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Alkaloid Based Chemical Constituents of *Ocimum santum* & Cinchona Bark: A Meta Analysis

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ABSTRACT

This article provides a concise summary of the recent developments that have been achieved in our comprehension of the asymmetric addition processes that are catalysed by native Cinchona alkaloids and their derivatives. This class of reactions includes cycloadditions, 1,4-adds, direct nucleophilic additions across carbon–oxygen or carbon–nitrogen double bonds, and direct nucleophilic additions across carbon–oxygen double bonds. Because of their capacity to catalyse the addition of a wide variety of functional groups to C9, many Cinchona alkaloids have been utilised in these processes as catalysts. These functional groups include amino, alkoxy, hydroxyl, amido, urea, and thiourea, among others. The importance of mechanical variables is emphasised in many different contexts. Additionally, the utilisation of adducts in future synthesis is sometimes broken down into its component steps. Ocimum basilicum was discovered to be mostly consisted of estragol (> 35.71 percent), (E)-ocimene (> 1.47 percent), trans-bergamotene (> 0.83 percent), a-cadinol (> 0.41 percent), eucalyptol (> 0.25 percent), and -caryophyllene (> 0.07 percent), whereas Ocimum sanctum is primarily composed of eucaly There is a greater concentration of chemical components in the leaves of Ocimum basilicum and Ocimum sanctum than there is in the actual inflorescence or flowers of the plant. The genetic distance between the two species was analysed in order to better understand the interspecies relationship, and the results showed that it was 2.86. The small difference in genetic makeup that exists between Ocimum basilicum and Ocimum sanctum is evidence that these two species are related to one another and share similar traits.

Keywords- *Ocimum sanctum,* Cinchona, Alkaloid, Herbal Plant.

I. INTRODUCTION

Since the beginning of time, people have been scouring the natural environment in search of cures and treatments for their various ailments. In the past, humans, like other animals, relied on their intrinsic awareness of the therapeutic virtues that plants offered. Because there was not enough knowledge accessible at the time, everything was dependent on experience because it was not possible to pinpoint the causes of the illnesses or the exact plant and how it could be used as a cure. It took some time, but eventually it was discovered

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why certain medicinal plants were used to treat certain disorders. As a consequence, the usage of medicinal plants progressively transitioned from a framework that was based on empirical evidence to one that was founded on explanatory facts. Medicinal and preventative treatments were traditionally drawn from plants up until the development of iatrochemistry in the 16th century. However, the decreasing efficacy and increasing contraindications of synthetic medications make the usage of natural drugs an issue that is once again in the spotlight. People have relied on natural products, particularly those that are derived from plants, to keep themselves healthy ever since the earliest days of recorded medical history. Due to the fact that it has been around for such a long time, traditional medicine has been extensively accepted and utilised by people throughout the ages. Since ancient times, there is a wealth of evidence supporting the use of plants for medical purposes. Medicines derived from plants have been the subject of research for decades due to the positive effects they have on human health and the low risk of adverse consequences they present. Plants that have a long history of use in ethnomedicine can be a rich source of chemicals for the treatment of a variety of illnesses and infectious diseases when it comes to the pharmaceutical business. These plants have been used to cure a wide range of conditions. It is believed that medicinal plants retain bioactive compounds that can have a broad variety of impacts on patients seeking treatment. Medicinal plants are associated with a wide variety of therapeutic effects, some of which include anti-inflammatory, antiviral, anticancer, antimalarial, and analgesic actions. It is believed that between 350,000 and practically half a million different species of vascular plants are used for medicinal purposes. This number represents approximately 10% of all vascular plant species. Since the beginning of human history, people have looked to plants for healing, and this practise is still common today. In the beginning, humans relied on the method of trial and error to discover useful plants that had positive advantages, such as healing ailments or simply making them feel better. Traditional medicine is the practise of employing several plants in a certain method that has been perfected over a long period of time by many generations of people. According to the definition provided by the World Health Organization, traditional medicine is "the totality of knowledge, skills, and practises based on the theories, beliefs, and experiences indigenous to different cultures, whether explicable or not, used in the maintenance of health, as well as the prevention, diagnosis, improvement, or treatment of physical and mental illnesses." Traditional medicine can be defined as "the totality of knowledge, skills, and practises based on the theories, beliefs, and experiences indigenous to different cultures, whether explicable or not."

Throughout the history of humanity, every society has created a form of medicine that is mostly derived from the local flora. Some authors even go so far as to claim that the custom of passing on information is what ultimately led to the development of the contemporary medical and pharmaceutical businesses. There are literally hundreds of higher plants that are still produced for the purpose of harvesting them for their medicinal and pharmacological qualities. Phytomedicines are the terms used to refer to medicines that are generated from plants that have medicinal properties.

Despite extensive familiarity with the curative benefits that medicinal plants had on the human body and the ways in which they were administered, it wasn't until the 18th century that researchers eventually isolated the active component that gave many medicinal herbs their therapeutic powers. One such example is Avicenna's (Ibn Sina) Canon of Medicine, which was widely utilised by physicians and scientists in the Islamic world all the way up until the early 18th century.

The development of modern science, in particular chemical analysis, and the accompanying instrumentation, such as the microscope, made it possible to separate the components of medicinal plants that were actually responsible for their therapeutic effects. This wasn't possible before the Renaissance. Since then, these biologically active components of medicines have been manufactured in laboratories via synthetic processes. The range of applications that medicine might address gradually expanded over time. It would appear that the use of medicinal plants in their natural state has been phased out in the era of modern medicine. The pharmaceutical business is the backbone of modern medicine. This industry develops new medications mostly based on the bioactive components of plants and, as a result, uses plants as their primary source of raw materials. However, many parts of the developing world are still unable to afford access to this contemporary medicine that is generated from synthetic compounds. As a result, many portions of the world continue to rely on ancient traditions that entail the direct use of medicinal plants.

II. MATERIAL & METHODS

Performs comprehensive searches of many databases, including PUBMED, SCI, and SCOPUS online. herbal medicine, herbs high in alkaloids Ocimum & Cinchona.

To create the Cinchona skeleton, an aliphatic quinuclidine ring and an aromatic quinoline ring are connected to one another by means of two single carbon–carbon bonds. The molecule as a whole contains a total of five stereocenters. There are pairs of cinchona alkaloids, each of which has a significant structural difference at the C8, C9, and N1 locations. Because of their potential to catalyse the creation of enantiomeric compounds, the eight primary Cinchona alkaloids that are displayed in Figure 1 are diastereomers, also known

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as pseudoenantiomers. The structural features of Cinchona alkaloids and their derivatives that are responsible for their catalytic activity in terms of yields and diastereoselectivity and enantioselectivity of products were highlighted in an earlier article that we had written as a review. 4 The bifunctional catalytic efficacy of Cinchona molecules has been proven by a number of separate research. When compared to the nitrogen found in quinoline, the nitrogen found in the quinuclidine ring's tertiary position makes it 103 times more basic. In this manner, the fundamental nature of the catalyst may be tracked back to the tertiary nitrogen content of the catalyst. Activating the electrophile is accomplished through the presence of hydrogen bonding groups, such as those found in hydroxyl, urea, and thiourea at the carbon 9 position. Because of the "chiral pocket" that is generated around the reactive site as a result of the relative orientation of the quinoline and quinuclidine rings, enantioselective product synthesis can be accomplished.

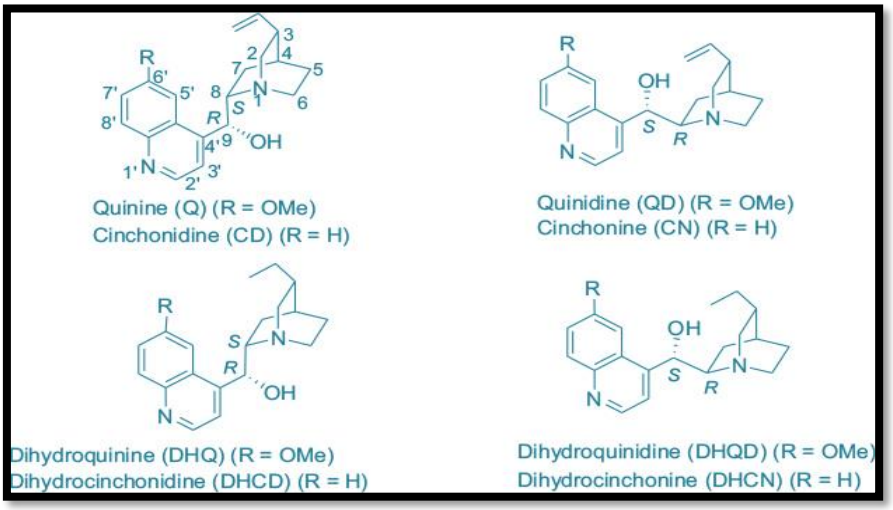

Fig. 1: Structure of 8 major Cinchona alkaloids

Alkaloids carrying out the purposes for anti-malarial action of Cinchona

Cinchona bark was the original source of the antimalarial drug quinine, which was originally isolated as an alkaloid. The medication is still highly effective despite the fact that it is being used to treat malaria that is resistant to many drugs. During the 1940s, a synthetic quinine derivative known as chloroquine was discovered. Chloroquine is a 4-aminoquinoline. Because of its effectiveness, low cost, and minimal toxicity, it was the drug of choice for treating malaria for a number of decades. On the other hand, as a result of parasite resistance, its application in modern treatment for malaria has been restricted. Mefloquine was created as a treatment for chloroquine-resistant malaria; however, despite its structural similarities to quinine, its use is limited because of resistance to the drug as well as severe effects on neuropsychiatric functioning. The Artemisia annua plant, often known as sweet warm wood, is the source of artemisinin, a natural endoperoxide that is derived from the plant. Artemisinin and its semi-synthetic equivalents, artemether, artether, and artesunate, are the antimalarial drugs that clinicians turn to when previous treatments have not been successful. The World Health Organization recommends treating patients with artemisinin analogues in combination with other treatments in order to slow the emergence of drug-resistant forms of malaria (ACT). There have been reports of instances in which parasites have developed resistance to the ACT.

In view of the fact that malaria parasites have developed resistant to many of the treatment regimens that are now in use, there has been an urgent need to discover innovative antimalarial chemotherapeutic medicines derived from natural sources, particularly medicinal plants. Quinine and artemisinin, two of the most powerful antimalarial lead compounds, were first extracted from plants, which explains why traditional medicine relied so heavily on them to cure malaria. Both quinine and artemisinin are still used today. The antimalarial activity of plants is due to the presence of phytoconstituents such alkaloids, terpenes, steroids, and flavonoids in the plant. Alkaloids are widely acknowledged as a significant class of chemicals due to the extensive range of biological roles that they perform. They are formed from amino acids and constitute a sizable collection of structurally distinct molecules that have nitrogen incorporated into a heterocyclic ring. Amino acids are the source of their creation.

Toxicity of quinine

Documentation is provided regarding the toxic effects of quinine in humans, and concerns regarding the management of quinine overdoses are brought to light. Patients have reported unpleasant reactions after eating quinine in tonic water, despite the fact that it is available

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therapeutically as sulphate or hydrochloride salts. These reactions occurred despite the fact that quinine is readily available. It is also utilised as an adulterant in heroin sold on the "street," which increases the risk of users accidentally overdosing on the drug. From what I understand, this is a problem that exists in the United States. Quinine is toxic to a wide variety of bacteria, yeasts, and trypanosomes, in addition to the plasmodia that are responsible for the disease malaria. Quinine possesses both local anaesthetic and irritant effects in equal measure. When it is utilised in therapeutic settings, the irritation that it causes may be a contributing factor in the feeling of sickness that patients have. In addition to that, it has a moderating influence on the temperature. Cinchonism is a term that is commonly used to describe a group of conditions that share specific characteristics. These conditions include acute quinine poisoning and quinine accumulation after treatment for malaria. A headache, gastrointestinal distress, vasodilation, increased perspiration, and otologic symptoms are all related with plasma quinine concentrations that are somewhat high. When these levels reach dangerously high levels, symptoms can start to appear in the cardiovascular system as well as the brain system. If you take far more than the recommended amount, you run the risk of experiencing severe nausea, as well as vomiting, abdominal discomfort, and diarrhoea. These symptoms are caused by a combination of the central effects that quinine has on the chemoreceptor trigger zone and the local irritating effects that quinine has on the gut. Tinnitus, increased sweating, and vasodilation are some of the most common symptoms. It is common for blindness to go undiagnosed for at least a day following the initial appearance of visual symptoms. Patients who are sensitive to aspirin have been shown to experience pseudo-allergic reactions to quinine, and similar reaction may also take place in people who are sensitive to other drugs. The consumption of quinine has been associated to the development of drug-induced thrombocytopenia and purpura. Plasmodium falciparum malaria is known to have a number of adverse effects, including renal failure, acute intravascular hemolysis, and anaemia. It appears that the widespread assumption that quinine can cause an abortion is not supported by the findings of scientific studies.

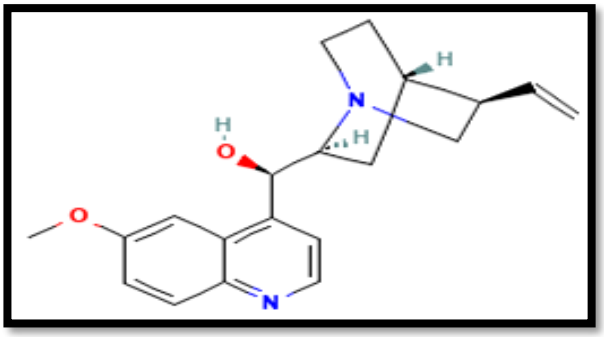

Fig. 2: Structure of Quinine

Cinchonine

The emergence of resistance to many drugs is one of the primary factors contributing to the ineffectiveness of chemotherapy in the treatment of diseases like gynaecological cancers (MDR). In rare instances, it has been demonstrated that hydrocinchonine, along with its equivalents quinidine and cinchonine, can reverse the effects of multidrug resistance. However, this effect has not been reported in uterine sarcoma cells. In the current study, our objective was to evaluate and contrast the efficacy of hydrocinchonine, quinidine, and cinchonine as MDR-reversing medicines for use in combination therapy with the anticancer agent paclitaxel (TAX). According to the results of the 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) assay, hydrocinchonine, cinchonine, and quinidine significantly increased the cytotoxicity of TAX in P-glycoprotein (gp)-positive MES-SA/DX5 cells. However, this effect was not observed in P-glycoprotein-negative MES-SA The rhodamine test demonstrated that the accumulation of the P-gp substrate rhodamine was much higher in TAX-treated MES-SA/DX5 cells compared to TAX-treated control cells. This was the case when comparing the two groups of cells. In addition, hydrocinchonine, cinchonine, and quinidine were effective at cleaving poly (ADP-ribose) polymerase (PARP), activating caspase-3, downregulating P-gp expression, and elevating the sub-G1 apoptotic fraction in MES-SA/DX5 cells that had been treated with TAX.

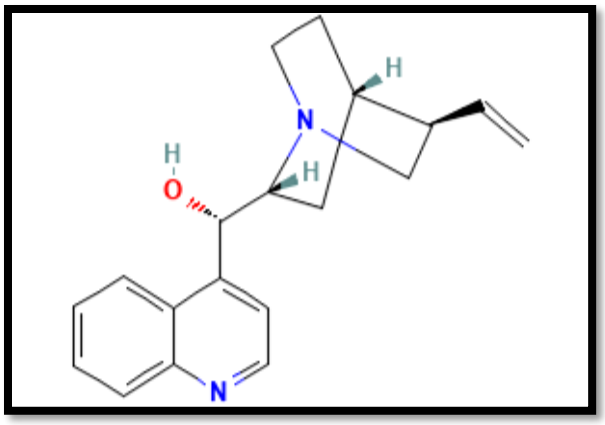

Fig. 3: Structure of Cinchonine

Quinidine

Quinidine, an alkaloid with antimalarial and class 1A antiarrhythmic effects, comes from the Cinchona tree. Quinidine comes from the Cinchona tree. The neuronal membrane is stabilised by quinidine, which works by binding to voltage-gated sodium channels and preventing those channels from letting sodium ions in. As a result, the threshold for excitation is raised, and there is less depolarization during phase 0 of the action potential. An increase in the effective refractory period (ERP), action potential duration

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(APD), and ERP/APD ratios are likewise the results of a slower conduction of nerve impulses. Because of its contact with the heme polymer (hemazoin) in the acidic feeding vacuole of the parasite, quinidine is able to inhibit further polymerization caused by the heme polymerase enzyme. This is how quinidine performs its antimalarial effect. This results in the parasite succumbing to an excessive amount of the toxic heme.

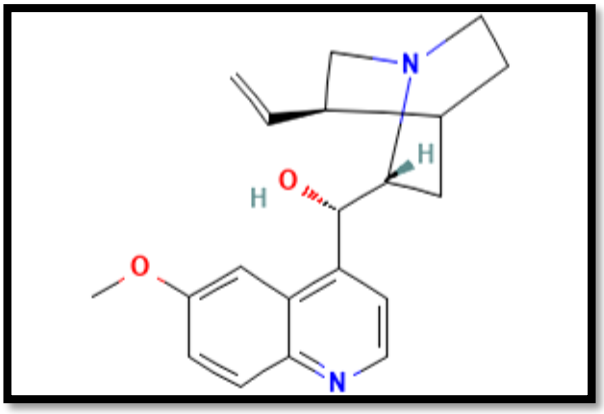

Fig. 4: Structure of Quinidine

Ocimum sanctum

O. basilicum and O. sanctum that were grown in Malaysia were subjected to chemical analysis so that their constituent parts could be determined. In order to determine the chemical components shared by both species, a GC-MS analysis and a Kovats index verification were carried out. The information obtained from the Kovats index retention index system is utilised extensively in the process of identifying chemical compounds through the use of gas chromatography. In order to get rid of the chemical components, we employed hydrodistillation, HS-SPME, and solvent extraction utilising methanol and dichloromethane as our solvents. Research was conducted on the plant's chemical components, and major substances that were found in the leaves, flowers, and inflorescence were isolated and identified. The many different chemical components of O. basilicum that has been cultivated in Malaysia are detailed in Table 1. It has been determined that O. basilicum contains a total of 47 distinct chemical compounds. The percentage of leaf extract obtained through hydrodistillation was 0.10 percent (v/w), whereas that obtained through dichloromethane extraction was 0.13 percent (w/w), and that obtained through methanol extraction was 0.83 percent (w/w), respectively. The volatiles of O. basilicum leaves were analysed using HS-SPME, and the results showed that the most prevalent compounds were estragole (59.67 percent), eucalyptol (9.02 percent), trans α bergamotene (8.60 percent), and β -caryophyllene (2.65 percent). Camphor made up 2.65 percent of the volatiles (1.62 percent). After undergoing hydrodistillation, the leaves of O. basilicum produced mainly estragole (35.71 percent), eucalyptol (13.26 percent), (E) β-ocimene (7.99 percent), trans-α bergaptene (5.72 percent), and β -cadinol (5.71 percent). After the leaves of O. basilicum were extracted in methanol, the compounds with the highest concentrations were found to be estragole (82.69 percent), (Z) β -ocimene (1.26 percent), trans β -bergamotene (0.83%), and eugenol methyl ether (0.83%). (0.40 percent). From a dichloromethane extract of O. basilicum leaves, estragol (at a concentration of 73.16 percent), eucalyptol (at a concentration of 6.17 percent), trans-bergamotene (at a concentration of 5.26 percent), (E) β -ocimene (at a concentration of 4.52 percent), and γ -cadinol (at a concentration of 2.56 percent) were isolated. Because there was not enough material of flowers and inflorescence to hydrodistill, we were forced to stick with just one plant for the entirety of the study. This allowed us to eliminate potential confounding factors, such as growing conditions and the availability of nutrients, which could have an effect on the chemical composition of the plant. Extractions of O. basilicum flowers were performed using dichloromethane extraction, methanol extraction, and high-speed solid-phase microextraction (HS-SPME). The yield of floral extracts obtained using dichloromethane and methanol extractions, respectively, was 0.05 percent (w/w) and 0.34 percent (w/w), respectively. When we extracted the compound with dichloromethane, we were able to separate 98.8 percent estragole and 1.1 percent (Z) β -farnesene. When we extracted the compound with methanol, we were able to isolate 99.2 percent estragole and 0.7 percent (Z) β -farnesene. The HS-SPME study discovered a number of important compounds, the most prominent of which were estragole (88.18 percent), trans β -bergamotene (2.82 percent), (E) β-ocimene (1.47 percent), eugenol methyl ether (0.72 percent), and -bulnesene (0.82 percent). (0.51 percent). With the help of HS-SPME, we were able to determine that the O. sanctum leaves contain the following compounds in the highest concentrations: eugenol methyl ether (34.34 percent), caryophyllene (22.15 percent), germacrene D (11.54 percent), α -elemene (9.16 percent), and copaene (4.62 percent). The hydrodistillation of O. sanctum leaves reveals a profile that is predominately composed of eugenol methyl ether (39.90 percent), caryophyllene (27.51 percent), germacrene D (9.62 percent), α -elemene (4.59 percent), and copaene (4.22 percent), with only a small variation in percentage between each of these components. The most abundant compounds in the extracts of O. sanctum leaves were eugenol methyl ether (57.46 percent), caryophyllene (18.02 percent), germacrene D (5.58 percent), α -elemene (5.26 percent), and copaene (1.80 percent). These were followed by germacrene D (5.58 percent), germacrene A (5.26 percent), and germacrene A (5.58 percent). Dichloromethane extraction of O. sanctum flowers resulted in a weight-percentage yield of 4.28 percent (w/w), while methanol extraction resulted in a yield of

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9.04 percent (w/w), respectively. The methanol extract of O. sanctum flowers contained 74.51 percent eugenol methyl ether, 13.76 percent caryophyllene, 9.34 percent germacrene D, and 2.39 percent copaene, whereas the dichloromethane extract contained 62.94 percent eugenol methyl ether, 13.35 percent caryophyllene, 8.29 percent germacrene D, and α -elemene (4.22 percent). An HS-SPME analysis of O. sanctum flowers indicated that the components with the highest concentrations were eugenol methyl ether (62.44 percent), germacrene D (12.73 percent), caryophyllene (11.09 percent), and α -elemene (6.61 percent). The least prevalent were copaene (1.49 percent) and α -elemene. The amount of inflorescence extract that could be harvested from dichloromethane and methanol extractions was 11.76 and 2.23 percent (w/w), respectively. An O. sanctum inflorescence methanolic extract was used to isolate eugenol methyl ether (59.84 percent), germacrene D (11.01 percent), caryophyllene (97.7 percent), a-elemene (5.28 percent), and b-cubebene (3.67 percent), while an O. sanctum inflorescence HS-SPME analysis found eugenol methyl ether (63.96 percent Both the O. basilicum and the O. sanctum strains were found to contain significant amounts of phenylpropene and terpenes. The primary constituent found in O. basilicum is estragole, whereas the primary constituent found in O. sanctum is eugenol methyl ether. The inflorescence and the flowers of O. basilicum have the lowest concentration of chemical components compared to the leaves, which have the maximum concentration. Estragole is the major chemical component that may be found in each of the three parts of the plant. Even though eugenol methyl ether may be detected in all three plant parts, the inflorescence and flowers of O. sanctum have a lesser concentration of the chemical components than the leaves do. The leaves have the highest concentration of chemical components. The current study demonstrates that hydrodistillation and HS-SPME were both capable of extracting new chemical components that were already known. The solubility of the chemical components is affected by the polarity of the solvent that is employed in the various extraction methods. This provides an explanation for the observed pattern. In the process of solvent extraction, polar solvents such as dichloromethane and methanol are utilised. On the other hand, the non-polar solvent PDMS is utilised in the process of HS-SPME, and water is utilised in the process of hydrodistillation. It is commonly believed that the extraction of lipophilic phenols is acceptable for the least polar solvents unless exceptionally high pressure is applied. On the other hand, it is commonly believed that the extraction of polyphenols is good for the polar solvents.

III. CONCLUSION

The use of catalysts produced from the cinchona alkaloid, which displays both diastereo and enantio selectivity, is greatly sought after. The advancement of stereoselective synthesis techniques owes a great deal to this category of catalysts. New catalysts that are tuned for specific reactions, such as the aldol addition, Mannich addition, Strecker reaction, and Michael additions/cyclization, have been devised and developed. The C6′ and C9 locations of the Cinchona alkaloids are typically modified to create these catalysts. Amine, urea, thiourea, alkoxy, hydroxyl, and amide groups are frequently found in these places. A number of dimeric Cinchona-alkaloid catalysts have also been used in a variety of synthesis procedures. Cinchona alkaloid-based catalysts containing NH_2, OH, and alkoxy groups at the C9 position are the primary active sites for these reactions.

The most typical strategy for these reactions is enamine catalysis by a C9 Cinchona-based amine. Using these catalysts in the Mannich and Strecker reactions of imines with nitroalkanes, -nitro esters, oxazolinones, butenolides, and -aryl isocyanoacetates has resulted in the production of the appropriate adducts with excellent yields and excellent enantioselectivities. Oils such as eugenol methyl ether, caryophyllene, germacrene D, β-elemene, and copaene are abundant in Malaysian-grown O. basilicum and O. sanctum, respectively. Eye pl (Chemical components from these two species can be extracted in greater quantities using HS-SPME and water distillation than with solvent extraction. As the solubility of chemical constituents in various extraction procedures is impacted by the polarity of solvent used, the chemical constituents extracted are largely dependent on the extraction methods. The process of solvent extraction is straight forward and uncomplicated.

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