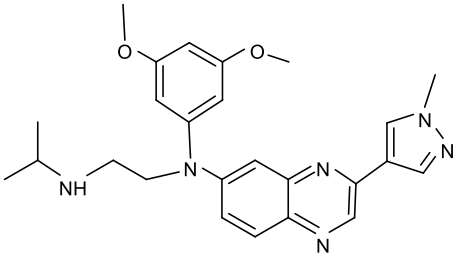
The Maestro 12.8 software includes tools for both protein and ligand optimization, such as assigning atomic charges to make proteins more polar, modifying ligands by assigning charge and rotatable bonds, calculating the energy contribution of de-solvation during ligand-binding on proteins, and assigning grid maps on protein surfaces in advance of ligand interaction by auto grid. The aforementioned facilities enhance molecular docking's speed, accuracy, and docking with a new scoring mechanism, effective optimization, and multithreading [38].

2.4 Protein docking with ligand (phytochemicals) molecules in a modeled TPP

In the current study, we have calculated the binding-free energy or docking, which reflects the binding affinity of 1 ligands and 1 prescription medicine (Standard drug Erdafitinib) to model TPP.According to the aforementioned docking research, phytochemical 3-O-alpha-L-Arabinoside present in leaves of Leea indica plant shows the highest binding affinity and the highest docking score (--6.559 kcal/mole), had higher binding energies than the prescription medications Erdafitinib whose docking score (-5.572). As a result, we chose a phytochemical ligand from 3-O-alpha-L-Arabinoside phytoconstitutent that exhibits superior docking energy. Table 2 lists the ligands that have the greatest affinity for the model TPP for further research [39]. As an alternative to Auto Dock Vina in the current investigation, the Schrodinger program's Glide energy (Maestro 12.8) drug discovery tool was used in the study. When docking calcineurin with inhibitors, Maestro 12.8 predicts binding affinity energy between -6.559 kcal/mole to-5.572 kcal/mole which is nearly identical to the findings of the current investigation [40].

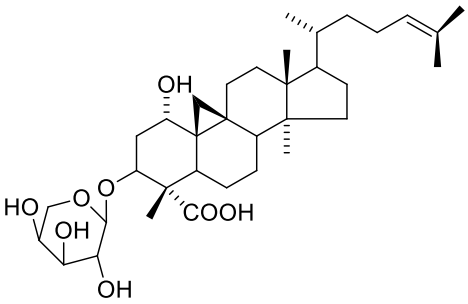
Table 2: *In-silico* screening of *Leea indica's* phytoconstituents' comparing with standard antineoplastic drug: -

S. No	Name of Phytoconstituents	Chemical Structure	Docking score	Glide energy
1.	3-O-alpha-L-Arabinoside		-6.559	-0.364

2.	**Erdafitinib**		-5.572	-0.169

❖***Leea indica's*** **phytoconstituents' chemical structure composition.**

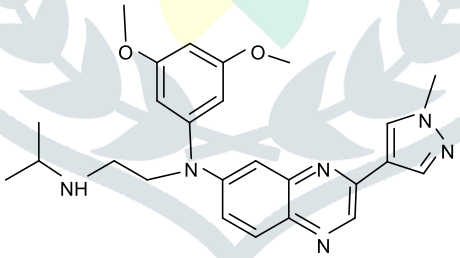
Mollic acid 3-O-alpha-L-Arabinoside



(2a*R*,5a*S*,8*S*,11*S*,11a*S*,12a*S*)-11-hydroxy-2a,5a,8-trimethyl-3-((*R*)-6-methylhept-5-en-2-yl)-9-(((2*S*,3*R*,4*S*,5*S*)-3,4,5-trihydroxytetrahydro-2*H*-pyran-2-yl)oxy)hexadecahydrocyclopenta[*a*]cyclopropa[*e*]phenanthrene-8-carboxylic acid

Figure 1: Chemical structure of 3-O-alpha-L-Arabinoside

Erdafitinib



N^1-(3,5-dimethoxyphenyl)-N^2-isopropyl-N^1-(3-(1-methyl-1*H*-pyrazol-4-yl)quinoxalin-6-yl)ethane-1,2-diamine

Figure 2: Chemical structure of Erdafitinib

3. **Result and Discussion:** The above *in silico* study experimental evaluation data shows that 3-O-alpha-L-Arabinoside phytoconstituent present in Leea indica medicinal plant shows the highest binding affinity and docking score (-6.559 kcal/mole), with receptor having PDB id (2KCE) and Erdafitinib international formulated antineoplastic drug shows docking score of (-5.572 kcal/mole) which is the least when compared to phytoconstituents present in Leea indica plant this result prove that 3-O-alpha-L-Arabinoside phytoconstituent shows tremendous result not only in treatment of CaSki (cervical cancer) cells but also for various different types of Malignant cells.

2KCE: Binding of the anticancer drug zd 1694 to E. coli thymidylate synthase: assessing specificity and affinity [41].
Classification: METHYL TRANSFERASE
Organism(s): Escherichia coli
Expression system: Escherichia coli
Mutation(s): No
Resolution: 2.20 Å

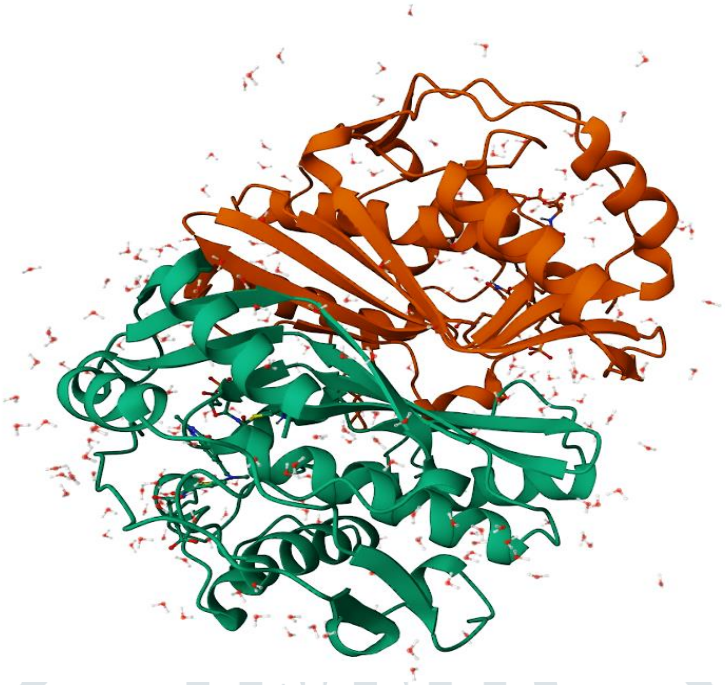


Figure 3: 3D- Structure of protein (2KCE)

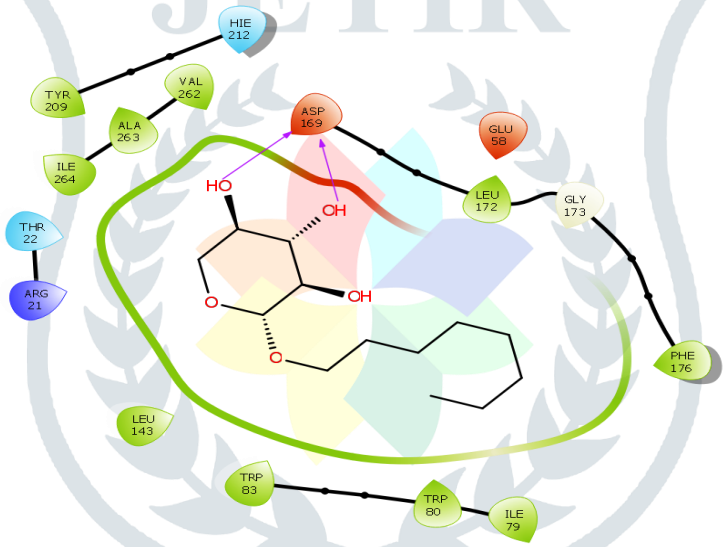


Figure 4: 3-O-alpha-L-Arabinoside 2D diagrams of docked conformation compound

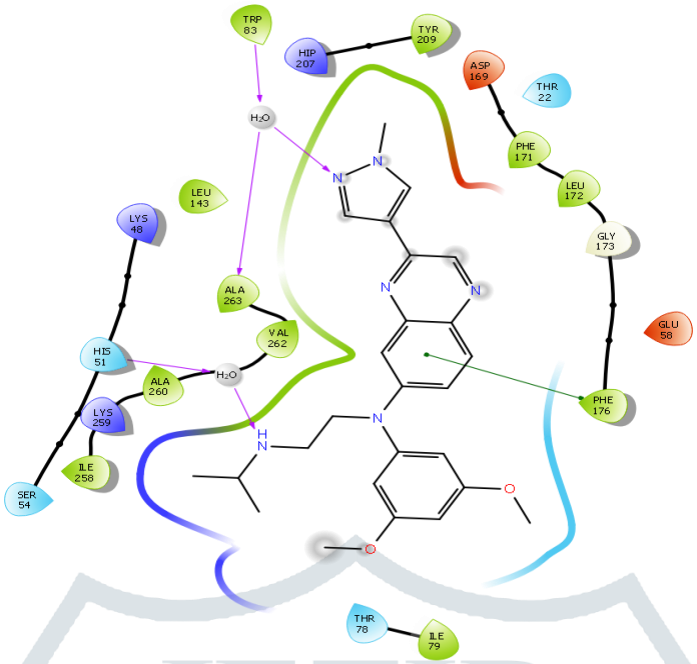


Figure 5: Erdafitinib 2D diagrams of docked conformation compound

4. Conclusion: Our research which is based on in-silico study assessment of Leea indica a medicinal plant containing phytoconstituents α-L-arabinoside conclude that phytoconstituents present Leea indica"s leaves show effective property and potent record against cancerous cells although our work is based on computational molecular docking but with great importance of this scientific tool which is known as Maestro 12.8 used for molecular docking analysis prove its authenticity.As these plants species were effective against several types of cancer cell prove in our study through molecular docking anaylsis it can be said that the unexplored plants of this genus may introduce a new era of cancer treatment in the future.

Compliance with ethical standards Acknowledgments
The authors thank the reviewers for their insightful suggestions.

Disclosure of conflict of interest
The authors declare there is no conflict of interest in this study.

Statement of informed consent
Informed consent was obtained from all individual participants included in the study.

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