Elettaria cardamomum is examined as a medicinal plant using *in-silico* screening analysis in order to discover novel possible cardiovascular disease (CVD) inhibitors from its phytoconstituents sabinene, α -terpineol, and α -pinene.

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Abstract- Cardiovascular disease (CVD) is an umbrella term for a number of linked pathologies, commonly defined as coronary heart disease (CHD), cerebrovascular disease, peripheral arterial disease, rheumatic and congenital heart diseases and venous thromboembolism. Globally CVD accounts for 31% of mortality, the majority of this in the form of CHD and cerebrovascular accident. 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-cardiac medication Quinapril as a standard drug with the phytoconstituents found in Elettaria cardamomum capsules contains Sabinene, α -terpineol, α –pinene. The outcomes show the potency of this screening approach, which can hasten the development of novel drugs to treat emerging infectious diseases and disorders. Use of Cardiac receptor having PDB id (1LXF) and the when compared to the anticardiac medicine Quinapril, whose docking score was -5.647, the phytoconstituents screening chemicals extracted from the medicinal plant Elettaria cardamomum, such as Sabinene (-6.715), α –terpineol (-6.161), α –pinene (-6.078) were more effective than standard anticardiac medication quinapril whose docking score is (-5.647). The docking results reveal that phytoconstituents found in *Elettaria cardamomum* plants have a great deal of potency against cardiovascular diseases condition and can be utilised to inhibit various cardiovascular diseases, making them an essential source for new anticardiac medications in the future that target cardiovascualar diseases.

Index Terms- Cardiovascular diseases, Quinapril, Sabinene, α -terpineol, α -pinene, Docking score, *In-silico* screening.

Introduction

Cardiovascular disease (CVD) is an umbrella term for a number of linked pathologies, commonly defined as coronary heart disease (CHD), cerebrovascular disease, peripheral arterial disease, rheumatic and congenital heart diseases and venous thromboembolism. Globally CVD accounts for 31% of mortality, the majority of this in the form of CHD and cerebrovascular accident [1]. The rate of CVD worldwide is predicted to increase as the prevalence of risk factors for CVD rises in previously low-risk countries. Currently 80% of CVD mortality occurs in developing nations [2] and CVD is expected to be the major cause of mortality in most developing nations by 2020, overtaking infectious disease [3].Not only is CVD a leading cause of mortality, but it is the leading cause of loss of disability-adjusted life years globally [2]. The World Health Organisation (WHO) estimate that over 75% of premature CVD is preventable and risk factor amelioration can help reduce the growing CVD burden on both individuals and healthcare providers [4]. Whilst age is a known risk factor for the development of CVD, autopsy evidence suggests that the process of developing CVD in later years is not inevitable,[5] thus risk reduction is crucial. The INTERHEART study elucidated the effect of CVD risk factors including dyslipidaemia, smoking, hypertension, diabetes, abdominal obesity, whilst it demonstrated the protective effects of consumption of fruits and vegetables, and regular physical activity. These risk factors were consistent throughout all populations and socioeconomic levels studied, helping to establish the viability of uniform approaches to CVD primary prevention worldwide [6]. In this research paper we look at the main components of primary prevention of CVD as by utilizing molceular docking (in-slico screening) and structural docking of phytoconsitutents present in Elettaria cardamomum medicinal plant which show best docking result when compared with standard drug this research paper indicates attempt to provide a summary of primary prevention guidelines in CVD for clinicians. Hyperlipidemiarelates to increasedoxidative stress causing significant production of oxygen free radicals, which may lead to oxidative modifications in low-density lipoproteins, which present a significant function inthe initiation andprogression of atherosclerosis and associated cardiovascular diseases [7].Hyperlipidemia is a potent risk factor for atherosclerosis and coronary heart disease (CHD) and is present in a substantial proportion of young adults. According to data from the National Health and Nutrition Examination Survey, 11.7% of adults aged 20 to 39 and 41.2% of adults aged 40 to 64 had elevated low-density lipoprotein cholesterol (LDL-C) levels, but only 10.6% of adults aged 20 to 39 and 47.7% of adults age 40 to 64 with hyperlipidemia were receiving treatment [8].

Elettaria Cardamomum

Elettaria cardamomum (L.) Maton is commonly known as small cardamom, green cardamom, or true cardamom and is grown in India, Guatemala, Sri Lanka, Nepal, Indonesia, Costa Rica, Mexico and Tanzania [9]. In India, cardamom is cultivated in altitudes ranging from 900 to 1400 m above msl (mean sea level) covering three southern Indian states (Kerala, Karnataka and Tamil Nadu). In Kerala, it is cultivated mainly in the Indian Cardamom Hills covering an area of 1050 square kilometers designated as Cardamom Hill Reserves [10]. The botanical name of cardamom, *Elettaria cardamomum*, originated from the Tamil word "*Elettari*" which refers to the seeds of cardamom [11]. In general, the cardamoms are the capsules of dried fruits in different genera of the Zingiberaceae family, primarily *Elettaria*, *Amomum* and *Aframomum*. Among them, *Elettaria cardamomum* (L.) Maton is most important and is grown predominantly in southern India [12]. Small cardamom is extensively cultivated in Nepal and Sikkim and to a limited extent with the large cardamom (*Amomum subulatum* Roxb.). However, international trade is now limited to Asian countries as far as small and large cardamom are concerned because of high prices. Worldwide, cardamom is recognized as the "queen of spices" for its pleasant aroma and taste, and is the third most expensive spice after saffron and vanilla. For centuries, cardamom capsules have been used for culinary and traditional medicine applications including controlling asthma, teeth and gum infections, digestive and kidney disorders [13,14] cataracts, nausea, diarrhea and cardiac disorders [15,16]. The essential oil and other bioactive metabolites accumulated in cardamom capsules contribute to their characteristic aroma and utility as a functional food, pharmaceutical, and nutraceutical [13].

Chemical composition of *Elettaria cardamomum* (L.)

The proximate composition of cured cardamom capsules includes carbohydrate 68.2%, protein 10.6 %, fat 2.4 % and ash 5.3 % [17]. One hundred g of cured capsules contained calcium (93 mg), magnesium (182 mg), potassium (124 mg), phosphorus (183 mg) sulphur (100 mg) and iron (13 mg) [17, 18, 19]. These are essential mineral elements for normal day-to-day physiological activities of humans. Cardamom capsules and leaves contain significant levels of manganese, zinc and copper. Reported nutritionally important metabolites of cardamom capsules that include flavonoids (catechin, myricetin, quercetin and kaempferol) and carotenoids (lutein and β-carotene[20].The profiling of EO of cardamom seeds sampled from southern India predominantly exhibited 1, 8-cineole (28.94%), α-terpinyl acetate (26.7%), α-terpineol (14.6%), sabinene (13.5%), nerol (5.0%) and α-pinene (2.4%)[20]. [21] indicated that seeds of cardamom collected across the cardamom growing region of India chiefly contained α-terpinyl acetate, 1, 8-cineole and α-terpineol.

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 3 ligands

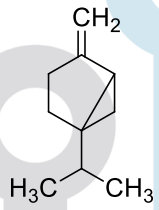
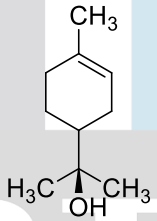
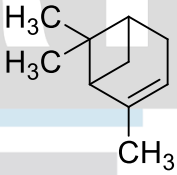
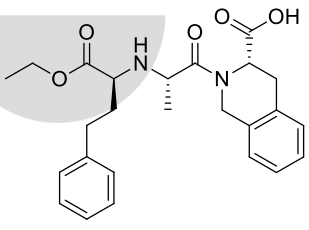
The Maestro 12.8 software includes tools for both protein and ligand optimization, such as assigning atomic charges to make proteins more polar, modifying ligands by assigning charge and rotatable bonds, calculating the energy contribution of de-solvation during ligand-binding on proteins, and assigning 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

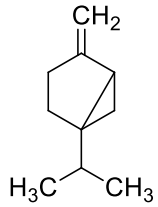
In the current study, we have calculated the binding-free energy or docking, which reflects the binding affinity of 3 ligands and 1 prescription medicine (Standard drug Quinapril) to model TPP. According to the aforementioned docking research, phytochemicals Sabinene, α -terpineol, α –pinene present in capsules of Elettaria cardamomum plant shows the highest binding affinity and the highest docking score and had higher binding energies than the prescription medications Quinapril whose docking score (-5.647). As a result, we chose a phytochemicals present in Elettaria Cardamomum′s as a ligand that exhibits superior docking energy's and glide energy when compared to standard drug. Table 1. 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 (-6.715 kcal/mole to-5.647 kcal/mole) which is nearly identical to the findings of the current investigation [40].

Table 1: *In-silico* screening of Elettaria Cardamomum′s phytoconstituents' comparing with standard anticardiac drug: -

S. No	Name of Phytoconstituents	Chemical Structure	Docking score	Glide energy
1.	**Sabinene**		-6.715	-13.16
2.	**α –terpineol**		-6.161	-18.025
3	**α –pinene**		-6.078	-14.325
4.	**Quinapril (Standard drug)**		-5.647	-42.195

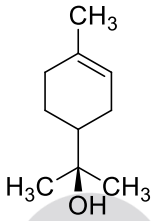
❖ **Elettaria Cardamomum's phytoconstituents' chemical structure composition.**

"Figure 1: Chemical structure of Sabinene"



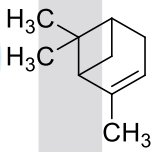
1-isopropyl-4-methylenebicyclo[3.1.0]hexane

"Figure 2: Chemical structure of α –terpineol"



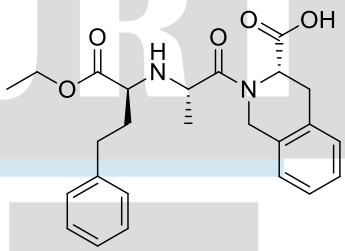
2-(4-methylcyclohex-3-en-1-yl)propan-2-ol

"Figure 3: Chemical structure of α –pinene"



2,6,6-trimethylbicyclo[3.1.1]hept-2-ene

"Figure 4: Chemical structure of Quinapril"



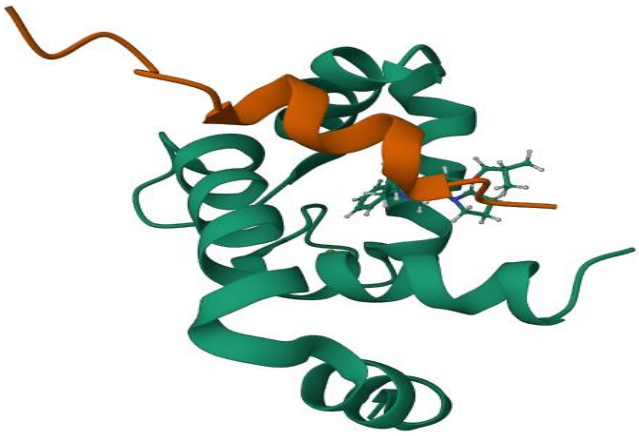
Quinapril

3. **Result and Discussion:** The above *in silico* study experimental evaluation data shows that Sabinene, α -terpineol, α –pinene phytoconstituent present in *Elettaria cardamomum* medicinal plant shows the highest binding affinity and docking score that is Sabinene (-6.715), α –terpineol (-6.161), α –pinene (-6.078), with receptor having PDB id (1LXF) and Quinapril international formulated anticardiac drug shows docking score of (-5.647 kcal/mole) which is the least when compared to Sabinene, α -terpineol, α –pinene phytoconstituents present in *Elettaria cardamomum* plant this result prove that phytoconstituent shows tremendous result not only in treatment of myocardial infarction but also for various different types of cardiovascular diseases.

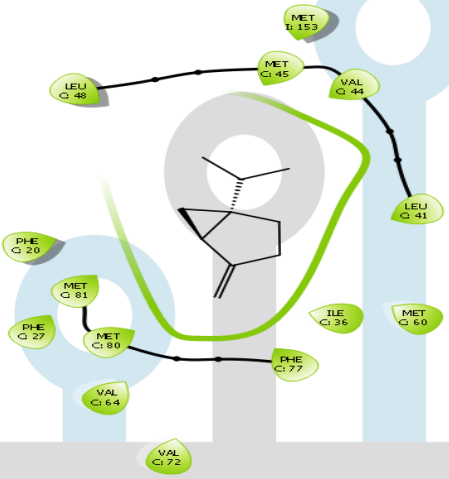
1LXF: Structure of the Regulatory N-domain of Human Cardiac Troponin C in Complex with Human Cardiac Troponin-I (147-163) and Bepridil [41].

- **Classification:** METAL BINDING PROTEIN, PROTEIN BINDING
- **Organism(s):** Homo sapiens
- **Expression system:** Escherichia coli
- **Mutation(s):** No

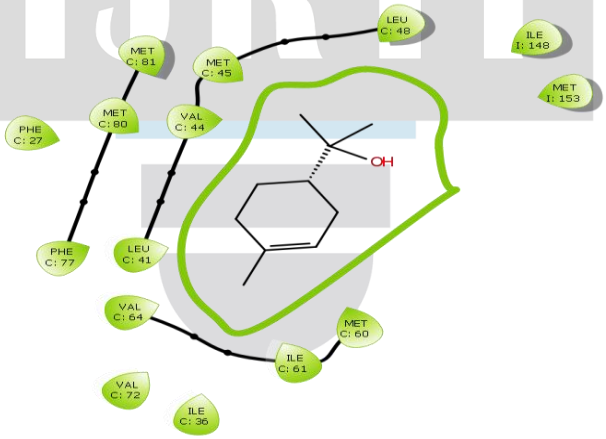
"Figure 5: 3D- Structure of protein (1LXF)"



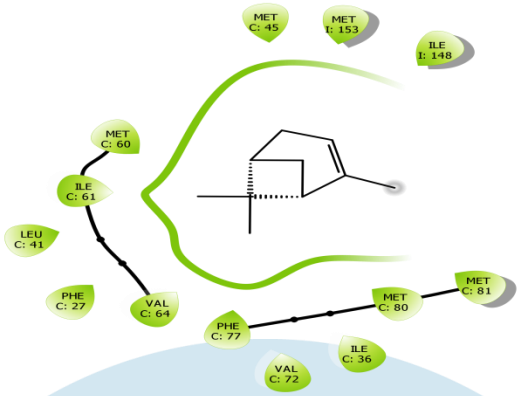
"Figure 6: Sabinene 2D diagrams of docked conformation compound"



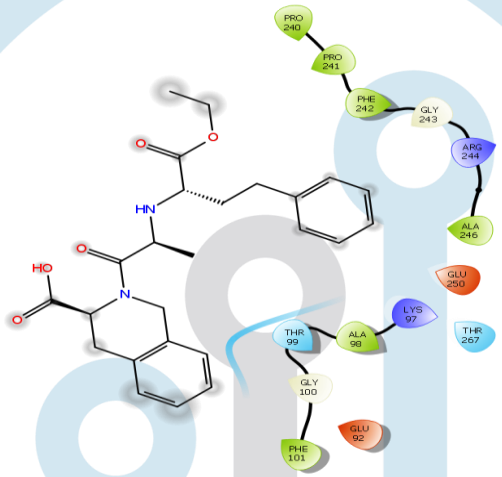
"Figure 7: α -terpineol 2D diagrams of docked conformation compound"



"Figure 8: α –pinene 2D diagrams of docked conformation compound"



"Figure 9: Quinapril 2D diagrams of docked conformation compound"



Conclusion: Our research which is based on *in-silico* study assessment of *Elettaria cardamomum* a medicinal plant containing phytoconstituents Sabinene, α -terpineol, α –pinene present conclude that phytoconstituents present in *Elettaria cardamomum* "s capsules show effective property and potent record against various cardiovascular diseases 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 cardiovascular diseases and potent inhibitor for hyperlipidemia condition and myocardial infarction prove in our study through molecular docking anaylsis it can be said that the unexplored plants of this genus may introduce a new era for treatment of cardiovascular diseases in future.

Compliance with ethical standards Acknowledgments
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Disclosure of conflict of interest
The authors declare there is no conflict of interest in this study.

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

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