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Isolation of Ace Inhibitors from Aromatic Plants

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ABSTRACT: Aromatic Plants have potential efficacy to treat hypertension. The main objective of this study is to know the ACE inhibition activity in these plants of aerial parts. Ace inhibition drugs were available such as ramipril, captopril, Quinapril, lisinopril, enalapril & benazepril. Among these drugs lisinopril has higher mortality rate when compared to ramipril. Some diseases such as HIV, amyloidosis, hyperthyroidism, gaucher's disease etc. may increase the level of Angiotensin converting enzyme. The term ARB refers to angiotensin II receptor blockers is one of the medication for hypertension, its function is to lower a blood pressure and has a lesser adverse effect while comparing with angiotensin converting enzyme inhibitor drugs. In the treatment of heart failure, ACE inhibitors are commonly used to hinder the development of angiotensin II, which lowering the both venous and arteriolar resistance. Their function is to interfering with the renin-angiotensin-aldosterone system in the body shortly known as RAAS that may controls the blood pressure in the body. Studies revealed that arb has the ability to reduce endanger of cardiovascular problems. The first approved ARB was losartan; people who are having diseases which can be related to kidney must avoid ARB drugs.

KEY WORDS: ACE inhibition activity, aromatic plants, ARBs, hypertension, gaucher's disease.

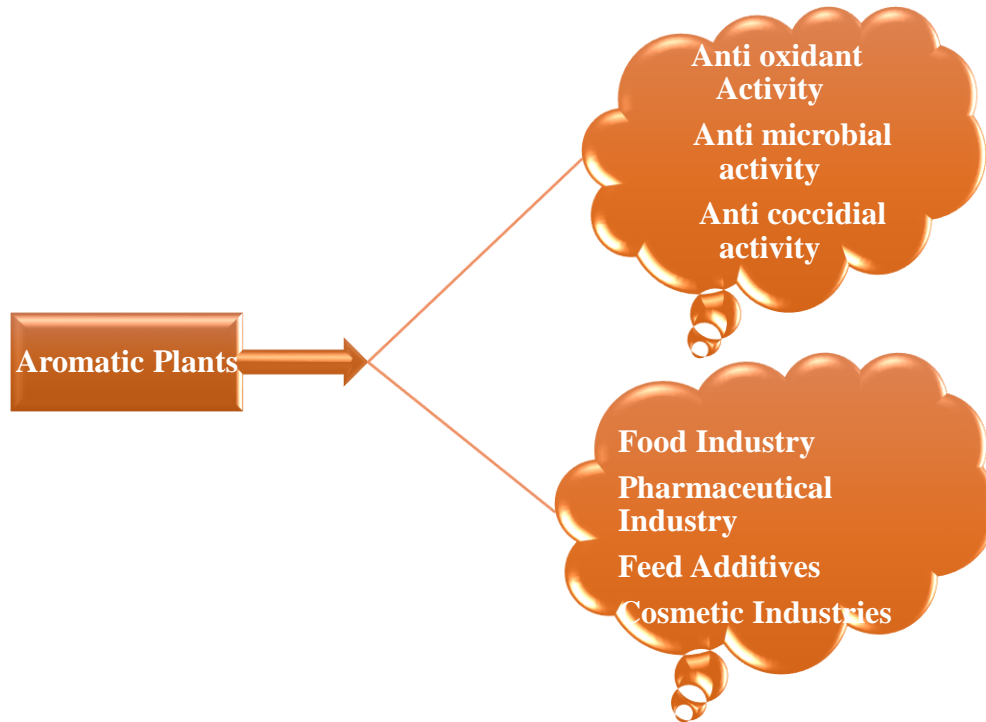
I.INTRODUCTION

Hypertension is a condition in which the blood pressure will be raised up resulting in severe harm to arteries that often occurred in old age people leads to stroke, heart failure, dysfunction of lungs & kidney problems. In some cases it doesn't shows any symptoms in people who has hypertension, In fact most of them do not know themselves for years. Symptoms may include bleeding in nose, breathing problem in extreme poor condition. People who have diabetes have a chance of getting high Bp not only that, it is also caused due to increased level of sodium, stress, unhealthy diet, obesity. Pregnancy women can also be affected if untreated the flow of blood, oxygen to the foetus will affect a mother's organ such as kidney. Some medications has the ability to increase the level of blood pressure such as steroids, birth control pills etc. ACE inhibitors diuretics, beta blockers, calcium channel blockers were employed to treat hypertension. The aim of this paper is to know the ace inhibition activity in aromatic plants by bioassay directed fractionation method which is nothing but it's a technique which is employed to identify & separating a target molecule in order to determine the inhibition activity in the plants on the basis of their properties. They have been shown the inhibition activity in the following plants.

Aromatic Plants

Aromatic plants are the plants which contain essential oils due the presence of volatile compound that can be extracted from the plants of leaves, bark, root which may be applied in the field of cosmetic and pharmaceutical industries because of its odor & flavor due to aromatic oxygenated compounds [1]. Aromatic Plants were associated with medicinal plants which is represented as MAP in short. It may be used as medicine too. Due to this property the scientific research can be going in these plants and also it had a great benefits in trade past for two decades. In natural medicine the aromatherapy holds an alternate system which may treat condition like pain reliever & also promote relaxation by massaging these essential oils with other substances. The classification and identification of plants were the initial step for study of Aromatic plants. These plants are composed of bioactive components which has the capacity to lower risk of cardiovascular diseases also cure respiratory related diseases. It consists of several chemical compounds so it named as chemical goldmines or natural biochemical factories. These plants were easily known by ancient Greek people; they also know the value of aromatic plants. The Greek physician father of medicine was generally referred as Hippocrates. He

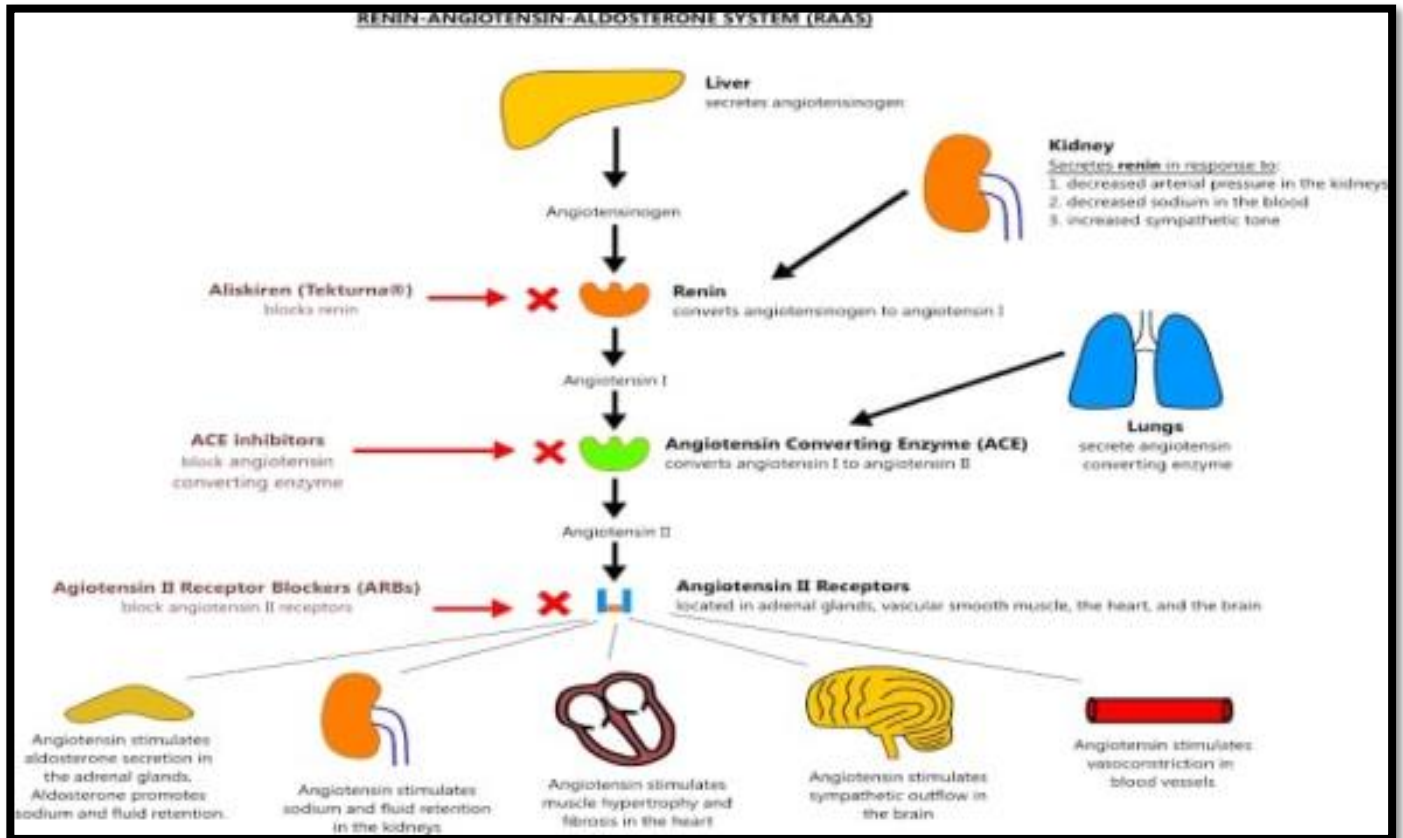
is popularly known for traditional medicine. He used aromatic oils as a disinfectant by spraying in streets to prevent spreading plaque disease in Athens.



Half of the people in the world have faith in extracts of aromatic plants for curing their health conditions. These oils from the plants can be separated by steam distillation process. Not all aromatic plants have medicinal properties, some herbs of aromatic oils, chemicals were included in drugs for formulation in countries. It can be used as therapeutics for mouth wash, oral intake and inhalation purpose [2,3]. Based on the utilization of aromatic plants, it can be categorized into groups namely, herbs, miscellaneous group, spices. Synthetic chemicals were employed in the field of food, pharma & cosmetic industries which resulting in hazardous to human health. So they commence to use natural fragrance and flavors derived from aromatic plants instead of using artificial fragrance.

Angiotensin Converting Enzyme & Inhibitors

ACE refers to Angiotensin Converting Enzyme is a class of gluzincin family which is mainly located in the alveoli of lungs, endothelial cells & epithelial cells of kidney. Its function is to converts a decapeptide which means polypeptide contains a string of ten aminoacids of angiotensin I into octapeptide angiotensin II by the removal of 2 free carboxyl aminoacid at the end. The patient's heart rate, potassium level should be monitored while taking ACEI medication. The University of California, Los Angels researchers conducted a study on ACEI, revealed that ace inhibitors doesn't shows that much of effectiveness in the initial treatment. If ACE level may be increased in the blood is due to sarcoidosis disorder which is caused by the cells were accumulated in the infection site to form nodules. That's why it can be used as a indicator to diagnosis this disorder. Normal level of angiotensin converting enzyme should be less than 40nmol/mL/min if it goes beyond this level, it shows a symptoms of sarcoidosis.



ACE Inhibitors are known as Angiotensin Converting Enzyme inhibitors which can be used in the treatment of hypertension, prevent stroke and some more diseases. ACEI initially were introduced in the year 1977 from snake venom, laterally developed into as captopril. In our human body liver produce angiotensinogen, kidney will produce renin. With the help of renin angiotensinogen were converted into angiotensinogen I; This angiotensinogen I will further converted into angiotensinogen II in our body. For that purpose lung produce angiotensin converting enzyme. Then the angiotensinogen II will bind to the receptor of AT1 in vascular smooth muscle which resulting in increasing blood pressure, in this case if the ace were inhibited means it doesn't convert angiotensinogen I into angiotensinogen II so that the blood pressure should be maintained in control. Such inhibitors were ended in pril like enalapril, moexipril, ramipril, lisinopril, captopril etc. known as angiotensin converting enzyme inhibitor drugs. These are collectively called as prodrugs besides, lisinopril and captopril. Enalapril can be given in emergencies by the route of administration (IV). Also these ace inhibitors were utilized to treat retinopathy, congestive heart failure, diabetic nephropathy and hypertension. It also has some side effects such as rashes, hyperkalemia and dry cough is due to increased level of bradykinin.

Isolation of ACE inhibitors from *Jasminum grandiflorum*

Jasminum species are available maximum in India being ancient period. Leaves, flowers, roots of the plant as various used in herbal medicine, also it has an enormous demand in producing aroma chemicals industries. The flowers of the plant generate aroma which makes pleasant mood. It is composed of isophytol, eugenol, benzyl benzoate and some chemical constituents. Jasmine flowers can be converted into jasmine oleoresin and jasmine concrete by using solvent extraction method that may applied in the field of perfumery industries. Wounds can be treated by the leaves of this plant as well as it helps to recover from toothaches and oral mucositis by chewing the leaves. The flowers helps to prevent breast cancer [4], their roots were employed to remove stone in kidney & alleviate pain in retention of urine *Jasminum grandiflorum* were prescribed for leprosy, involved in treating baldness as hair oil. It has anticonvulsant, antiulcer,

anticancer, antioxidant and anti-inflammatory properties. This plant has higher angiotensin converting enzyme inhibition activity which was detected by in vitro enzymatic test [6,7]. The purified ACE inhibitor ranges between 26-66mM [5]. The plant sample of *Jasminum grandiflorum* & *Jasminum azoricum* species were collected from the forest near kerala. Leaves, stem, roots and flowers are kept in tropical botanical garden herbaricum. Before extraction, the sample should be dried properly; with the help of soxhlet apparatus the powdered sample (plant) were withdrawn by 2l of dichloromethane. The extraction was undergoes process to separate the components known as fractionation by vacuum chromatography. This was monitored by aid of thin layer chromatography to get suitable assay of angiotensin converting enzyme. Sixty, percent of enzyme were begins to remove the adsorbed substance by using ethyl acetate, dichloromethane at 1:1 ratio that can be fractionated in a medium pressure liquid chromatography with the gradient of dichloromethane in ether, methanol in ethyl acetate, R-O-R in C_6H_{14} and ethyl acetate in dichloromethane makes up to 25% of volume for 50 ml fraction size. By using dichloromethane and ethyl acetate mixture the forbidden material were rinsed off. The purification may done to remove with the use of methanol, toluene and dichloromethane in a ratio of 1:16:4 in a medium pressure liquid chromatography followed by silica in the addition of dichloromethane & methanol. Again in the ratio of 9:1 DCM, methanol was involved to elute on sephadex column. Finally we get angiotensin converting enzyme inhibitor from the fractions of eighteen milligram. Also, fractionating extract in the initial step, while isolating inhibitor some compounds were collected. Such as 1.1g of urolic acid that will settled down in initial stage. At the end of a purification isoquercitrin were obtained from *Jasminum grandiflorum* has pharmacological activities so it will be involved in preparations of medicines by acquired them in plants [8],[9],[10].

Osmium Sanctum

Osmium sanctum is otherwise called as Basil or Thulasi. It belongs to lamiaceae family of perennial aromatic plant. It has essential oil so that it may be applied in traditional medicine [11]. The leaves were collected, dried to make a powder that should be mixed with MeOH & kept in room temperature for 48 hours for extraction. By using rotary evaporator the extract was filtered, under the reduced pressure to evaporate. This step may be carried out thrice to get crude extract of methanol with the yield of 13.8 percentage. Then osmium sanctum extract (methanol) was remained in H_2O that will be fractioned by $C_4H_8O_2$ & $C_4H_{10}O$. To obtain ethyl acetate, $C_4H_{10}O$ the fractions allow to evaporate with the help of rotary evaporate all these fractions and the extract should be kept aside for further analysis. Chaudhary and his colleague made few modifications in ACEI assay which has already illustrated by Cushman & Cheung based on discharge of hippuric acid catalysed by angiotensin converting enzyme from hippuryl-histidyl-leucine. Fifty μ l of angiotensin converting enzyme was combined with sample solution should be incubated previously for ten minutes at $37^\circ C$ for half an hour. By adding one molar hydrochloric acid the reaction were wind up or get terminated, $C_4H_8O_2$ was added to that solution that will be placed in a centrifuge. The supernatant was then transferred into test tube and it will evaporate in room temperature. The absorbance was measured in UV spectrophotometer at 228 nm by adding DH_2O in 1ml of hippuric acid. Here catapril may be used as standard. Percentage of ACE inhibition was calculated by $(A-B)/(A-C) \times 100$. A refers to OD value with only angiotensin converting enzyme, B refers to presence of ACE & Inhibitors in OD, C refers to optical density alone. By this calculation we can able to calculate the percentage of inhibition [12,13].



Allium Sativum

Allium sativum refers to garlic also known as stinging rose of amaryllidaceae. The flavor from the plant is due to phytochemical present in it. It consists of H₂O, carbohydrate, protein, dietary fiber & less amount of fat [14]. It is one of the most vital aromatic plants. It acts against diseases like influenza, hypertension, cold and also for snake bite. It has antiageing, antimicrobial, anticancer, antifungal properties. The garlic skin were removed for homogenize in DH₂O which was purified and kept at 4°C for 20 h [15-17]. By filtrate them, it will form a precipitate than can be dissolved by demineralized water.



This process were done in column chromatography whereas deionized or demineralized h₂O may be used to elute impurities in column for that lowry's method is employed to estimate the protein content in a fractions. Some μ l of solution should be taken from the sample was mixed with angiotensin converting enzyme solution along with HHL solution in sodium chloride borate buffer to maintain ph upto 8.3. the solution must be kept in the incubator for one hour at 37°C, to that solution 0.5 normality of hydrochloric acid were added to terminate the reaction; then hippuric acid was separated. Finally the absorbance was measured in 228nm to estimate the activity of ACEI & calculated the percentage of inhibition by using formulas. In this study reveals that Allium sativum has a capacity to fight against hypertension which will reduce blood pressure in human due to the existence of dipeptides in garlic [18,19].

CONCLUSION

In this paper discussed about aromatic plants having the activity of angiotensin converting enzyme inhibition in Jasminum grandiflorum, Osmium sanctum & Allium sativum plants which can be used to treat hypertension and also aid in the growth of modern medicine.

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