Review

Plectranthus amboinicus (Lour.) Spreng: Botanical, Phytochemical, Pharmacological and Nutritional Significance

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Abstract: Plectranthus amboinicus (Lour.) Spreng. is a perennial herb belonging to the family Lamiaceae which occurs naturally throughout the tropics and warm regions of Africa, Asia and Australia. This herb has therapeutic and nutritional properties attributed to its natural phytochemical compounds which are highly valued in the pharmaceutical industry. Besides, it has horticultural properties due to its aromatic nature and essential oil producing capability. It is widely used in folk medicine to treat conditions like cold, asthma, constipation, headache, cough, fever and skin diseases. The leaves of the plant are often eaten raw or used as flavoring agents, or incorporated as ingredients in the preparation of traditional food. The literature survey revealed the occurrence 76 volatiles and 30 non-volatile compounds belonging to different classes of phytochemicals such as monoterpenoids, diterpenoids, triterpenoids, sesquiterpenoids, phenolics, flavonoids, esters, alcohols and aldehydes. Studies have cited numerous pharmacological properties including antimicrobial, antiinflammatory, antitumor, wound healing, anti-epileptic, larvicidal, antioxidant and analgesic activities. Also, it has been found to be effective against respiratory, cardiovascular, oral, skin, digestive and urinary diseases. Yet, scientific validation of many other traditional uses would be appreciated, mainly to discover and authenticate novel bioactive compounds from this herb. This review article provides comprehensive information on the botany, phytochemistry, pharmacology and nutritional importance of P. amboinicus essential oil and its various solvent extracts. This article allows researchers to further explore the further potential of this multi-utility herb for various biomedical applications.

Keywords: Plectranthus amboinicus; Indian borage; pharmacology; biological activities; nutrition; phytochemistry; botany; medicinal plant

1. Introduction

At present, plant-based medicines are widely employed in various public health practices throughout the globe as they are safe and cost-effective, and efficiently combat various deadly diseases and help in maintaining good health [1]. Herbal medicines are very commonly used in Unani, Ayurveda, Sidda, folk and other traditional practices of healthcare management [2]. According to the estimation by the World Health Organization, about 80% of people on the globe are still dependent on traditional herb-based medications due to their low cost, easy accessibility and likely negligible side effects in comparison to allopathic medicines [2–4]. Certainly, many of the leading active drug molecules of plants and their derivatives used presently in allopathic medicine are mainly due to the understanding of traditional medical practices for curing diseases [2]. Modern drug discovery research is governed by natural plant-based compounds and their products, followed by synthetic chemical
drugs. Currently, natural products are considered as a major source of medicaments and, hence, they are extensively used by pharmaceutical industries. This has led towards increased global demand for medicinal plants in the modern era of natural medicine, leading to exploration and exploitation of new plant sources for their medicinal properties [3,5,6]. The Lamiaceae members of plant species belonging to commercially important genera, such as *Plectranthus*, *Salvia*, *Ocimum* and *Mentha*, are attributed with a rich diversity of ethnobotanical benefits. More than 300 species of *Plectranthus* are reported all over the tropical and warm regions of the old world, including Asia, Africa and Australia [7]. In over 85% of the literature, documentation of *Plectranthus* is on the therapeutic values of this genus followed by its nutritional and horticultural properties attributed to its aromatic nature and essential oil producing capability [8,9]. *Plectranthus amboinicus* (Loureiro) Sprengel is one of the most documented species in the family Lamiaceae. *P. amboinicus*, also commonly known as Indian borage, and is a fleshy, succulent herb famous for its distinct oregano-like flavor and odor. It is one of the most cited species in the Lamiaceae family, especially for its medicinal properties, accounting for 68% of all customary applications of this genus [10]. This herb is widely used by indigenous people of tropical rain forests, either in folk medicine or for culinary purposes. This is mainly due to its natural production of an essential oil with high amounts of bioactive compounds such as Carvacrol [11], Thymol [12] β-Caryophyllene, α-Humulene, γ-Terpine, p-Cymene, α-Terpineal and β-Selinene, identified in the oil component of its leaves [13,14]. These biochemical components exhibit various biological properties [15,16] and are widely used in folk medicine to treat conditions like cold, asthma, constipation, headache, cough, fever and skin diseases. The leaves of the plant are often eaten raw or used as flavoring agents, or incorporated as ingredients in the preparation of traditional food. The chopped leaves are also used as a substitute for sage (*Salvia officinalis*) in meat stuffing [17]. With this background, the present review was undertaken to present complete facts on the multifarious medical benefits of *P. amboinicus*. This review is a compiled survey of information on various aspects of *P. amboinicus* including botany, distribution, wild relatives, phytochemistry, medicinal and nutritional properties and other benefits. The available information was retrieved from many search engines including ScienceDirect, Google Scholar, PubMed, Scopus and SciFinder etc.

2. Botanical Description

2.1. Taxonomy

*P. amboinicus* (Loureiro) Sprengel is a member of the family, Lamiaceae. The paleotropical oil-rich genus, *Plectranthus* belongs to the subfamily Nepetoideae. It comprises about 300 species of annual or perennial herbs or subshrubs which are often succulents [18]. Many species of *Plectranthus* have economical and medicinal values. Among them, *P. amboinicus* is one of the most important aromatic medicinal succulent plants that possess distinctive smelling leaves with short soft erect hairs.

2.2. Morphological Features

*P. amboinicus* is a succulent shrub with a tendency for climbing or creeping. It can reach over 1 m in height and even more in width in the wild [18–20]. This sprawling large succulent herb is fleshy and highly aromatic. The fleshy stems grow about 30–90 cm, either with long rigid hairs (hispidly villous), or tomentose (densely covered with soft, short and erect hairs, pubescent) [18,19]. Leaves are undivided (simple), broadly ovate to suborbicular with a tapering tip (ovate) and very thick; they are pubescent (thickly studded with hairs), with the lower surface possessing the most numerous glandular hairs, giving a frosted appearance [20]. The taste of this leaf is pleasantly aromatic with an agreeable and refreshing odor. Flowers are on a short stem (shortly pedicelled), pale purplish in dense whorls at distant intervals in a long slender raceme. Flowers have a bell shaped calyx and the throat is smooth inside with two lips, the upper lip being ovate and thin, the lower lip having four narrow teeth. The corolla is pale purplish and five times longer than the calyx, with a short tube, inflated...
throat and short lips [19,20]. Fruit nutlets are smooth, pale brown in color, 0.7 mm long and 0.5 mm wide. *P. amboinicus* rarely flowers and seeds are difficult to collect [19].

### 2.3. Origin, Wild Relatives and Geographical Distribution

The name *Plectranthus* derives from the Greek words “plectron”, meaning spur, and “Anthos”, meaning flower, in reference to the spur-shaped flowers of some members of the genus [21]. Due to lack of precise morphological features to distinguish species within the genus *Plectranthus* and its closely associated genera, numerous taxonomic problems with the naming of species have resulted in misplacement of species in some closely linked genera such as *Coleus*, *Solenostemon* and *Englerastrum* [10]. The species *P. amboinicus* was originally classified under the genus *Coleus* but was moved to the *Plectranthus* genus, although both names are sometimes seen in the literature today. This species also has the greatest number of synonyms (Table 1). The synonyms of *P. amboinicus* include *P. aromaticus* Roxb., *Coleus aromaticus* Benth. and *C. amboinicus* Lour. [10]. *P. amboinicus* is of unknown origin, but is possibly from Africa and India [18], and it has since been distributed and cultivated pantropically. The type specimen of the species was collected in Amboina, Moluccas, resulting in its species name *amboinicus* [22]. Taxonomic revisions of *Plectranthus* have taken place on a regional rather than international basis and thus have contributed to a misunderstanding of the same species [10]. The traditional uses around the world are represented in Table 1.

**Table 1.** Vernacular names and traditional uses of *Plectranthus amboinicus* commonly used by locals in their respective countries.

| Country   | Vernacular Names                                      | Traditional Uses          |
|-----------|-------------------------------------------------------|----------------------------|
| Barbados  | Poor man’s pork, Broad leaf thyme                     | Folk medicine, Culinary   |
| Cambodia  | Sak dam ray                                           | Folk medicine, Culinary   |
| China     | Da shou xiang                                         | Folk medicine, Home garden|
| Cuba      | orégano; orégano de Cartagena                        | Folk medicine, Culinary   |
| Fiji      | Rhaivoki, Sage                                        | Folk medicine, Culinary   |
| Germany   | Jamaika thymian                                       | Folk medicine, Culinary   |
| Guyana    | Thick leaf thyme, broad leaf thyme                    | Folk medicine, Culinary   |
| India     | Indian Borage, Pashan Bhedi, Karpooravalli, Patharchur| Folk medicine, Culinary, Home garden |
| Indonesia | Torbangun, Daun Kutjing                               | Folk medicine, Culinary, Home garden |
| Malaysia  | Daun bangun-bangun, Pokok bangun-bangun               | Folk medicine, Culinary, Home garden |
| Philippines | Latai, Suganda, Oregano                             | Folk medicine, Culinary, Home garden |
| Puerto Rico | Puerto Rican oregano brujo, Cuban oregano          | Folk medicine, Culinary   |
| South Africa | Sup mint, French thyme, Indian mint                | Folk medicine, Culinary, Home garden |
| Thailand  | Hom duan huu suea, Niam huu suea                     | Folk medicine, Culinary   |
| USA       | Indian Borage, Country borage, Spanish thyme, Mexican mint, French thyme, Indian mint | Culinary, Home garden |
| Vietnam   | Can day la                                           | Folk medicine, Culinary   |
| West Indies | French thyme, Spanish thyme, Broad-leaf thyme     | Folk medicine, Culinary   |

### 2.4. Cultivation

*P. amboinicus* is a fast-growing plant usually propagated by stem cuttings. This preferred propagation through vegetative means is because it rarely seeds or sets seed [23]. The herb grows easily in a well-drained, semi-shaded location. It is found to grow well under tropical and subtropical locations. It was also found to adapt well in cooler climates if grown in a pot and brought indoors, or moved to a warm, sheltered position during winter [19]. The plant should be watered only sparingly. *P. amboinicus* grows best in rich, compost soil with neutral pH and high humidity, but if there is excess
water in the ground its roots might start to rot. On the other hand, it copes well with severe droughts, as it has lots of water stored in its succulent flesh. It also survives well with severe heat and scorching sun, as well as strong shade, but grows best under partial shade. For all those reasons, it is very easy to grow indoors and that is why it is becoming more and more popular as a house plant in northern Europe. *P. amboinicus* cannot withstand temperatures lower than 0 °C and is stressed even when it is colder than 10 °C. In general, very meager information is available on the methods/practices used for commercial cultivation and harvesting of this herb.

3. Phytochemistry

A large and growing body of literature has investigated the chemical composition and pharmacological properties of *P. amboinicus*. The literature survey has emphasized the occurrence of different classes of phytocompounds including 76 volatiles and 30 non-volatile compounds. More recently, interest among phytochemists and biologists has focused on the isolation of specific bioactive compounds of *P. amboinicus* and comprehending their pharmacological importance. However, the chemical profile and the accumulation pattern of bioactive constituents in different parts of the plant and their essential oil content varies depending on various parameters, such as geographical features, climate and different stages of plant material collection [2]. Moreover, the method of extraction and identification can also lead to variations in phytochemical composition. Presently, only a few reports have stated the isolation and authentication of individual compounds of *P. amboinicus*. Therefore, correct identification, isolation and quantification of phytocompounds is very much necessary in order to understand their pharmacological and biological significance. *P. amboinicus* is reported to contain several classes of phytochemicals including monoterepenoids, diterpenoids, triterpenoids, sesquiterpenoids, phenolics, flavonoids and esters. The details of these bioactive constituents are discussed in this section.

3.1. Volatile Composition of *P. amboinicus*

The essential oil obtained from the leaves and stem explants was shown to contain a total of 76 volatile constituents. The essential oil contained a copious quantity of the two major phenolic compounds, namely, carvacrol and thymol, which are pharmaceutically appreciated for various culinary properties. The quality as well as quantity of chemical compounds occurring in the essential oil is directly related to its biological functions. *P. amboinicus* oil is rich in oxygenated monoterpenes, monoterpenic hydrocarbons, sesquiterpene hydrocarbons and oxygenated sesquiterpenes [10]. The leaf essential oil of *P. amboinicus* is particularly rich in phenolic monoterpenes such as Thymol and Carvacrol, which are speculated to exert various pharmacological properties [10,17,20,24]. Table 2 represents the details of these volatile compounds, while Figure 1 depicts the structural details of some of these major compounds.

A hydro distillation method using a Clevenger type apparatus for 3–4 h is commonly employed for extracting *P. amboinicus* essential oil. However, volatile constituents of *P. amboinicus* leaf obtained by using hexane extraction, steam distillation and supercritical CO₂ extraction methods were shown to have a chemical difference [25]. The hexane extraction method produced the highest oil yield (6.52%) compared to steam distillation (0.55%) and supercritical CO₂ extraction methods (1.40%). It was also noticed that there was a difference in aroma of the extracts which was attributed to qualitative and quantitative dissimilarity in chemical composition. In another study, a solid phase micro extraction (SPME) method showed the presence of eucalyptol in *P. amboinicus* leaves [17,26]. The volatile constituents of *P. amboinicus* leaves collected from Uganda were extracted with head space solid phase microextraction (HS-SPME) and their analysis using the gas chromatography–mass spectroscopy (GC-MS) electron impact ionization method revealed the presence of Linanol (50.3%) as the major component [27,28]. The other volatiles observed were Carvacrol (10.3%), Geranyl acetate (11.75), Nerol acetate (11.6%), γ-Terpinene (3.2%), p-Cymene (2.9%), Nerol (2.3%), α-4-Carene (1.3%), Caryophyllene (1.2%) and β-Myrcene (0.8%).
## Table 2. The known volatile constituents of *P. amboinicus.*

| Compound Name          | Formula | Plant Origin/Part                                      | Method          | References               |
|------------------------|---------|-------------------------------------------------------|-----------------|--------------------------|
| **Monoterpe hydrocarbons** |         |                                                       |                 |                          |
| 2,3-Carene            | C₁₀H₁₄  | India, Malaysia, Morocco, Mauritius/Leaf              | GC-MS           | [20,22]                  |
| α-Cymene              | C₁₀H₁₄  | Brazil, India, Cambodia, Malaysia, Venezuela/Aerial parts, Leaf | GC-MS           | [12–14,29,32–38]        |
| Limonene              | C₁₀H₁₄  | India, Mauritius/Leaf                                  | GC-MS           | [29,30]                  |
| β-Methylene            | C₁₀H₁₄  | Cambodia, India, Venezuela /Leaf                      | GC-MS           | [13,25,29,36,38]        |
| Oxime                 | C₁₀H₁₄  | Morocco /Leaf                                          | GC-MS           | [29,31]                  |
| α-Phellandrene         | C₁₀H₁₄  | India, Comoros, Mauritius, Venezuela/Leaf             | GC-MS           | [29,31,38]               |
| β-Phellandrene         | C₁₀H₁₄  | India/Leaf                                             | GC-MS           | [14,35]                  |
| α-Pinene              | C₁₀H₁₄  | India, Cambodian /Leaf                                 | GC-MS           | [29,36]                  |
| β-Pinene              | C₁₀H₁₄  | India/Leaf                                             | GC-MS           | [29]                     |
| Sabinene              | C₁₀H₁₄  | Cambodia, India, Morocco /Leaf                         | GC-MS           | [29,31,38]               |
| α-Terpineene          | C₁₀H₁₄  | India, Mauritius/Leaf                                  | GC-MS           | [14,25,30,34,35,39]     |
| γ-Terpineene          | C₁₀H₁₄  | Brazil, Cambodia, Malaysia, Mauritius, India, /Leaf   | GC-MS           | [13,14,29,30,32,34–37]  |
| α-Terpinolene         | C₁₀H₁₄  | Morocco, Brazil /Leaf                                  | GC-MS           | [37,39]                  |
| α-Terpinylol           | C₁₀H₁₄  | Cambodia, India, Venezuela /Leaf                      | GC-MS           | [14,29,31,35,38]        |
| Menthol               | C₁₀H₁₄  | India, Comoros, Venezuela /Leaf                      | GC-MS           | [14,29,31,35,38]        |
| Thymol                | C₁₀H₁₄  | Brazil, Cambodia, India, Venezuela /Aerial parts, Leaf | GC-MS           | [14,29,33,35,37–41,44,45]|
| Thymol methyl ether   | C₁₁H₁₄  | Brazil /Leaf                                           | GC-MS           | [37]                     |
| **Oxygenated monoterpenes** |         |                                                       |                 |                          |
| Camphor               | C₁₀H₁₄O | Comoros, India, Mauritius/Leaf                         | GC-MS           | [30–32]                  |
| Carvacrol             | C₁₀H₁₄O | Cambodia, India, Malaysia, Mauritius, Venezuela /Aerial parts, Leaf | GC-MS           | [12–14,28–30,32–35,38–43]|
| Carvone               | C₁₀H₁₄O | India /Leaf                                            | GC-MS           | [29]                     |
| 1,8-Cineole           | C₁₀H₁₄O | India /Leaf                                            | GC-MS           | [12,26,27,29,41]        |
| Eugenol               | C₁₀H₁₄O | Cambodia, India /Leaf                                   | GC-MS           | [29,36,29,41,44]        |
| Germacrene            | C₁₀H₁₄O | Mauritius /Leaf                                         | GC-MS           | [30]                     |
| Linalool              | C₁₀H₁₄O | Comoros, Mauritius /Leaf                                | GC-MS           | [30,31]                  |
| Methyl carvacrol       | C₁₁H₁₄O | India /Leaf                                            | GC-MS           | [29]                     |
| Methyl eugenol        | C₁₁H₁₄O | Cambodia /Leaf                                          | GC-MS           | [29,36]                  |
| α-Terpinolin          | C₁₀H₁₄O | India, Comoros, Venezuela /Leaf                        | GC-MS           | [29,31,36]               |
| Terpinen-4-ol         | C₁₀H₁₄O | India, Mauritius /Leaf                                  | GC-MS           | [12,13,28–31,37,39]     |
| Thymol                | C₁₁H₁₄O | Brazil, Cambodia, India, Venezuela /Aerial parts, Leaf | GC-MS           | [12–14,29,33,35,37–41,44,45]|
| Thymol methyl ether   | C₁₁H₁₄O | Brazil /Leaf                                           | GC-MS           | [37]                     |
| **Sesquiterpene hydrocarbons** |         |                                                       |                 |                          |
| α-Amorphene            | C₁₅H₂₀  | Cambodia /Leaf                                          | GC-MS           | [36]                     |
| Aracomendrene         | C₁₅H₂₀  | Brazil, India /Leaf                                     | GC-MS           | [34,37]                  |
| trans-α-Bergamotene    | C₁₅H₂₀  | Brazil, Comoros, India, Venezuela /Aerial parts, Flower | GC-MS           | [13,31,33,37,38]        |
| trans-β-Bergamotene    | C₁₅H₂₀  | Cambodia /Leaf                                          | GC-MS           | [38]                     |
| γ-Cadinene            | C₁₅H₂₀  | Cambodia /Leaf                                          | GC-MS           | [38]                     |
| δ-Cadinene            | C₁₅H₂₀  | Cambodia /Leaf                                          | GC-MS           | [38]                     |
| α-Calocorene          | C₁₅H₂₀  | India/Aerial parts                                      | GC-MS           | [33]                     |
| cis-Calocorene         | C₁₅H₂₀  | Cambodia /Leaf                                          | GC-MS           | [38]                     |
| β-Caryophyllene        | C₁₅H₂₀  | Brazil, India, Venezuela / Leaf, Flower                 | GC-MS           | [13,29,31,33,37,38,41]  |
| γ-Caryophyllene        | C₁₅H₂₀  | India /Leaf                                             | GC-MS           | [42]                     |
| α-Copaene             | C₁₅H₂₀  | Comoros, India /Leaf                                    | GC-MS           | [29,51]                  |
| α-Cubebene            | C₁₅H₂₀  | India /Leaf, Aerial parts                               | GC-MS           | [33,35]                  |
| (E,Z)-α-Farnesene      | C₁₅H₂₀  | France /Leaf                                            | GC-MS           | [29,46]                  |
| Germacrene            | C₁₅H₂₀  | Cambodia /Leaf                                          | GC-MS           | [36]                     |
| α-Farnesene            | C₁₅H₂₀  | Cambodia /Leaf                                          | GC-MS           | [36]                     |
| γ-Gurjunene            | C₁₅H₂₀  | India/Aerial parts                                      | GC-MS           | [33]                     |
| Humulene              | C₁₅H₂₀  | Brazil, Cambodia, India, Venezuela /Aerial parts, Leaf  | GC-MS           | [14,31,33,35,38,45]     |
| α-Murolene            | C₁₅H₂₀  | Cambodia, France, Mauritius /Leaf                      | GC-MS           | [30,36,46]               |
| Patchouline            | C₁₅H₂₀  | India, Mauritius /Leaf                                  | GC-MS           | [30,42]                  |
| β-Selinene            | C₁₅H₂₀  | India, Comoros /Leaf                                    | GC-MS           | [14,31,35,44]            |
| β-Phellandrene         | C₁₅H₂₀  | Cambodia /Leaf                                          | GC-MS           | [46]                     |
Table 2. Cont.

| Compound Name                  | Formula | Plant Origin/Part | Method     | References |
|-------------------------------|---------|-------------------|------------|------------|
| Oxygenated sesquiterpenes     |         |                   |            |            |
| Caryophyllene oxide           | C_{15}H_{24}O | India, Cambodia, Venezuela /Leaf, Aerial parts | GC-MS | [13,14,29,38,39,44] |
| β-Cedrene epoxide             | C_{30}H_{40}O | India/Aerial parts | GC-MS | [14,35]    |
| 1-Epi-cubenol                 | C_{15}H_{24}O | India/Aerial parts | GC-MS | [14,35]    |
| β-Himachalene oxide           | C_{30}H_{40}O | India/Aerial parts | GC-MS | [29]       |
| Humulene oxide                | C_{30}H_{40}O | India/Leaf        | GC-MS | [29]       |
| Spathulenol                   | C_{30}H_{40}O | India/Leaf        | GC-MS | [32,39]    |
| Others (Terpenes, phenylpropanoids, esters, fatty acids, alcohols, aldehydes) |         |                   |            |            |
| 1,2-Benzenediol-4-(1,1-dimethylethyl) | C_{30}H_{41}O | India/Leaf        | GC-MS | [44]       |
| Methyl chavicol               | C_{20}H_{30}O | India/Aerial parts | GC-MS | [14,33,35] |
| α-Carocalone                  | C_{30}H_{41}O | India/Aerial parts | GC-MS | [33]       |
| Dihydro carveol               | C_{30}H_{41}O | India/Aerial parts | GC-MS | [14,35]    |
| Durohydroquinone              | C_{20}H_{30}O | India/Leaf        | GC-MS | [44]       |
| 1,4-Eicosadiene               | C_{20}H_{40}O | India/Leaf        | GC-MS | [44]       |
| Ethyl Salicylate              | C_{15}H_{20}O | France/Leaf       | GC-MS | [29,46]    |
| (Z)-3-Hexen-1-ol              | C_{15}H_{20}O | India/Aerial parts | GC-MS | [34,35]    |
| 1-Octen-3-ol                  | C_{14}H_{22}O | India, Mauritius, Venezuela/Leaf | GC-MS | [29,30,36,39] |
| Oleic acid                    | C_{18}H_{36}O | India/Leaf        | GC-MS | [44]       |
| 2-Phenyl ethyl fglate         | C_{30}H_{41}O | India/Aerial parts | GC-MS | [14,35]    |
| Phytol                        | C_{20}H_{30}O | India/Leaf        | GC-MS | [44]       |
| Squalone                      | C_{30}H_{40}O | India/Leaf        | GC-MS | [44]       |
| Tetradecanal                  | C_{14}H_{20}O | India/Aerial parts | GC-MS | [14,35]    |
| 3,7,11,15-Tetramethyl-2-hexadecan-1-ol | C_{30}H_{41}O | India/Leaf        | GC-MS | [44]       |
| Thymol acetate                | C_{12}H_{20}O | India/Leaf        | GC-MS | [29,39]    |
| Trans-sabinene hydrate        | C_{12}H_{20}O | India/Aerial parts | GC-MS | [14,35]    |
| Undecanal                     | C_{11}H_{12}O | India/Aerial parts | GC-MS | [14,35]    |
The chemical constituents of *P. amboinicus* essential oil differed with the collected samples from diverse geographical places. In India, *P. amboinicus* essential oil was reported to possess volatiles such as Carvacrol (43.1%), Thymol (7.2%), Eugenol (6.4%), Chavicol (5.3%) and Et-salicylate (3.2%) [40], which varied from the constituents observed by Baslas and Kumar [41] with Thymol (41.30%), Carvacrol (13.25%), 1,8-Cineole (5.45%), Eugenol (4.40%) and β-Caryophyllene (4.20%). Likewise, analysis of essential oil obtained from wild growing *P. amboinicus* plants in Bangalore, India showed the presence of 36 compounds [29]. The major compounds identified were Carvacrol (53%–67%), *p*-Cymene (6.5%–12.6%), β-Caryophyllene (7.4%), Caryophyllene oxide (2.2%) and α-Terpine (5.9%–15.5%). For the first time, there was an occurrence of the compounds eugenol and methyl eugenol in Indian (Andra Pradesh) *P. amboinicus* oil [12].

**Figure 1.** Cont.
Figure 1. The structures of some of the volatile chemical constituents.

GC and GC-MS techniques have indicated the occurrence of Thymol (94.3%), followed by Carvacrol (1.2%), 1,8-Cineole (0.8%), p-Cymene (0.3%), Spathulenol (0.2%) and Terpinen-4-ol (0.2%) as the major constituents of Indian *P. amboinicus* leaf essential oil. Investigation of volatiles of *P. amboinicus* collected from Mysore, Karnataka, India showed the existence of Carvacrol (70%), β-Caryophyllene (6.2%), *p*-Cymene (5.6%) and α-Terpinolene (5.3%) as the main components [13]. The volatile composition of aerial parts and flowers of *P. ambonicus* growing in Belgaum, Western Ghats region of North West Karnataka, India have been studied by Joshi et al. [33] using gas chromatography outfitted with a flame ionization detector (GC-FID) and GC-MS. The results revealed the occurrence of
12 components from aerial parts oil and 4 constituents from flower oil and represented 94.29% and 90.25% of the total oil, respectively. In both the essential oils, the major compound observed was Carvacrol (50.98% in flowers and 77.16% in aerial parts oils). They also noticed the chemotype nature of the plants with minor quantities of α-Calacorene, Methyl chavicol and α-Corocalene from aerial parts oil. However, *P. amboinicus* collected from Western Ghats (Siruvani hills), Tamilnadu, India contained only 14% of Carvacrol. Other chief constituents observed were Thymol (18%), *cis*-Caryophyllene (18%) and *p*-Cymene (10.83%) [34]. Yet, the presence of chemical variation in the leaf essential oils had been evident from the plants collected from the same state [42,44]. A total of 10 volatile compounds were identified with dominant constituents as Carvacrol (50.7%), β-caryophyllene (13.1%) and patchoulane (8.7%) [42], while the occurrence of Carvacrol was not evident from the study of Uma *et al.* [44]. They reported the occurrence of 3-Methyl-4-isopropyl phenol (31.70%) as the major constituent followed by Squalene (10.07%), Caryophyllene (2.36%) and Phytol (8.44%). Similarly, the essential oil of *P. amboinicus* leaves obtained from the Cuddalore district of Tamilnadu, India was shown to contain a total of 26 compounds, with Carvacrol (28.65%) and Thymol (21.66%) observed as the major compounds [14]. Some of the other major components included α-Humulene (9.67%), γ-Terpinene (7.76%), Undecanal (8.29%), *p*-Cymene (6.46%), α-Terpineol (3.28%), β-Selinene (2.01%) and Caryophyllene oxide (5.85%).

Likewise, plants growing in the same locality were shown to contain 26 compounds and among them Carvacrol (29.25%), Thymol (21.66%), Undecanal (8.29%) and α-Humulene (9.67%) were the major compounds [35]. About 28 volatile compounds were revealed from the aerial parts of *P. amboinicus* cultivated in Uttarakhand, India by using GC and GC-MS analysis. Among the 16 identified compounds, Thymol (83.39%) was the major component. The other important components observed were 1-Octen-3-ol, Caryophyllene oxide, Terpine-4-ol, *trans*-Caryophyllene, Eugenol and α-Cadinol [39]. Likewise, chemical investigation of essential oil of *P. amboinicus* collected from Himalayan foothill and mid-hill regions of India were reported by Verma *et al.* [47]. They identified 44 constituents representing 86%–99% of the oil composition using GC and GC-MS analysis. Some of the major components observed were Thymol (57.7%–66.4%), γ-Terpinene (5.8%–11.7%), *p*-Cymene (4.1%–14.2%), (*E*)-Caryophyllene (2.6%–3.6%), Caryophyllene oxide (1.3%–1.5%) and 1-Octen-3-ol (1.0%–1.8%). Essential oil of *P. amboinicus* from Mauritius was characterized by Gurib-Fakim *et al.* [30] using capillary GC and GC-MS analysis and the results revealed Carvacrol (41.3%) and Camphor (39%) as the dominant volatiles.

The leaf essential oil obtained from Martinique, France was found to contain Carvacrol (72%) as a chief phenolic component along with newly identified compounds such as (Z)-1,3-Hexadiene (0.1%), (*E,Z*)-α-Farnesene (0.2%), (*Z*)-3-Hexenol (0.6%), α-Murolene (0.2%) and (*E,E*)-α-Farnesene (0.2%) [46]. *P. amboinicus* oil from Cambodia was shown to contain largely Thymol (57.4%). Other major constituents such as Carvacrol (13.5%), *p*-Cymene (5.2%) and γ-Terpinene (5.6%) were also noticed [36]. Likewise, 64.3% of Thymol was identified from Brazilian *P. amboinicus* leaf essential oil [37]. Other major compounds identified were *p*-Cymene (10.3%), β-Caryophyllene (2.8%) and γ-Terpinene (9.9%). Liquid-solid chromatography (LSC), Gas-liquid chromatography (GLC) and GC-MS analysis of *P. amboinicus* plants from Cuba revealed Carvacrol (64%) as the major component among the identified 13 terpene hydrocarbons and seven oxygenated compounds [43]. Similarly, Velasco *et al.* [38] identified 15 volatile constituents in the essential oil of *P. amboinicus* collected from Venezuela and the major component observed was Carvacrol (65.2%). Capillary GC and GC-MS analysis of *P. amboinicus* essential oil from the Archipelago of Comoros was carried out by Hassani *et al.* [31] and the results showed the existence of Carvacrol (23.0%), Camphor (22.2%), δ-3-Carene (15.0%), γ-Terpinene (8.4%), *p*-Cymene (7.7%) and α-Terpineol (4.8%) as the major constituents of the oil. The essential oil from Uganda consisted of Linalool (50.3%), Carvacrol (14.3%), Nerol acetate (11.6%) and Geranyl acetate (11.7%) as the major components as revealed by GC-MS analysis [40]. Essential oil of *P. amboinicus* leaves from Serdang, Malaysia was shown to contain Carvacrol (19.29%), 3-Carene (20.78%) and Camphor (17.96%) as the major volatile constituents [32].
The essential oil yield and its main chemical constituents are also influenced by the environmental factors and different seasons. Mallavarupu et al. [29] have revealed that the quality of essential oil will be superior when collected during September. The oil content was found to be higher in the plants harvested during September in comparison to the plants harvested during May. Moreover, the compositions also differed among the two harvest times. About 68% of oxygenated monoterpenes, 11% of sesquiterpenes and 3.3% oxygenated sesquiterpenes were found in the oil distilled from the September harvest time, whereas, the oil obtained from the May harvest comprised higher amounts of monoterpenes (35.7%). The major compounds such as Carvacrol (67.0%), β-Caryophyllene (7.4%), α-Humulene (2.1%) and Caryophyllene oxide (2.2%) were found to be higher in oil obtained during September, while the oil distilled during May showed the presence of p-Cymene (12.6%), γ-Terpinene (15.5%), Carvacrol (53.0%) and β-Caryophyllene (4.3%). A GC-MS study was carried out by Roja et al. [45] to identify the chemical constituents of P. amboinicus oil from the leaves of the tissue culture plants, in vitro root cultures as well as parent plants. The results revealed the presence of similar volatile constituents, though the parent plants and root cultures contained 21 compounds in comparison to only 15 compounds noticed in the tissue culture plants. The concentration of Thymol compound was found to be 0.012, 0.29 and 0.009% (fresh weight) in the tissue culture plants, in vitro roots and the parent plants, respectively. They also suggested that thymol and cis-Caryophyllene can be produced from the tissue culture plants as oil yield and Thymol concentration was found to be similar to the parent plants. Interestingly, the root cultures had a three times higher Thymol content after a period of four weeks of day growth. This suggested the possible use of root cultures for producing Thymol and cis-Caryophyllene on a large scale.

3.2. Non-Volatile Chemical Constituents of P. amboinicus

A total of 30 non-volatile constituents have been identified from P. amboinicus according to our literature survey [17,48]. These non-volatile chemical components included phenolic acids, flavonoids, monoterpenes, sesquiterpenes, oxygenated monoterpenes, and esters. The details of these phytocompounds are exemplified in Table 3 and some of the important and major compound structures are illustrated in Figure 2. The chloroform extract of P. amboinicus air-dried leaves was subjected to fractionation using the silica gel column chromatography technique to separate non-volatile compounds [49]. Later, the isolated compounds were identified by using ultraviolet (UV), 1-D nuclear magnetic resonance (NMR) and 2-D NMR spectroscopy as three flavones, namely, Cirsimaritin, Salvigenin and Chrysoeriol. High pressure liquid chromatography (HPLC) analysis was carried out to analyze the major compound, Carvacrol, present in the aqueous extract of P. amboinicus plants obtained from Taichung of Taiwan [50]. The results showed an abundance of Carvacrol occurrence in the aqueous extract, with 1.88 mg/g of the extract. Eight compounds from the ethyl acetate fraction of P. amboinicus leaves collected from Egypt were isolated and identified [48]. Based on the UV, NMR spectra and their physical data, these isolated compounds were identified as 5,4′-Dihydroxy-3,7′-dimethoxy flavone (3-methoxy genkwanin), 5,4′-Dihydroxy-6,7-dimethoxy flavone (Crisimaritin), p-Coumaric acid (Hydroxy cinnamic acid), Caffeic acid, 3,5,7,3′,4′-Pentahydroxy flavanone (Taxifolin), Rosmarinic acid, Apigenin and 5-O-Methyl-luteolin. For the first time, they reported the occurrence of 3-Methoxy genkwanin, p-Coumaric acid and 5-O-Methyl-luteolin in this plant. In the same study, total phenolic content was higher in the stem extract (9.6 mg/g) compared to the leaf extracts (8.4 mg/g) and the root extracts (5.4 mg/g).
Table 3. The known non-volatile constituents of *P. amboinicus*.

| Compound Name          | Formula   | Plant Origin/Part                                      | Analytical Method                  | References |
|------------------------|-----------|--------------------------------------------------------|------------------------------------|------------|
| **Phenolic acids**     |           |                                                        |                                    |            |
| Caffeic acid           | C_{9}H_{8}O_{4} | India, Egypt/Leaf, stem, root (Methanol extract)       | UV/NMR/UPLC/MS/HPLC                | [48,51]    |
| Gallic acid            | C_{7}H_{6}O_{5} | India/Stem (Methanol extract)                           | HPLC                              | [51]       |
| p-Coumaric acid        | C_{9}H_{8}O_{3} | India, Egypt/Leaf, stem, root (Methanol and ethyl acetate fraction) | UV/NMR/UPLC/MS/HPLC                | [48,51]    |
| Rosmarinic acid        | C_{18}H_{16}O_{8} | India, Egypt, Thailand/Leaf, stem, root (Methanol and ethyl acetate fraction) | UV/NMR/UPLC/MS/HPLC                | [48,51,52] |
| Salvianolic acid A     | C_{26}H_{22}O_{10} | Thailand/Aerial parts (Water extract)                  | UV/NMR/MS/HPLC                    | [52]       |
| Shimobashiric acid     | C_{36}H_{32}O_{16} | Thailand/Aerial parts (Water extract)                  | UV/NMR/MS/HPLC                    | [52]       |
| **Flavonoids**         |           |                                                        |                                    |            |
| Chrysoeriol            | C_{16}H_{12}O_{6} | Philippines, Egypt/Leaf, stem, root (Chloroform extract, Ethyl acetate fraction) | UV/NMR/UPLC/MS                    | [48,49]    |
| Cirsimaritin           | C_{17}H_{14}O_{6} | Philippines/Leaf (Chloroform extract)                  | UV/NMR                            | [49]       |
| Eriodictyol            | C_{15}H_{12}O_{6} | Egypt/Leaf, stem, root (Ethyl acetate fraction)        | UV/NMR/UPLC/MS                    | [48]       |
| Luteolin               | C_{15}H_{12}O_{6} | Egypt/Leaf, stem, root (Ethyl acetate fraction)        | UV/NMR/UPLC/MS                    | [48]       |
| Rutin                  | C_{15}H_{12}O_{6} | India/Stem (Methanol extract)                           | HPLC                              | [51]       |
| Salvigenin             | C_{18}H_{16}O_{6} | Philippines/Leaf (Chloroform extract)                  | UV/NMR                            | [49]       |
| Thymoquinone           | C_{17}H_{14}O_{6} | Thailand/Aerial parts (Water extract)                  | UV/NMR/MS/HPLC                    | [52]       |
| 5,4'-Dihydroxy-6,7-dimethoxy flavone | C_{27}H_{26}O_{10} | Egypt/Leaf, stem, root (Ethyl acetate fraction) | UV/NMR/UPLC/MS/HPLC                | [48,51]    |
| 5,4'-Dihydroxy-3,7-dimethoxy flavone | C_{27}H_{26}O_{10} | Egypt/Leaf, stem, root (Ethyl acetate fraction) | UV/NMR/UPLC/MS                    | [48]       |
| 5-O-Methyl-luteolin    | C_{27}H_{26}O_{10} | Egypt/Leaf, stem, root (Ethyl acetate fraction)        | UV/NMR/UPLC/MS                    | [48]       |
| 3,5,7,4',5'-Pentahydroxy flavone | C_{37}H_{26}O_{10} | Egypt/Leaf, stem, root (Ethyl acetate fraction)        | UV/NMR/UPLC/MS                    | [48]       |
| 4',5',5''-Trihydroxyflavone (apigenin) | C_{37}H_{26}O_{10} | Egypt/Leaf, stem, root (Ethyl acetate fraction)        | UV/NMR/UPLC/MS                    | [48]       |
The tannin content was found to be highest in the root extracts (126 μg/g), followed by the leaf (90 μg/g) and stem extracts (81 μg/g). The use of high resolution Ultra Performance Liquid Chromatography (UPLC)-MS analysis identified the presence of Rosmarinic acid, Chrysoeriol, Caffeic acid and \( p \)-Coumaric acid in the ethyl acetate fractions of stems and roots. However, the compounds, Eriodyctiol, Luteolin and Quercetin were found only in the ethyl acetate fractions of stems [48]. Bhatt et al. [51] have analyzed the phytochemicals present in the methanolic stem extracts of \textit{P. amboinicus}. Their study revealed the existence of total phenolic content (49.9 mg gallic acid equivalent (GAE)/g extract), condensed tannins (0.7 mg tannic acid equivalent (TAE)/g extract) and total flavonoids (26.6 mg rutin equivalent (RE)/g extract). Further, HPLC analysis of the extract confirmed the occurrence of bioactive polyphenols such as Rosmarinic acid (6.16 mg/g extract), Rutin (0.32 mg/g extract), Caffeic acid (0.77 mg/g extract), Gallic acid (0.26 mg/g extract), \( p \)-Coumaric acid (0.10 mg/g extract) and Quercetin (0.15 mg/g extract). The chemical composition of aqueous leaf extracts of \textit{P. amboinicus} was reported to contain tannins, flavonoids, saponins, polyuronides and
steroid glycosides [28]. In the same study, about 11 phytocompounds constituting 97.6% of the total extract were confirmed using GC-MS analysis. The major components included Linalool (50.3%), Carvacrol (14.3%), Geranyl acetate (11.7%) and Nerol acetate (11.6%). Chen et al. [52] have isolated and identified four bioactive compounds with transcription factor inhibition activity from aerial parts (stem and leaves) of *P. ambonicus* collected from Thailand. They separated the compounds from water extracts using HPLC column-based fractionation to detect the compounds using mass spectrometry and NMR analysis. The identified non-volatiles included Rosmarinic acid, Thymoquinone, Shimobashiric acid and Salvianolic acid.

4. Bioactivities of *P. amboinicus*

4.1. Antimicrobial Activities

*P. amboinicus* extract, from crude extract to an essential oil, contains innumerable biological constituents owing to its chemical diversity. Plant phytochemicals possess antimicrobial activity against a wide range of bacteria, yeast and mold, but vary in quantity and quality depending on the bioactive constituents [3,4,53]. Its wide range of chemical diversity containing phytochemicals such as terpenes, alcohols, acetones, phenols, acids, aldehydes and esters is often used as components in the pharmaceutical industry. Table 4 provides the detailed antimicrobial activities of different parts of *P. amboinicus* and its major compounds.

4.1.1. Antibacterial Activities

Bacteria are prokaryotic microorganisms usually found on the surface of the skin, mucosal layer and intestinal tract of humans and animals. The genus *Staphylococcus* is one example of common bacteria found to reside on the skin and in mucous membrane and is mostly harmless. Yet, there are dangerous bacteria classified as human pathogens, causing contagious diseases with a fatal prognosis [54]. These bacteria are usually inhibited by taking antibiotics. However, recently drug resistance developed by microbes is increasingly observed and is a global phenomenon. Therefore, continuous exploration of medicinal plants for effective drugs is an ongoing process. From early years, *P. amboinicus* has been used as folk medicine to fight pathogenic bacterial activity. In Cuba, a decoction of the leaves was given to patients suffering from chronic cough or tuberculosis and later scientific studies revealed *P. amboinicus* having anti-*Mycobacterium tuberculosis* activity [55]. Hot water extract of *P. amboinicus* leaves inhibited growth of pathogens, *Escherichia coli* and *Salmonella typhimurium* while stimulating the growth of *Lactobacillus plantarum* [56]. This antibacterial activity of plant extracts is most likely due to the combined effect of adsorption of polyphenols to bacterial membranes with membrane disruption and subsequent leakage of cellular contents [57,58], and the generation of hydro peroxide from polyphenols [59]. Further, it was shown that unsterilized ethanolic leaf extract of *P. amboinicus* exhibits antibacterial activity against diabetic wound pathogens, *E. coli*, *S. aureus*, *P. mirabilis*, *P. aeruginosa* and *K. pneumonia* [60]. Current attention is focused on inhibition of antibiotic-resistant bacteria as it is gradually becoming a major problem in the medical industry. Essential oil of *P. amboinicus* is reported to have a synergistic effect on the antibiotic toxicity toward resistant bacterial strains when combined with aminoglycosides. This makes *P. amboinicus* essential oil a possible source of a natural product with bacterial resistance-modifying activity [61]. In another study, Vijayakumar et al. [62] used leaf extract of *P. amboinicus* to biologically synthesize zinc oxide nanoparticles (Pam-ZnO NPs). These Pam-ZnO NPs successfully controlled the growth of methicillin-resistant *Staphylococcus aureus* biofilms (MRSA ATCC 33591) at the concentration of 8–10 g·mL⁻¹.
Table 4. Pharmacological properties of *P. amboinicus* different parts.

| Pharmacological Activity | Plant Part Used | Bioactive Compound | Potential Effect | References |
|--------------------------|-----------------|--------------------|------------------|------------|
| **Antibacterial activity** | Leaf extract/Essential oil/Decoction | Biogenic zinc oxide nanoparticles | Pam-ZnO NPs control the growth of methicillin-resistant *Staphylococcus aureus* biofilm, inhibits growth of *Escherichia coli*, *Salmonella typhimurium* & *Mycobacterium tuberculosis*. | [54–61] |
| **Antifungal activity** | Leaf extract/Decoction | Carvacrol, *p*-Cymene, *α*-Terpinolene & *β*-caryophyllene | Fungitoxic properties against *Aspergillus flavus*, *Aspergillus niger*, *Aspergillus oryzae*, *Candida versatilis*, * Fusarium sp.* - *GF-1019*, *Penicillium sp.*, *Saccharomyces cerevisiae*, *Candida albicans*, *C. krusei* & *C. stellatoidea*. | [54,63] |
| **Antiviral activity** | Leaf/Ethanolic extract | - | Exhibited antiviral activity against viruses (HSV, H5N1 & HIV) | [20,64–66] |
| **Activity against Respiratory diseases** | Leaf extract/Decoction or juice/Essential oil | - | Used as folk medicine in Brazil for influenza, cough, expectorant, bronchitis and throat problems; given orally to control asthma & catarrh, used as bronchodilator. | [11,12,67–72] |
| **Laviecidal potential** | Leaf extract/Essential oil | Pam-ZnO NPs (zinc oxide nanoparticles) | Exhibited up to 100% mortality in *Aedes aegypti*, *Culex quinquefasciatus* & *Culex tritaeniorhynchus*. | [14,47,62,73–75] |
| **Oral Diseases** | Essential oil | Carvacrol | Antimicrobial effect when used with mouthwash. | [79] |
| **Digestive diseases (Diarrhea, Constipation, dyspepsia, indigestion & as carminative)** | Leaf extract/Juice | - | Inhibited the growth of *Escherichia coli* & *Salmonella typhimurium*; relieved constipation troubles; prevents formation of gas in the gastrointestinal tract & facilitates expulsion of gas. | [30,56,67,68,77] |
| **Antitumor activity** | Leaf extract/Crude hydro alcoholic extracts | Flavone (Luteolin), flavonols | Inhibited the growth of sarcoma 180 & Ehrlich ascite carcinoma tumors in mice; showed significant antitumor activity through inducing apoptosis in A549 (human lung cancer) cell line. | [79,79] |
| **Antinflammatory activity** | Aerial part/Ethanol, methanol & hexane extract | Rosmarinic acid, Shimobashiric acid, alvianolic acid L, Rutin, Thymoquinone, Quercetin | Concentration of 0.1 mg/mL inhibited 10%–50% DNA binding activities; inhibited the binding of AP-1 to its consensus DNA sequence; decreased carrageenan-induced paw edema up to 40%; significantly increased IgG, IgM & lysozyme activity in rats. | [34,50,52,78,80] |
| **Analgesic activity** | Leaf extract | - | Provides remedy for headache, backache & musculo-skeletal problems. | [52,81–83] |
| **Wound healing activities** | Leaf & Root Aqueous extract | - | Increased wound healing activity in experimentally induced diabetic mice & against mules. | [60,84–87] |
| **Cardiovascular disorders** | Leaf aqueous extract | - | Positive inotropic activity in the isolated frog heart; effective for treating congestive heart failure. | [67,88] |
| **Skin disease (Anti-dandruff, Cuts, Skin Allergy; Burns)** | Leaf extract/Essential oil/Leaf juice/Paste | Thymol, 1,8-Cineole, *β*-Pinene, *α*-pinene, phenolic compounds | Inhibited the growth of *Malassezia furfur*, applied on cut as antiseptic promoted better healing, paste was effective against skin allergies, skin burns. | [68,89–92] |
| **Insect bites** | Leaf aqueous extracts | - | Potency as antidote for scorpion (*Heterometrus laoticus*) venom with >50% efficiency. | [68,93] |
| **Lactogenic properties** | Leaf | Nutrient content (iron & carotene) | Increased breast milk in new mothers. | [80] |
| **Antiseizure activity** | Leaf, stem, root Extract (aqueous & alcoholic) | Alkaloids, flavonoids & saponins | Effective as an anticonvulsant and/or antiepileptic medicine. | [11,68,94] |
| **Activity against Geriatric diseases** | Leaf Decoction/Ethanolic & aqueous leaf extract | - | Effective against urinary diseases in the Amazon & India; to relieve kidney troubles, treat vaginal discharges; used after childbirth; increased urine volume & electrolyte concentration in male albino rats. | [67,89,95–98] |
| **Antioxidant activity** | Leaf extracts/Essential oil | Carvacrol & Thymol | Exhibited significant inhibition in DPHH free radical & hydroxyl radical formation. | [16,34,99,100] |
| **Other diseases** | Leaf | - | Fevers, meningitis, eye diseases. | [67,101–103] |
4.1.2. Antifungal Activities

There is also vast evidence that *P. amboinicus* plays a crucial role in hindering the growth of disease causing fungus. However, little is known of the derivatives and its effectiveness when used together with industrial drugs. In evaluating the interference of *P. amboinicus* essential oil on the anti-*Candida* activity of some clinically used antifungals (itraconazole, ketoconazole and amphotericin B), it showed a diverse level of interference. Essential oil exhibited prominent interference on the activity of itraconazole, providing a synergic effect on *C. albicans*, *C. tropicalis*, *C. krusei* and *C. stellatoidea*. Whereas, interference on the anti-yeast activity of ketoconazole was antagonic and synergic when interacting with *C. albicans*, *C. guilliermondii* and *C. stellatoidea*. Amphotericin B, on the other hand, showed a small interference on the anti-yeast activity [63]. In another research, antifungal activity of the volatile oil was studied against various fungi by an agar well diffusion susceptibility test. In that, growth of *Aspergillus ochraceus*, *Aspergillus niger* and *Penicillium* sp. was inhibited by 60%, 64% and 60%, respectively, with 10 µL of volatile oil [13].

4.1.3. Antiviral Activities

A large number of active agents are available for the symptomatic treatment of sexually transmitted diseases (STDs) and acquired immune deficiency syndrome (AIDS). Nevertheless, the emergence of drug-resistant strains and dose-limiting toxic effects has complicated the treatment of these diseases and necessitated the search for new antimicrobial substances from various sources. In the last decade, major advancements have been reported in the field of “microbicides”, i.e., compounds or formulations which, when applied topically can prevent the transmission of STDs including AIDS [28]. These include a few from plant sources such as gossypol derivatives, praneem polyherbal preparations and plantibodies. Likewise, extracts of *P. amboinicus* were tested and reported to have antiviral activity against Herpes Simplex Virus-1 (HSV1) [64] and anti-HIV inhibition activity [65]. Besides that, ethanolic extract of *P. amboinicus* was reported to have selective antiviral activity on Vero cell lines at 0.1 mg/mL minimum inhibitory concentration when tested against HSV1 and Vesicular Stomatitis (VSV) viruses [66].

4.2. Respiratory Disorders

*P. amboinicus* is frequently cited in the treatment of chronic coughs, asthma, bronchitis and sore throat in India and the Caribbean Islands [67–69]. In accordance with that, leaves of *P. amboinicus* had positive bronchodilator activity when tested on guinea pigs [70]. In Eastern Cuba, essential oil from aerial parts of *P. amboinicus* is used to treat asthma [11]. Decoction or juice made from leaves together with other herbs is also taken orally to control asthma. This decoction is also used to treat catarrhal infections where it clears the excessive build-up of thick phlegm or mucus in an airway or cavity of the body [71]. Collectively, the reason behind this could be high amounts of Carvacrol [11] and Thymol [12] found in the essential oil of the plant. Carvacrol and Thymol are an excellent expectorant and used to treat various respiratory disorders. It is suggested that a drink or a bath of *P. amboinicus* juice/decoction can be a worthy treatment for influenza, cough, bronchitis and throat problems [72].

4.3. Activity against Digestive Diseases

*P. amboinicus* is a popular treatment for dyspepsia, indigestion and diarrhea, and a carminative in India and Africa [30,67,68,77]. In India, the leaves of *P. amboinicus* are consumed along with buttermilk, yogurt, or any other probiotic sources during pathogen-induced diarrhea. The leaves are known to have a prebiotic effect on the probiotic bacteria *Lactobacillus plantarum*. They utilize the phytoconstituents of the leaves by producing necessary metabolic enzymes. A detailed examination by Shuba and Bhatt [56], describes the mode of hot water extract (HWE) of *P. amboinicus* leaves on growth inhibition of *Escherichia coli* and *Salmonella typhimurium* (pathogens) while stimulating the growth of *Lactobacillus plantarum*. Sodium dodecyl sulfate polyacrylamide gel electrophoresis (SDS-PAGE)
gel showed the presence of phenolic acid decarboxylase enzyme induced in the presence of HWE, which indicated the utilization of polyphenols by the bacteria. Cells grown on HWE also showed β-galactosidase activity, indicating their ability to utilize sugars present in HWE. This provides evidence in the traditional use of the leaves in the alleviation of diarrhea by accelerating microbial gut balance during infection. In addition, *P. amboinicus* juice obtained from pounded leaves is used as a drink to cure constipation in Indonesia and Malaysia [77].

4.4. Antiepileptic Activity

Various literatures have reported the use of *P. amboinicus* in the treatment of nervous disorders, including epilepsy and convulsions [68]. In Cuba, it is used as an anticonvulsive and antiepileptic drug [11]. Bhattacharjee and Manjumder [94], tested the anticonvulsant activity of the leaf, stem and root alcoholic extract separately on Swiss albino mouse models by maximal electric shock-induced seizures and pentylentetrazole-induced seizures. They found significant anticonvulsant activity in both the models with alcoholic leaf extract recording the highest activity. They also predicted that the presence of alkaloids, flavonoids and saponins in these extracts may be responsible for this activity.

4.5. Antitumorigenic Activities

The antitumor activity of hexane extracts of *P. amboinicus* has been reported [78]. The results showed a significant inhibition on the growth of Sarcoma-180 tumor in mice treated with the hexane extracts of *P. amboinicus*. A dose of 350 mg/kg of hexane extracts of *P. amboinicus* significantly reduced the growth of S-180 tumor with 66% inhibition, while doses of 100, 150 and 250 mg/kg reduced the inhibition to 44%, 45% and 47%, respectively. There were no significant differences in body weight before and after the treatments. This was comparable to metrotexat, a cancer-treating drug which may cause very serious, life-threatening side effects but reduces 100% of tumoral growth. Nevertheless, hexane extracts of *P. amboinicus* is plant-based, therefore, the severity of side effects can be reduced while the tumoral growth is being destroyed. *P. amboinicus* ethanolic extract showed significant anticancer activity through inducing apoptosis in the A549 (human lung cancer) cell line [79].

4.6. Anti-Inflammatory Activities

The hexane extract (HE) of *P. amboinicus* was also shown to exhibit anti-inflammatory activity [78]. A significant reduction of the paw edema was observed at doses of 150, 250 and 350 mg/kg of the HE of *P. amboinicus*. The highest percentages of reduction of the paw edema were observed in the groups treated with 250 (41%) and 350 mg/kg (33%) of the HE of *P. amboinicus*. Interestingly, the lowest percentage of inhibition of paw edema was observed in the groups that were treated with 10 mg/kg of the indomethacin, a non-steroidal antiinflammatory drug. Rheumatoid arthritis is a chronic inflammatory disease. The activator protein-1 (AP-1) controls the expression of inflammatory cytokines, whereas tumor necrosis factor (TNF-α) plays a key role in the pathogenesis of inflammatory bone resorption. The active constituents of *P. amboinicus* were shown to possess AP-1 and TNF-α inhibitory activities [52]. However, they further suggested validating the AP-1 and TNF-α inhibitory potential of *P. amboinicus* for the treatment of rheumatoid arthritis. Treatment of leaf methanolic extracts of *P. amboinicus* resulted with moderate to high anti-inflammatory activity in experimental mice [34]. *In vitro* and *in vivo* studies have revealed the potent anti-inflammatory activity of aqueous extract of *P. amboinicus* [50]. The anti-inflammatory activity was related to modulation of antioxidative enzymes in the liver with a decreased malondialdehyde level. Also, they observed the production of TNF-α and cyclooxygenase 2 (COX-2) in the tissue of edema paw induced in mice. *In vitro* studies revealed the production of proinflammatory mediators in RAW 264.7 cells. Most recently, Silitonga et al. [80] reported the significant improvement of immunoglobulin levels (IgG, IgM) and lysozyme activity in rats when treated with ethanolic leaf extract of *P. amboinicus*. 
4.7. Wound Healing Activities

Few studies have investigated the ability of *P. amboinicus* to reduce blood sugar levels. Some of the phytochemicals found in *P. amboinicus* have been proven to play an important role towards blood sugar level lowering mechanisms (Table 4). This herb has the ability to prevent or decrease the risk of infection and its complications in diabetic patients [84]. Application of a paste prepared using *P. amboinicus* showed an enhanced wound healing ability by immune-stimulation in diseased giant murrels [85]. Likewise, *P. amboinicus* leaves and root derived paste (10%) has been shown to exhibit thorough epithelialization on the excision wound in albino rats after 12 days of application [86]. The use of polyherbal suspension prepared from *P. amboinicus* and *Punica granatum* was shown to exhibit good wound healing properties in laboratory mice [87]. Further, ethanolic extract of *P. amboinicus* reduced the wound area by up to 76.6% in diabetic mice induced by monosodium glutamate. It was observed that the plant extract promoted wound healing by increased wound contraction, enhancing collagen deposition and reducing the wound epithelialization period [60].

4.8. Effects against Skin Diseases

*P. amboinicus* has been used in Brazil since the early days for the treatment of skin ulcerations caused by *Leishmania braziliensis* [89]. In India, the juice of the leaves is used to treat skin allergies [90]. It is also used to treat burns in Asian regions [68]. When the leaf paste is baked on a flame and applied to cuts or burns, it acts as an antiseptic and promotes healing [91]. Essential oil of *P. amboinicus* also inhibits the growth of dandruff-causing fungus *Malassezia furfur*, and was tested using the agar diffusion method and compared against Ketoconazole-based shampoo as the standard [92].

4.9. Effects against Animal and Insect Bites

Leaves of *P. amboinicus* are also used as a poultice for centipede and scorpion bites in Asian regions, including Malaysia [68]. It is reported that aqueous extracts (0.706 mg/mL and 0.406 mg/mL) of *P. amboinicus* to be more than 70% efficient when tested against fibroblast cell lysis [93]. This implies the aqueous extracts to have a tendency to be scorpion (*Heterometrus laoticus*) venom antidotes. However, the same paper also reported its cytotoxicity to be questionable.

4.10. Lactogenic Activity

In Indonesia, *P. amboinicus* is used as a traditional food in soup to stimulate lactation for the month or so following childbirth. The leaves are commonly consumed by mothers who have given birth in North Sumatra, in particular the Batak tribe. The leaves of this herb are believed to increase the production of breast milk due to the high content of nutrients, especially iron and carotene. Consumption of leaves significantly increases minerals such as iron, potassium, zinc and magnesium in milk, thus, improving the infant's weight and health holistically [80].

4.11. Antioxidant Activities

The essential oil *P. amboinicus* possesses a significant antioxidant property against stress-created in cell line-induced lung cancer in both (*in vitro* and *in vivo*) models which could be due to the presence of phytochemical compounds such as Carvocrol and Thymol. Non-enzymatic antioxidant-reduced glutathione was found to be increased in the *P. amboinicus* essential oil treated mice. The presence of important bioactive compounds confirms the possibility of its use in pharmaceutical drug formulations. The use of essential oil of *P. amboinicus* is cheaper than natural drug formulation and also without any side effects on the animal model reported [34]. For the first time, the aqueous leaf extract of *P. amboinicus* was reported to possess higher superoxide- scavenging, nitric oxide-scavenging and ferrous ion-chelating capacity [99]. A report by Bhatt and Negi [16] showed the highest polyphenolic content with appreciable total antioxidant and 1,1-diphenyl-2-picrylhydrazyl (DPPH) free radical-scavenging properties in the solvent extract of *P. amboinicus* leaves. Similarly,
Khanum et al. [100] found lower content of total flavonoids and total phenolics and antioxidant activity in an ethanolic leaf extract of *P. amboinicus*.

4.12. Oral Diseases

Caries and periodontal disease are especially of concern to public health, where they affect a large part of the population. *P. amboinicus*, rich in carvacrol, has shown an antagonistic effect when used with mouthwash to avoid bacterial growth in the oral cavity [76]. This could be a potential alternative treatment for diseases related to oral cavities.

4.13. Larvicidal Potential

Mosquitoes have the ability of carrying and transmitting human and animal diseases across countries causing hundreds of millions of clinical cases and millions of deaths annually. Senthilkumar and Venkatesalu [14] reported the possible use of *P. amboinicus* essential oil as a low cost eco-friendly resource for inhibiting the malarial vector mosquito population. The LC50 values of the oil were found to be 33.5 and 28.3 ppm after 12 and 24 h, respectively. Likewise, Lima et al. [73] reported larvicidal activity (LC50 value: 58.9 ± 0.4 µg/mL) of the essential oil of *P. amboinicus* against the mosquito (*Aedes aegypti*) which is a chief vector of dengue, yellow fever and dengue hemorrhagic fever. In another study, the essential oil of *P. amboinicus* was shown to act as a good larvicidal agent against the mosquito, *Anopheles gambiae* after 48 h [47]. In an investigation by Baranitharan et al. [74], the highest larvicidal activity against *Aedes aegypti*, *Anopheles stephensi* and *Culex quinquefasciatus* was found in the ethyl acetate leaf extracts of *P. amboinicus*. More recently, Jayaraman et al. [75] have reported the larvicidal potential of different solvent extracts of *P. amboinicus* leaves against *Aedes aegypti*, *Culex quinquefasciatus*, and *Anopheles stephensi*. *P. amboinicus* zinc oxide nanoparticles (Pam-ZnO NPs) showed 100% mortality of fourth instar mosquito larvae of *Anopheles stephensi*, *Culex quinquefasciatus* and *Culex tritaeniorhynchus* at the concentration of 8 and 10 g/mL. The histopathological studies of Pam-ZnO NPs-treated *A. stephensi* and *C. quinquefasciatus* larvae revealed the presence of damaged cells and tissues in the mid-gut. The damaged tissues suffered major changes, including rupture and disintegration of the epithelial layer and cellular vacuolization [62]. This biological control could be slow, but a long-lasting, inexpensive alternative and harmless to the ecosystem.

4.14. Activity against Cardiovascular Disorders

*P. amboinicus* is also used in the Caribbean, to treat congestive heart failure [67]. The aqueous extracts of the fresh leaves of *P. amboinicus* exhibited dose-dependent positive inotropic activity in the isolated frog heart without affecting the heart rate [88]. This may be attributed to the increase in sodium influx thereby causing greater intracellular availability of calcium. In this report the bioactivity of the tissue-cultured extracts of *P. amboinicus* to the parent plant was also described. Both extracts from tissue-cultured and parent plant produced a comparable significant effect indicating that they both can be used as a source of biochemical production.

4.15. Activity against Genitourinary Diseases

The leaves of *P. amboinicus* are frequently utilized in the treatment of urinary diseases in the Amazon and India [69,95]. This species is also reported to relieve kidney troubles and treat vaginal discharges, and is taken as a drink after childbirth [67]. Urolithiasis is a condition when stony concretions form in the bladder or urinary tract. Many remedies have been employed during the treatment of urinary stones. The juice of *P. amboinicus* has been used as a natural remedy to dilute the crystals in the urinary tract in India from ancient times [96]. The antilithiatic activity of the concentrated fresh juice of the leaves of *P. amboinicus* is proved by Jose et al. [97]. The said study on urine analysis revealed significant reduction in calcium, oxalates and total protein level compared to the control. Further histopathological results showed an absence of crystal and normal-sized tubules with a single epithelial lining. He suggested this antilithiatic activity could be associated with calcium oxalate
origin. The diuretic properties of ethanolic and aqueous extracts of *P. amboinicus* were evaluated by determination of urine volume and electrolyte concentration in male albino rats. Furosemide (10 mg/kg) was used as a standard, while normal saline (0.9%) was used as a control. Both ethanolic and aqueous extracts (500 mg/kg) have shown a significant increase in the volume of urine and urinary concentration of Na, K and Cl ions and were comparable to furosemide. This study concludes that the leaves of *P. amboinicus* possess diuretic activities [98].

4.16. Analgesic Activity

In Africa, *P. amboinicus* is used as a remedy for headaches [81]. The aqueous extract of *P. amboinicus* leaves showed an analgesic and anti-inflammatory property, mainly modulated by controlling inhibition of proinflammatory mediators [52]. It is also used to treat musculo-skeletal conditions such as a stiff neck and backache [82,83].

4.17. Activity against Other Diseases

*P. amboinicus* is an important herb in Asia and South America for the treatment of infectious diseases such as fevers [67,101], cholera and meningitis [102]. It also used to treat sensory disorders associated with ear and eye problems. For example, *P. amboinicus* seed oil is a treatment for acute edematous otitis acuta in Polynesia [103], whereas in India its leaves are rubbed into the eyes to alleviate conjunctivitis [67].

5. Culinary Uses

5.1. Nutritional Values

Herbs have been used extensively in culinary purposes since ancient times. Many delicious cuisines we enjoy contain various dietary herbs to increase the taste and flavor of the food. Herbal plants also have lots of health benefits attributed to their nutritional content [17,27]. Hence, *P. aromaticus* can be a good source of nutritive compounds which help to enhance the taste and also prolong the shelf life of food products. A study validates the presence of high minerals, precisely calcium and potassium, at 0.158% and 0.138%, respectively [17]. The detailed nutritional components are presented in Table 5 [17,19,27]. These minerals are necessary to build and maintain strong bones and to retain normal function of heart, kidneys, muscles and nerves. *P. amboinicus* also has a significant content of iron at 0.262%. Iron is an important component of hemoglobin aids red blood cells to carry oxygen throughout the body. Hemoglobin represents about two-thirds of the body’s iron and its deficiency causes anemia. Adding to that, this plant also contains total Xanthophylls (0.356 mg/g of dry weight of the plant) which consist of Neoxanthin, Violaxanthin, Leutin, Zeaxanthinics. It also has α-Carotene (0.157 mg/g of dry weight) and β-Carotene (0.0035 mg/g of dry weight) [104]. All this makes *P. amboinicus* a unique dietary supplement.

| No. | Principles | Nutrient Content |
|-----|------------|------------------|
| 1.  | Proteins   | 0.6%             |
| 2.  | Vitamins   |                  |
| +   | Ascorbic acid | 0.003%         |
| +   | Thiamine   | 0.00008%         |
| 3.  | Minerals   |                  |
| +   | Calcium    | 0.159%           |
| +   | Phosphorous | 0.016%           |
| +   | Potassium  | 0.138%           |
| +   | Sodium     | 0.047%           |
| +   | Magnesium  | 0.088%           |
| 4.  | Trace metals |                |
| +   | Iron       | 0.262%           |
| +   | Zinc       | 0.0003%          |
| +   | Copper     | 0.00002%         |
| +   | Chromium   | 0.000022%        |
| 5.  | Soluble dietary fibers | 0.33%        |
| 6.  | Insoluble dietary fibers | 1.56%       |
| 7.  | Phyto acid | 0.00092%         |
| 8.  | Soluble oxalate | 0.02%            |
5.2. Use as a Food Additive

The highly aromatic leaves of *P. amboinicus* are used in cooking to enhance the taste and aroma of food. The herb is often used as a substitute for oregano in the food trade. The leaves of *P. amboinicus* are added when marinating food, for food stuffings [104] and for flavoring meat dishes, e.g., beef, lamb and chicken [105,106]. The strong oregano-like flavor of this herb is an excellent choice to disguise the smell of meat while enhancing the taste. It is also used for the same reason in seafood cuisines such as fish and shellfish [67] to mask the smell of fish, which may prevent someone from enjoying their meal. In addition to this, *P. amboinicus* is used to spice dishes containing tomato sauces [10]. In India, the leaves are sometimes eaten raw with bread and butter or added to fritters. The tender and soft leaves are crunchy and have an astringent taste when chewed raw. They also may be added to beer and wine for flavoring [67].

6. Ornamental and Other Social Uses

*P. amboinicus* is grown as an ornamental in home gardens and hanging baskets for its attractive heart-shaped foliage and expression of fresh aroma when touched [10]. The variegated version with white-edged leaves, *Plectranthus amboinicus* “Variegata”, looks particularly attractive as an ornamental plant, especially when planted in hanging baskets or grown as a garden border. This plant is resistant to diseases and is able to survive drought due to its succulent leaves which can retain water. They can grow beautifully with minimum maintenance. Added to their culinary and medicinal value, *P. amboinicus* makes a preferred potted plant in many home gardens. *P. amboinicus* has scented leaves and these are often rubbed into the hair and body after bathing to replace body odor with a refreshing scent [67]. Many health and wellness spas around the world use essential oils of this plant to induce a calming sensation for aromatherapy. In the Amazon, the leaves are mixed with sugar and used as an intoxicant [68]. Whereas, in Tonga and Martinique, the leaves are used for the cleaning of textiles and to perfume them [10,46]. *P. amboinicus* is also used for spiritual and religious purposes and offered to the spirits when a house is being built in some community [67].

7. Conclusions and Recommendations

*P. amboinicus* is an important aromatic medicinal herb packed with many bioactive constituents and nutrients, which are important for maintaining good health. The plant has shown a wide range of biological properties and proved to be effective in curing respiratory, cardiovascular, oral, skin, digestive and urinary diseases. The biological properties are attributed to the occurrence of a wide range of bioactive compounds in the plant extracts as well as an essential oil. Thus, it can be stated that *P. amboinicus* has huge future prospects in meeting the global demand for natural, cost-effective and safer bioactive molecules in pharmaceutical and nutraceutical industries. However, additional research efforts are required to isolate, identify and interpret or authenticate the effectiveness of bioactive compounds from *P. amboinicus*. Though several classes of phytocompounds are isolated and authenticated from this herb, their bioactivity and toxicity studies under *in vivo* conditions using animal models are limited to only a few compounds. Till now, no scientific evidence is available on the human safety aspects of *P. amboinicus* even though it is used widely in folk medicine. Further, some detailed investigations should be aimed at understanding the effectiveness of these isolated compounds in treating other human illnesses.

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Abbreviations

The following abbreviations are used in this manuscript:

- **SPME**: Solid phase micro extraction
- **GC**: Gas chromatography
- **LSC**: Liquid-solid chromatography
- **GLC**: Gas-liquid chromatography
- **GC-MS**: Gas chromatography-mass spectroscopy
- **GC-FID**: Gas chromatography outfitted with flame ionization detector (GC-FID)
- **NMR**: Nuclear magnetic resonance
- **UV**: Ultra violet
- **HPLC**: High pressure liquid chromatography
- **UPLC**: Ultra performance liquid chromatography
- **GAE**: gallic acid equivalent
- **TAE**: Tannic acid equivalent
- **RE**: Rutin equivalent
- **Pam-ZnO NPs**: *P. amboinicus* Zinc oxide nanoparticles
- **TNF-α**: Tumor necrosis factor
- **COX-2**: Cyclooxygenase 2
- **AP-1**: Activator protein-1
- **HWE**: Hot water extract (HWE)
- **HE**: Hexane extract
- **SDS-PAGE**: Sodium dodecyl sulfate polyacrylamide gel electrophoresis
- **HSV 1**: Herpes simplex virus-1
- **STDs**: Sexually-transmitted diseases
- **AIDS**: Acquired immune deficiency syndrome (AIDS)
- **HIV**: Human immunodeficiency virus
- **VSV**: Vesicular stomatitis virus

References

1. Kumara Swamy, M.; Pokharen, N.; Dahal, S.; Anuradha, M. Phytochemical and antimicrobial studies of leaf extract of *Euphorbia nerifolia*. *J. Med. Plants Res.* 2011, 5, 5785–5788.
2. Swamy, M.K.; Sinniah, U.R. A comprehensive review on the phytochemical constituents and pharmacological activities of *Pogostemon cablin* Benth.: An aromatic medicinal plant of industrial importance. *Molecules* 2015, 20, 8521–8547. [CrossRef] [PubMed]
3. Swamy, M.K.; Sinniah, U.R.; Akhtar, M.S. *In vitro* pharmacological activities and GC-MS analysis of different solvent extracts of *Lantana camara* leaves collected from tropical region of Malaysia. *Evid. Based Complement. Altern.* 2015, 1, 1–9. [CrossRef] [PubMed]
4. Sandhya, S.; Kumar, S.P.; Vinod, K.R.; David, B.; Kumar, K. Plants as potent anti-diabetic and wound healing agents: A review. *Hygeia. J. Drugs Med.* 2011, 3, 11–19.
5. Mohanty, S.K.; Malappa, K.; Godavarthi, K.; Subbanarasiman, B.; Maniyam, A. Evaluation of antioxidant, *in vitro* cytotoxicity of micropropagated and naturally grown plants of *Leptadenia reticulata* (Retz.) Wight & Arn.: An endangered medicinal plant. *Asian Pac. J. Trop. Med.* 2014, 7, 267–271.
6. Kumara, S.M.; Sudipta, K.M.; Lokesh, P.; Neeki, A.; Rashmi, W.; Bhaumik, H.; Darshil, H.; Vijay, R.; Kashyap, S.S.N. Phytochemical screening and *in vitro* antimicrobial activity of *Bougainvillea spectabilis* flower extracts. *Int. J. Phytochem.* 2012, 4, 375–379.
7. Retief, E. Lamiaceae (Labiatae). In *Seed Plants of Southern Africa*; Leistner, O.A., Ed.; National Botanical Institute: Cape Town, South Africa, 2000; pp. 323–334.
8. Alasbahi, R.H.; Melzig, M.F. *Plectranthus barbatus*: A review of phytochemistry, ethnobotanical uses and pharmacology—Part 1. *Planta Med.* 2010, 76, 653–661. [CrossRef] [PubMed]

9. Grayer, R.J.; Eckert, M.R.; Lever, A.; Veitch, N.C.; Kite, G.C.; Paton, A.J. Distribution of exudate flavonoids in the genus *Plectranthus*. *Biochem. Syst. Ecol.* 2010, 38, 335–341. [CrossRef]

10. Lukhoba, C.W.; Simmonds, M.S.J.; Paton, A.J. *Plectranthus*: A review of ethnobotanical uses. *J. Ethnopharmacol.* 2006, 103, 1–24. [CrossRef] [PubMed]

11. Castillo, R.A.M.; Gonzalez, V.P. *Plecthranthus amboinicus* (Lour.) Spreng. *Rev. Cuba. Plantas Med.* 1999, 4, 110–115.

12. Singh, G.; Singh, O.P.; Prasad, Y.R.; Lampsonosa, M.P.; Catalan, C. Studies on essential oils. Part 33. Chemical and insecticidal investigations on leaf oil of *Coleus amboinicus* (Lour). *Flavour Frag. J.* 2002, 17, 440–442. [CrossRef]

13. Murthy, P.S.; Ramalakshmi, K.; Srinivas, P. Fungitoxic activity of Indian borage (*Plectranthus amboinicus*) volatiles. *Food Chem.* 2009, 114, 1014–1018. [CrossRef]

14. Senthilkumar, A.; Venkatesalu, V. Chemical composition and larvicidal activity of the essential oil of *Plectranthus amboinicus* (Lour.) Spreng against *Anopheles stephensi*: A malarial vector mosquito. *Parasitol. Res.* 2010, 107, 1275–1278. [CrossRef] [PubMed]

15. Gonçalves, T.B.; Braga, M.A.; Oliveira, F.F.M. Effect of subinhibitory and inhibitory concentrations of *Plectranthus amboinicus* (Lour.) Spreng essential oil on *Klebsiella pneumoniae*. *Phytomedicine* 2012, 19, 962–968. [CrossRef] [PubMed]

16. Bhatt, P.; Negi, P.S. Antioxidant and antibacterial activities in the leaf extracts of Indian borage (*Plectranthus amboinicus*). *Food Nutr. Sci.* 2012, 3, 146–152. [CrossRef]

17. Khare, R.S.; Banerjee, S.; Kundu, K.K. *Coleus aromaticus* Benth. A nutritive medicinal plant of potential therapeutic value. *Int. J. Pharma. Bio. Sci.* 2011, 2, 488–500.

18. Wagner, W.L.; Lorence, D.H. Flora of the Marquesas Islands website. Available online: http://botany.si.edu/pacificislandbiodiversity/marquesasflora/index.htm (accessed on 18 January 2016).

19. Khan, M.C.P.I. *Current Trends in Coleus Aromaticus: An Important Medicinal Plant*; Booktango: Bloomington, IN, USA, 2013.

20. Roshan, P.; Naveen, M.; Manjul, P.S.; Gulzar, A.; Anita, S.; Sudarshan, S. *Plectranthus amboinicus* (Lour) Spreng: An overview. *Pharm. Res.* 2010, 4, 1–15.

21. Stearn, W.T. *Stearns Dictionary of Plant Names for Gardeners: A Handbok on the Origin and Meaning of the Botanical Names of Some Cultivated Plants*; Cassell: London, UK, 1992.

22. Roux, J.P. *Flora of South Africa*; Compton Herbarium: South African National Biodiversity Institute: Cape Town, South Africa, 2003.

23. Staples, G.W.; Kristiansen, M.S. *Ethnic Culinary Herbs: A Guide to Identification and Cultivation in Hawaii*; University of Hawaii Press: Honolulu, HI, USA, 1999.

24. Can Baser, K.H. Biological and pharmacological activities of carvacrol and carvacrol bearing essential oils. *Curr. Pharm. Design.* 2008, 14, 3106–3119. [CrossRef]

25. Pino, J.A.; Garcia, J.; Martinez, M.A. Comparative chemical composition of the volatiles of *Coleus aromaticus* produced by steam distillation, solvent extraction and supercritical carbon dioxide extraction. *J. Essent. Oil Res.* 1996, 8, 373–375. [CrossRef]

26. Knab, A.; McKinney; Heather, E.; Maurer; Marta, K. Isolation of the compounds. In *Mentha piperita, Mentha spicata and Coleus amboinicus*; Abstracts of Papers, 238th ACS National Meeting; Washington, DC, USA, 2008; pp. 16–20.

27. Rout, O.P.; Acharya, R.; Mishra, S.K.; Sahoo, R. Pathorchur (*Coleus aromaticus*): A review of the medicinal evidence for its phytochemistry and pharmacology properties. *Int. J. Appl. Biol. Pharm. Technol.* 2012, 3, 348–355.

28. Asiimwe, S.; Borg-Karlsson, A.K.; Azeem, M.; Mugisha, K.M.; Namutebi, A.; Gakunga, N.J. Chemical composition and Toxicological evaluation of the aqueous leaf extracts of *Plectranthus amboinicus* (Lour.) Spreng. *Int. J. Pharm. Sci. Invent.* 2014, 3, 19–27.

29. Mallavarapu, G.R.; Rao, L.; Ramesh, S. Essential oil of *Coleus aromaticus* Benth. *Int. J. Essent. Oil. Res.* 1999, 11, 742–744. [CrossRef]
30. Gurib-Fakim, A.; Sewraj, M.D.; Narod, F.; Menut, C. Aromatic Plants of Mauritius: Volatile Constituents of the Essential Oils of Coleus aromaticus Benth., Triphasia trifolia (Burm. f.) and Eucalyptus kirtontiana (F. Muell.). J. Essent. Oil Res. 1995, 7, 215–218. [CrossRef]
31. Hassani, M.S.; Zainati, I.; Zrira, S.; Mahdi, S.; Oukessou, M. Chemical Composition and Antimicrobial Activity of Plectranthus amboinicus (Lour) Spring. Essential Oil from Archipelago of Comoros. J. Essent. Oil Bear. Pl. 2012, 15, 637–644. [CrossRef]
32. Erny Sabrina, M.N.; Razali, M.; Mirfat, A.H.S.; Mohd Shukri, M.A. Antimicrobial activity and bioactive evaluation of Plectranthus amboinicus essential oil. Am. J. Res. Commun. 2014, 2, 121–127.
33. Koba, K.; Garde, D.; Sando, K.; Raynaud, C.; Chaumont, J.P. Chemical composition and antimicrobial properties of the leaf essential oil of Coleus aromaticus Benth. From Cambodia. Inter. J. Essent. Oil Ther. 2007, 1, 16–20.
34. Joshi, R.K.; Badakar, V.; Kholkute, S.D. Carvacrol rich essential oils of Coleus aromaticus (Benth.) from Western Ghats region of North West Karnataka, India. Adv. Environ. Biol. 2011, 5, 1307–1310.
35. Dutta, S. Essential oil of Coleus amboinicus of Indian origin. Indian Oil Soap J. 1959, 25, 120.
36. Baslas, R.K.; Kumar, P. Chemical examination of essential oil of Coleus aromaticus Benth. J. Indian Chem. Soc. 1981, 58, 103–104.
37. Mangathayaru, K.; Pratap, D.V.V.; Thirumurgan, D.; Patel, P.S.; David, D.J.; Karthikeyan, J. Essential oil composition of Coleus amboinicus Lour. Indian J. Pharma. Sci. 2005, 67, 122–123.
38. Prudent, D.; Perineau, F.; Bessiere, J.M.; Michel, G.M.; Baccou, J.C. Analysis of the essential oil of wild oregano from Martinique (Coleus aromaticus Benth.): Evaluation of its bacteriostatic and fungistatic properties. J. Essent. Oil Res. 2012, 15, 174–179. [CrossRef]
39. El-hawary, S.S.; El-sofany, R.H.; Abdel-Monem, A.R.; Ashour, R.S. Phytochemical Screening, DNA Fingerprinting, and Nutritional Value of Plectranthus amboinicus (Lour.) Spreng. Pharmacogn. J. 2012, 4, 10–13. [CrossRef]
40. Chiu, Y.J.; Huang, T.H.; Chiu, C.S.; Lu, T.C.; Chen, Y.W.; Peng, W.H.; Chen, C.Y. Analgesic and anti-inflammatory activities of the aqueous extract from Plectranthus amboinicus (Lour.) Spreng. both in vitro and in vivo. Evid Based Complement. Altern. Med. 2012, 2012, 1–11.
41. Bhatt, P.; Joseph, G.S.; Negi, P.S.; Varadaraj, M.C. Chemical composition and nutraceutical potential of Indian borage (Plectranthus amboinicus) stem extract. J. Chem. 2013, 2013, 1–7. [CrossRef]
73. Lima, M.A.; Oliveira, F.F.M.; Gomes, G.A.; Lavor, P.L.; Santiago, G.M.; Nagao-Dias, A.T.; Arriaga, A.M.; Lemos, T.L.; Carvalho, M.G. Evaluation of larvicidal activity of the essential oils of plants species from Brazil against *Aedes aegypti* (Diptera: Culicidae). *Afr. J. Biotecnol.* 2011, 10, 11716–11720.

74. Baranitharan, M.; Dhanasekaran, S. Mosquitocidal efficacies of medicinal plant of *Coleus aromaticus* Benth (Lamiaceae) leaf extracts Chikungunya vector, *Aedes aegypti* (Linn.) (Diptera: Culicidae). *Int. J. Curr. Res. Chem. Pharm. Sci.* 2014, 1, 61–67.

75. Jayaraman, M.; Senthilkumar, A.; Venkatesalu, V. Evaluation of some aromatic plant extracts for mosquito larvicidal potential against *Culex quinquefasciatus*, *Aedes aegypti*, and *Anopheles stephensi*. *Parasitol. Res.* 2015, 114, 1511–1518. [CrossRef] [PubMed]

76. Santos, F.A.V.; Serra, C.G.; Roberto, J.A.C.; Figueredo, F.G.; Matias, E.F.F.; Menezes, R.A.; Jose, G.M.; Henriques, D.M. Antibiacterial activity of *Plectranthus amboinicus* Lour (Lamiaceae) essential oil against *Streptococcus mutans*. *Eur. J. Integr. Med.* 2015. [CrossRef]

77. Ong, H.C.; Nordiana, M. Malay ethno-medico botany in Machang, Kelantan, Malaysia. *Fitoterapia* 1999, 70, 502–513. [CrossRef]

78. Gurgel, A.P.; da Silva, J.G.; Grangiero, A.R.; Oliveira, D.C.; Lima, M.P.; Silva, A.C.; Oliveira, A.G.; Souza, I.A. *In vivo* study of the anti-inflammatory and antitumor activities of leaves from *Plectranthus amboinicus* (Lour.) Spreng (Lamiaceae). *J. Ethnopharmacol.* 2009, 125, 361–363. [CrossRef] [PubMed]

79. Ramalakshmi, P.; Subramanian, N.; Saravana, R.; Mohanakrishnan, H.; Muthu, M. Anticancer effect of *Coleus aromaticus* (Karpoovali) on human lung cancer cell line (A549). *Int. J. Dev. Res.* 2014, 4, 2442–2449.

80. Silitonga, M.; Ilyas, S.; Hutahaean, S.; Sipahutar, H. Levels of apigenin and immunostimulatory activity of *Punica granatum* leaf extracts. *Int. J. Dev. Res.* 2010, 9, 369–373. [CrossRef]

81. De Padua, L.S. Some Medicinal Plants for Common Ailments; Techguid Series No. 14; National Book Store, Inc.: Mandaluyong, Philippines, 1988.

82. Githinji, C.W. Ethnobotanical and Chemotaxonomic Study of Some Kenyan Medicinal Labiate Species. Master’s Thesis, University of Nairobi, Kenya, 1990.

83. Githinji, C.W.; Kokwaro, J.O. Ethnomedicinal study of major species in the family Labiatae from Kenya. *J. Ethnopharmacol.* 1993, 39, 197–203. [CrossRef]

84. Warriner, R.; Burrell, R. Infection and the chronic wound: A focus on Silver. *Adv. Skin Wound Care* 2005, 18, 2–12. [CrossRef] [PubMed]

85. Sunitha, K.S.; Haniffa, M.A.; Milton, M.J.; Manju, A. *Coleus aromaticus* Benth act as an immunostimulant in *Channa marulius*. *Int. J. Bio. Tech.* 2010, 1, 55–59.

86. Jain, A.K.; Dixit, A.; Mehta, S.C. Wound healing activity of aqueous extract of leaves and roots of *Coleus aromaticus* in rats. *Acta Pol. Pharm. Drug. Res.* 2012, 69, 1119–23.

87. Soni, H.; Nayak, G.; Patel, S.S.; Mishra, K.; Singhai, A.K. Synergistic effect of polyherbal suspension of *Punica granatum* and *Coleus aromaticus* in evaluation of wound healing activity. *J. Herb. Med. Toxicol.* 2011, 5, 111–115.

88. Hole, R.C.; Juvekar, A.R.; Roja, G.; Eapen, S.; D’Souza, S.F. Positive inotropic effect of the leaf extracts of parent and tissue culture plants of *Coleus amboinicus* on an isolated perfused frog heart preparation. *Food Chem.* 2009, 70, 119–123. [CrossRef]

89. Franca, F.; Lago, E.L.; Marsden, P.D. Plants used in the treatment of leishmanial ulcers due to *Leishmania* (*Viannia*) *braziliensis* in an endemic area of Bahia, Brazil. *Rev. Soc. Bras. Med. Trop.* 1996, 29, 229–232. [CrossRef]

90. Harsha, V.H.; Hebbar, S.S.; Shripathi, V.; Hedge, G.R. Ethnomedicobotany of Uttara Kannada District in Karnataka, India; plants in treatment of skin diseases. *J. Ethnopharmacol.* 2003, 84, 37–40. [CrossRef]

91. Bhat, P.; Hegde, G.; Hegde, G.R. Ethnomedicinal practices in different communities of Uttara Kannada district of Karnataka for treatment of wounds. *J. Ethnopharmacol.* 2012, 143, 501–514. [CrossRef] [PubMed]

92. Selvakumar, P.; Naveena, B.E.; Prakash, B.D. Studies on the antidiarrheal activity of the essential oil of *Coleus amboinicus* and *Eucalyptus globulus*. *Asian Pac. J. Trop. Med.* 2012, 5, S715–S719. [CrossRef]

93. Uawonggul, N.; Chaveerach, A.; Thammasirirak, S.; Arkaravichien, T.; Chuachan, C.; Daduang, S. Screening of plants acting against *Heterometrus laoticus* scorpion venom activity on fibroblast cell lysis. *J. Ethnopharmacol.* 2006, 103, 201–207. [CrossRef] [PubMed]

94. Bhattacharjee, P.; Majumder, P. Investigation of phytochemicals and anti-convulsant activity of the plant *Coleus amboinicus* (Lour.). *Int. J. Green Pharm.* 2013, 7, 211–215.
95. Yoganarasimhan, S.N. *Medicinal Plants of India, Tamil Nadu*; Srinivasan, V., Kosal Ram, N., Eds.; Cyber Media: Bangalore, India, 2000.

96. Orient Longman. *Indian Medicinal Plants*; Microprint: Madras, India, 1995.

97. Jose, A.M.; Ibrahim; Janardhanan, S. Modulatory effect of *Plectranthus amboinicus* Lour. on ethylene glycol-induced nephrolithiasis in rats. *Indian J. Pharmacol.* 2005, 37, 43–44. [CrossRef]

98. Patel, R.; Mahobia, N.K.; Gendle, R.; Kaushik, B.; Singh, S.K. Diuretic activity of leaves of *Plectranthus amboinicus* (Lour) Spreng in male albino rats. *Pharmacogn. Res.* 2010, 2, 86–88. [CrossRef] [PubMed]

99. Kumaran, A.; Karunakaran, J. Antioxidant and free radical scavenging activity of an aqueous extract of *Coleus aromaticus*. *Food Chem.* 2006, 97, 109–114. [CrossRef]

100. Khanum, H.; Ramalakshmi, K.; Srinivas, P.; Borse, B.B. Synergistic antioxidant action of Oregano, Ajowan and Borage extracts. *Food Nutr. Sci.* 2011, 2, 387–392. [CrossRef]

101. Harsha, V.H.; Hebbar, S.S.; Hegde, G.R.; Shripathi, V. Ethnomedical knowledge of plants used by Kunabi tribe of Karnataka in India. *Fitoterapia* 2002, 73, 281–287. [CrossRef]

102. Neuwinger, H.D. *African Traditional Medicine. A Dictionary of Plant Use and Applications*; Medpharm Scientific Publishers: Stuttgart, Germany, 2000; pp. 406–408.

103. Zepernick, B. *Arzneipflanzer der Polynesier*; Dietrich Reimer: Berlin, Germany, 1972.

104. Purseglove, J.W. *Tropical Plants. Dicotyledons*; Longman Scientific & Technical: London, UK, 1987.

105. Bodner, C.C.; Gereau, R.E. A contribution to Bontoc ethnobotany. *Econ. Bot.* 1988, 42, 307–369. [CrossRef]

106. Brown, D. Grenada: Isle of spices. *Herbs* 1997, 22, 6–7.

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