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Review paper

Cambodian medicinal plants: an overview

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ABSTRACT

Context: Medicinal plants in Cambodia have been used to cure various conditions and illnesses. Objective: To review the therapeutic activities and properties of Cambodian medicinal plants. **Methods:** A keyword search was conducted in 2023, using databases like PubMed, Google Scholar, and Science Direct. Keywords included " Cambodia*, " " medic*, " " plant*, " " pharmacognosy, & quot; " ethnopharmacology, " and & quot;ethnobotanical. " Articles selected were published within the last 30 years. The analysis followed PRISMA guidelines. **Results:** Most of the research focused on laboratory experiments with plant extracts; the balance relied on surveys to collect local knowledge about Cambodian medicinal plants. Demonstrated were diverse therapeutic effects addressing cardiac issues and liver diseases to malaria and chronic illnesses. Laboratory experiments demonstrated multiple activities from antimicrobial and anti-malarial to anti-cancer. Ethnobotanical research provided insights into plant names, habitats, descriptions, and medicinal uses, detailing treatment methods and dosages. **Conclusion:** Cambodian medicinal plants, known for their safety and effectiveness, can complement traditional treatments and Westernmedicine for various illnesses. However, limited research calls for further exploration to uncovernew bioactive compounds with therapeutic properties.

***Keywords**:* Cambodia, ethnobotanical, ethnopharmacology, pharmacognosy,

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INTRODUCTION

Medicinal plants have played an important role in maintaining the healthcare structure in both developing and developed countries that utilize knowledge of traditional medicine (Ullah et al., 2020). Since ancient times, ten percent of the worlds known vascular plants have been used for therapeutic purposes. Civilizations have known their therapeutic properties and employed them as traditional medicine since the 18th century (Salmerón-Manzano et al., 2020). Rural communities throughout the world have been using plants as traditional medicines since ancient times and continue to do so today as an important alternative to Western therapy (Phumthum et al., 2018). The area of Cambodia is 181,035 square kilometers and is surrounded to the west by Thailand, the north by Laos, and the east by Vietnam (Cui et al., 2020). Cambodia resides in a regional tropic at 10 and 14° latitude north of the equator, and it has a warm and moist temperature (MoE, 2009). The annual regular climate and moisture are at 25 to 30°C and 80 to 90%, respectively (World Bank, 2021). Cambodia is famous for its affluent biodiversity, a unique ecosystem and an array of natural resources found within its forests. This includes a wide variety of wildlife, wood fuels such as charcoal production and common firewood, as well as many plants used for the purposes of traditional medicine (MoE, 2016). Within the country, almost 1,200 medicinal plants have been used to cure diseases (Cui et al., 2020). In Cambodia, medicinal plants have been used for approximately a thousand years to cure a wide array of conditions and illnesses. They are used widely and are considered effective therapy and safe (Chassagne et al., 2017). In Cambodia, patients mostly use them to treat chronic diseases with approximately half of the population using one form of medicinal herbs in the last 12 months (Pearson et al., 2018). Studies have identified Cambodian medicinal plants' fundamental phytochemical constituents as being flavonoids, tannins, alkaloids, and phenolic acids which have various bioactive properties. These include anti-diabetic, antifungal, anti-cancer, anti-oxidant, anti-allergic, anti-microbial, anti-inflammatory and anti-rheumatic properties (Chhouk et al., 2018).There is little information on the origin of traditional medication in Cambodia, but strong evidence proposes that indigenous medicine was developed during the Angkor period from preexisting Ayurvedic and Chinese medicine procedures and practices. It is well documented that the local population created a medical system that relied primarily on natural products (Ashwell & Walston, 2008). During the Angkor period from 9 to 15 century AD, indigenous Khmer medicine was developed by borrowing from Ayurvedic and Chinese medicine systems. Insight into the history of Angkor period Khmer medicine stems from the architectural and archaeological data surviving from that era. The Khmer temple, called Neak Poan, which was built under the Buddhist King Jayavarman VII (1181 – 1218) served as the Angkorian seat of traditional medicine. The surviving ruins of the hospital attest to the strong Indian influence on the medical practices of the day (Wiart, 2002). Because Western teachings were banned during the Khmer Rouge regime during the 1970s, traditional remedies were the only medical care available to the local population. Following the fall of the Khmer Rouge regime in 1979, Khmer traditional medicine was formally encouraged and promoted by the Cambodian government. This was primarily due to the fact that those with knowledge of Western medical practices had either been killed or had fled the country during the period

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(Ashwell & Walston, 2008). Currently, at least 40-50% of the population in rural or remote areas of Cambodia still depend on traditional medicine. This is particularly true among elder family members who compound their own mixture of medicine or seek cures from traditional healers called "Kru Khmer". Current biomedicine is only considered as the last option for this group of the population (Richman et al., 2010, Lim et al., 2022). Traditional Khmer Medicine uses plants, animals, and minerals with a combination of local beliefs and superstition to create a unique medical system (Keo et al., 2018). For almost a thousand years, many locals have considered Khmer traditional medicine which is based on a variety of remedies and practices, as the major medical system in Cambodia. In 1997 the government gave validity and status to Khmer medicine by constructing the National Center of Traditional Medicine (NCTM) in the capital city of Phnom Penh. The NCTM's aim is to promote traditional medical knowledge and to ensure the quality, safety, and efficacy of traditional medicine products. About 250 traditional healers from all over the country were trained at NCTM from 2009 to 2012. The course of training was created to share and improve knowledge of traditional medicine. This includes information on medicinal plants, pharmaceutical formulation, marketing, and basic medical education. Currently, they also strive to promote the safety and efficacy of accepted practices, as well as licensing the practitioners of traditional medicine (Chassagne et al., 2017). A particular type of shaman called a 'ruup' (physical body) is a medium that acts as an intermediate between the physical world and one's spirit by using guidance from the spirit to treat various ailments. This approach to healthcare continues to be practiced in remote areas across Cambodia. A traditional healer called Kru Khmer (Khmer teacher) is a person who is occasionally called upon to cure or treat patients by using traditional medicine at their home or that of the patients. They may use remedies such as liquid spraying, traditional medicine grinding, scarification, and body pinching (Chassagne et al., 2017). They treat their patients using medicaments prepared by mixing various products mostly derived from medicinal plants. Each Kru Khmer specializes in the treatment of a particular ailment or complaint (Hiegel, 1981). Treatments are derived from a large variety of herbal plants and are then delivered to the patient by medical assistants, nurses, village health workers, or midwives without physician supervision. This approach to treatment is not recognized by Western doctors and is inconceivable in the Western medical field (Richman et al., 2010). Local people use different parts of various plants including the leaves, fruit, or flowers to manage different illnesses and disorders. These conditions include fever, pain, cough, headache, malaria, stomach complaints, wounds, burns, backache, or diarrhea (Keo, Dim, et al., 2018). Traditional medicine may use medicinal plants to treat various bacterial complications such as urinary tract infections, bronchitis, and cutaneous abscesses (Chea et al., 2007). In the past, several studies have been conducted on Cambodian Medicinal Plants. So far, there has not been any credible reviews conducted on the properties and therapeutic activities of the commonly used plants. In order to properly devise a collaboration plan that will guide any future research agendas, it needs to be determined what credible research has already been conducted and what the imitations of those studies may be. This study aims to review the traditionally used Cambodian herbs and identify them by their locally used names and what individual plant parts are used. Additionally, we aim to recognize by what form the medication is administered as well as the method employed by Cambodian healers to treat various diseases.

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MATERIALS AND METHODS

An integrative review was undertaken, which combined experimental and non-experimental studies with theoretical and empirical data to provide an in-depth and structured review of the topic. A key word search using the words Cambodia, Medicinal, Plant, Pharmacognosy, Ethnopharmacology, and Ethnobotanical to search databases including PubMed, Google Scholar, and Google from August 01 to September 30, 2023. The inclusion criteria to select articles were full articles published in Khmer, English, and French from 2006 to 2023. Analysis and synthesis of the articles were undertaken using the PRISMA guidelines and reporting list. The flow diagram of the review id given Figure 1.

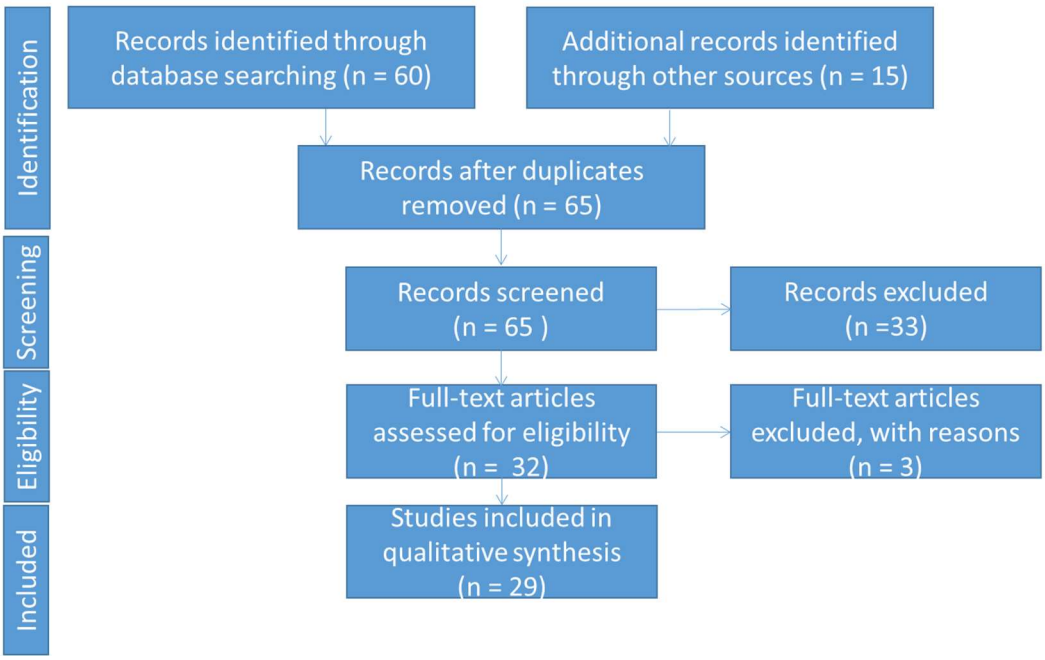

Figure 1. Flow diagram

RESULTS

The results presented within this study present the most widely utilized families of medications used by the indigenous and local people in Cambodia (Table 1). The review reported that 58 families and 212 species of plants have been safely used as natural products in the Cambodian common traditional medical system. The highest number of species was found in the Fabaceae family. This included 22 species of herbal plants. Traditional medical plants are sources of antimicrobial drugs that are commonly used to treat bacterial infections, illnesses, and wounds. Based on the reports reviewed, the most frequently used arrangement method of Cambodian plants meant to serve as alternative medicine was decoction. Moreover, leaves, whole

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plants, seeds, and aerial parts were the most commonly employed plant parts used during the preparation of Khmer traditional medicine. Roots, stems, bulk, fruits, and bark are also used as well. According to the study conducted by Hout et al. 2006, various plant extractions were tested for their *in vitro* activity against a chloroquine-resistant strain of *Plasmodium falciparum* (W2). Out of the total 26 extractions obtained from 8 plants belonging to 6 different families, it was found that nine extractions exhibited slight activity, with IC_{50} values ranging between 5 and 10 micrograms/ml. Additionally, seventeen extractions demonstrated effectiveness, with IC50 values falling within the range of 1 to 5 micrograms/ml. These findings suggest the potential of these plant extractions as candidates for further investigation in the development of anti-malarial treatments. In the study of Chea, Hout, et al., 2007, *Stephania rotunda* Lour. (កុមារពេជ្រ/komaPéch) was investigated, revealing that alkaloid dehydroroemerine, cepharanthine (SA), and SD1 (dichloromethane extracts from this plant) exhibited notable activities against *Plasmodium falciparum* W2, with IC50 values of 0.36, 0.61 µM, and 0.7 µg/ml, respectively. Their IC50 values on human monocytic THP1 cells were 10.8 µM, 10.3 µM, and >250 µg/mL, respectively. Administration of SD1 and SA at a dose of 150 mg/kg resulted in a reduction of parasitemia by 89% and 74% respectively through intra-peritoneal injection and by 62.5% and 46.5% respectively through oral administration. Cepharanthine at a dose of 10 mg/kg showed a decrease of 47% of parasitemia through intra-peritoneal injection and 50% through oral administration. The study conducted by Seng et al. 2007 has provided limited evidence suggesting an anthelmintic effect of *Manihot esculenta* Crantz. (known as ដំឡងមី or damlong mee) when included in the diet of goats. During the study, goats were fed with *Manihot esculenta* Crantz. for three weeks starting from the larval dosing period initiation and three weeks after the worm infection. It was observed that this dietary inclusion led to a beneficial effect on Faecal Egg Counts (FEC) by reducing the number of eggs noted in the feces. In the study of Chea et al., 2007, reference antibiotics were employed as positive controls for each strain, while blank disks soaked in dimethyl sulfoxide (DMSO) served as negative controls. Minimal Inhibitory Concentration (MIC) and Minimal Bactericidal Concentration (MBC) were determined. Among the 27 tested plants, only *Costus speciosus* (J.Koening) Sm. (ត្រចុក/trothok*)* and *Flueggea virosa* (Roxb. ex Wild.) Royle (លាជផ្ទះ/liëchPhtuhs) demonstrated activity against E. coli, with 25 extracts exhibiting strong activity as evidenced by a diameter of inhibition zone greater than 10 mm in the disk diffusion method. However, none of the extracts showed activity against *P. aeruginosa*. In the study by Jonville et al., 2008, a scoiridoid aglycone with an unusual skeleton named fagraldehyde (1), was isolated along with several known secoiridoids, gentiopicroside (2), sweroside (3), and swertiamarin (4) from the bark and leaves of *Fagraea* fragrans Roxb. (តាត្រាវ/Tatrav) collected in Cambodia. Compound 1 exhibited weak activity, with an IC50 value against *P. Falciparum* W2=22.4+/-1.8 µg/ml. According to the study of Chea et al., 2010, all of the tested alkaloids, including 2-norcepharanthine, cepharanoline, and fangchinoline, exhibited significant activity against a chloroquine-resistant *P. falciparum* strain (W2), with IC50 values of 0.3, 0.2, and 0.3 mM, respectively, and yielded a selectivity index (SI) of 41, 61, and 40, respectively. These findings are particularly noteworthy compared to the IC50 value obtained for cepharanthine in their previous study (IC50= 0.61Mm).

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Based on the study by Laval et al., 2011, it was found that 96% of the interviewees reported using medicinal plants. Among these, 81% of households used them for treating diseases, 71% consumed them daily for illness prevention, and 64% utilized them for alleviating pains associated with pregnancy and childbirth. The most common uses of medicinal plants were for treating malaria, colds, stomachaches, and headaches. The study conducted by Khay et al. 2012 revealed that *Vernonia cinerea* (L.) Less. (ស្មៅរុយ/smavruy) exhibited the most promising cytotoxic activity, followed by *Dracaena cambodiana* Pierre ex Gagnep. (អង្រែដែក/angraèdaèk) and *Harrisonia perforata* (Blanco) Merr. (ដើមទន្ទ្រានព្រៃ/daemtuntrien prey). Dichloromethane extracts from the roots of *D. cambodiana* (root) and the bark and roots of *Harrisonia perforata* (Blanco) Merr. demonstrated significant cytotoxic activity against the HT29 cell line, with a cell viability prevalence of 23.3%. Furthermore, moderate cytotoxic activity against the Hep G2 cell line was observed from three bark extracts of *H. perforata*. Dichloromethane extracts came from both the bark and root, with cell viability prevalences of 44.7%, 38% and 41.1%, respectively. These findings indicate the potential cytotoxic effects of these plant extracts, particularly against specific cancer cell lines. The study conducted by Keo et al. 2012 identified significant cytoprotective effects in eight ethanol extractions. Specifically, the bark of *Anacardium occidentale* L. (ស្វាយចន្ទី/svaychanti), bark and sapwood of *Bauhinia pulla* Craib (ខ្លែងពណ៌/khlengpor), flower of *Borassus flabellifer* L. (ត្នោត/thnaot), stems and leaves of *Coix lacryma-jobi* L. (ស្លួយ/skuey), bark and sapwood of *Diospyros nitida* Merr. (ឈើភ្លើង/chheuphleung), sapwood of *Dipterocarpus obtusifolius* Teijsm. Ex Miq. (ត្បែង/tbeng), stems of *Oryza rufipogon* Griff. (ស្រែដែ/sraa nae), and fruit of *Phyllanthus emblica* L. (កន្ទួតព្រៃ/kantuot prey) demonstrated important cytoprotective properties against glutamate-induced cell damage and deterioration in HT22 cells. These findings suggest the potential of these plant extracts in protecting cells from oxidative stress and neuronal damage, which could have implications for neuroprotection and related research areas. The study of Baghdikian et al., 2013 showed that a novel aporphine alkaloid called vireakin (2) was discovered, alongside two previously identified alkaloids, stephanine (1) and pseudopalmatine (8). Additionally, five known alkaloids tetrahydropalmatine (3), xylopinine (4), roemerine (5), cepharanthine (6) and palmatine (7) were isolated and identified. All tested compounds exhibited significant antiplasmodial activities, with IC(50) values ranging from 1.2 μM to 52.3 μM. Notably, pseudopalmatine displayed a particularly promising selectivity index, with an IC(50) greater than 25 μM against K562S cells.

The study conducted by Ningsih, 2014 demonstrated that the leaf of *Plumeria acutifolia* (Poir.) Woodson (ចំប៉ី/champy) was extracted with a concentration of 100 ppm to inhibit the growth of the bacteria *Staphylococcus aureus*. An inhibition zone of 1.33 mm was observed, indicating effective prevention of bacterial growth. Furthermore, it was found that a concentration as low as 30 ppm also exhibited inhibitory effects, suggesting that even lower concentrations of the extract could potentially inhibit bacterial growth. Based on the study of Kouloura et al., 2014 it was revealed that the traditional medical use of *Micromelum falcatum* (Lour.) Tanaka (រលាយស្មង/romleaysmorng) can be attributed to its anti-inflammatory properties. This assertion was supported by the significant inhibition of nitric oxide (NO) production observed in the ethyl acetate (EtOAc) extraction of the plants.

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Interestingly, despite the presence of representative coumarin derivatives in the assays, they did not exhibit significant anti-inflammatory activity. These findings suggest that the observed anti-inflammatory properties are likely due to other compounds present in the EtOAc extraction of *Micromelum falcatum* (Lour.) Tanaka., highlighting the complexity of its pharmacological effects. The study conducted by Grape V.H. et al., 2016 involved interviews with mothers, focus group discussions, and the collection of voucher specimens of postpartum plants. A total of sixty-eight plant species from 33 families were documented, with the most prevalent families being *Rubiaceae* (n=10), *Lauraceae* (n=4), *Leguminosae* (34.2%), used for improving blood circulation (25.7%), and stimulating milk production (22.8%). These findings shed light on the diverse array of plant species utilized by mothers for various postpartum health purposes and highlights the importance of traditional botanical knowledge in maternal care practices. The study conducted by Chassagne et al., 2016 revealed that the Bunong people utilize a diverse range of 214 plants in 72 families, along with 1 mushroom and 22 animals, for treating various illnesses. Among these, the *Fabaceae* family was the most commonly used for medicinal use. Specific plants such as *Chromolaena odorata* (L.) R.M.King & H.Rob. (កន្ត្រោនខេត្ត/kantraingkhaet) from *Asteraceae* family, *Zingiber montanum* (J.Koening) Link ex A.Dietr. (ពន្លៃ/pun lai) from the *Zingiberaceae* family, and *Kalanchoe pinnata* (Lam.) Pers. (កបិលភ័ស/kabellapoahs) from the *Crassulaceae* family were highlighted for their efficacy in treating four prevalent illnesses: diarrhea, cold/fever, stomachache, and postpartum disorders. These are common ailments within their community. These findings underscore the rich traditional knowledge of medicinal plants among the Bunong people and highlight the importance of preserving and understanding their indigenous healthcare practices. The study by Garcia T. et al., 2017 demonstrated that 30% of the medication utilized by communities to address and alleviate postpartum ailments came from traditional plants. These ailments included appetite stimulation, promoting milk production, enhancing blood circulation, and reducing uterine size. Additionally, these plants were also employed to manage fever (20%), skin issues (17%), and stomach problems (10%). Examining 83 plant families, the most frequently encountered ones were Leguminosae (10%), followed by Rubiaceae (8%), Annonaceae (4%), Apocynaceae (4%), Malvaceae (4%), and Dipterocarpaceae (3%). These findings provide insights into the utilization of medicinal plants by both the Kuy and Khmer communities in Prey Lang, Cambodia, and highlight their reliance on specific plant families for various healthcare needs. The studies of Lee et al., 2017 revealed significant hepatoprotective activities in nineteen plant extracts. These plants include *Ampelocissus martini* (Planch.) (ទំពាំងបាយដូព្រៃ/tumpeangbaaychuu prey), *Bauhinia bracteata* (Benh.) Graham ex Baker (ខ្លែងពណ៌/kleynpoa), *Bombax ceiba* L. (រកា/roka), *Borassus flabellifer* L. (ត្នោត/taout), *Cardiospermum halicacabum* L. *(*អំបែងបែក*/ambeng bek)*, *Cayratia trifolia* (L.) Domin *(*វល្លិក្រដែត*/voatradet)*, *Cinnamomum caryophyllus* (Lour.) S. Moore (ក្រវានដើម/kravanhdaem), *Cyperus rotundus* (L,) (ស្មៅក្រវាញជ្រូក/smavkravvanchruuk), *Dasymaschalon lomentaceum* Finet & Gagnep. (ជើងចាប/Cheung chap), *Ficus benjamina* L. (ជ្រៃក្រឹម/chreykrem), *Mangifera duperreana* Pierre (ស្វាយព្រៃ/svaay prey), *Morinda citrifolia* L. (ញស្រុក/ñoosrok), *Pandanus humilis* Lour. (រំចេកស្រុក/rumchaeksrok), *Peliosanthes weberi* (L.Rodr.) N.Tanaka (ត្បាលដែក/thbaldaek*)*, *Phyllanthus emblica* L.

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(កន្ទួតព្រៃ/kantut prey), *Quisqualis indica* L. (ដើមសក់សេះ/daemsakset), *Smilax glabra* Roxb. (ប៉ប្រើស/papraha), *Tinospora crispa* (L.) Hook.f. & Thomson (បណ្ដូលពោធ្រ/bânndôôlpéch), and *Willughbeia cochinchinensis* (Pierre) K.Schum. (វល្លិគុយ/voakuy). These extracts exhibited a partial maximum efficient combination scope ranging from 59.23 to 157.80µg/ml. This indicates their potential efficacy in protecting the liver from various damaging agents. The study by Chassagne et al., 2017, identified 42 herbal medicines among 83 medicinal plants from 40 families that were used to treat liver disorders. The main families with the most indicated plants included Leguminosae and Poaceae. Some of the prominently used plants were *Cananga latifolia* Finet & Gagnep. (ឆ្កែស្រែង/chhkaesraen), *Andrographis paniculata* (Burm.f.) Wall. Ex Nees (ស្មៅប្រម៉ាត់មនុស្ស/smavbramat moa nuh), *Smilax* glabra Roxb. (ប៉ប្រើស/paprashs), *Gomphrena celosioides* Mart. (ស្មៅក្រចៀកទន្សាយ/pkaatoumhou), *Passiflora foetida* L. (ស៉ាវម៉ាវព្រៃ/saavmaav prey), and *Physalis minima* L. (ប៉េងបោះស្រោម/peng poasrom). These medicinal plants were often utilized in multiple-ingredient recipes and were typically administered via oral decoction. This indicates the significance of traditional herbal remedies in addressing liver-related ailments and highlights the importance of multiple-ingredient formulations in traditional medicine practice. The study by Keo et al., 2017, identified various compounds present in different plants parts of several medicinal plants. These include tannins, phenolic, steroids, flavonoids, cardiac, glycosides, terpenoids, and saponins. Resins were found in leaves of *Nicotiana tabacum* L. (ថ្នាំជក់/tnamchoek), whole plant of *Vernonia cinerea* (L.) Less. (ស្មៅរុយ/smavruy), barks of *Azadirachta indica* A.Juss (ស្ដៅ/sdav), leaves of *Annona muricata* L. (ទៀបចារាំង/tiebbarang), rhizomes *of Zingiber cassumunar* Roxb. (ពន្លៃ/pun lai), and rhizomes of *Curcuma longa* L. (រមៀត/rameut). These findings highlight the diverse array of bioactive compounds present in these traditional medicinal plants, which may be contributing to their perceived pharmacological activities and therapeutic properties. The study of Tang et al., 2017, investigated the effects of *Moringa oleifera* Lam. (ម្រុំ/morum) extract on diabetic mice. C57BLS/J lar-m+/Leprdb mice were treated with 150mg/kg of the *Moringa oleifera* Lam. leaf extract. The results showed that *Moringa oleifera* Lam. treatment significantly improved various parameters compared to the control group. Specifically, the study observed notable improvements in altered fasting plasma glucose levels, which decreased from 483 to 312 mg/dL, triglyceride levels which decreased from 42.12 to 23 mg/dl, low-density lipoprotein cholesterol levels which decreased from 107.21 to 64.25 mg/dl, and insulin level increase from 946-92 to 1678-268 mg/ml. Moreover, the histopathological damage and expression level of inflammatory markers such as tumor necrosis factor-alpha, interleukin (IL)-1b, IL-6, cyclooxygenase-2, and inducible nitric oxide synthase in renal tissue were reduced. These findings suggest the potential antidiabetic benefits of *Moringa oleifera* Lam. ethanolic leaf extract and highlight its therapeutic potential in managing diabetes-related complications.

The study of Meng et al., 2017, investigated the ethanolic extractions of *Morinda citrifolia* L. (ញ្ញស្រុក/ñoosrok) and identified various compounds in different parts of the plants. Compounds detected in roots included steroids, cardiac glycosides, coumarins, and phenols. Compounds found in the fruit included steroids, cardiac glycosides, phenols, alkaloids, tannins, and coumarins. Compounds present in the

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leaves included coumarins, saponins, phenols, tannins and alkaloids. These findings provide insight into the chemical composition of different parts of *Morinda citrifolia* L., suggesting its potential pharmacological activities and therapeutic uses. The study of Oeung et al., 2017 demonstrated the presence of various phytochemical compounds in different extractions of *Nicotiana tabacum* L. (ថ្នាំជក់/tnamchoek) leaves. These compounds include phenolics, tannins, alkaloids, cardiac glycosides, steroids, flavonoids, terpenoids, polypeptides, saponins, essential oils, quinones, and resins. These findings provide valuable information about the chemical composition of *Nicotiana tabacum* L. leaves, highlighting its potential pharmacological activities.

According to Houdkova et al., 2018, *Alphinia oxymitra* K.Schum. (ក្រគី/krakei) oil showed effectiveness against *Haemophilus Influenza*, both in liquid and solid forms. The main categories of compounds identified in the oil analysis were monoterpenoids and sesquiterpenoids, except for *Citrus lucida* (Scheff.) Mabb. (ក្រសាំង/krasang) where esters were the primary essences. The analysis highlighted key antimicrobial constituents, including β-caryophyllene, caryophyllene epoxide, 1,8-cineole, decanal, α-pinene, β-pinene, and terpinene-4ol, found in many commonly used essential oils. These constituents were observed to disrupt the cell membrane structure of germs, contributing to the antimicrobial properties of the oils. The study of Soeurn et al., 2018 revealed that the bark of *Dillenia ovata* Wall. ex Hook.f. & Thomson (ភ្លូធំ/phlouthom) contains a variety of phytochemical compounds. These compounds include terpenoids, polypeptides, alkaloids, saponins, resins, cardiac glycosides, coumarins, phenolics, flavonoids, and tannins, suggesting a rich pharmacological profile. These compounds have been associated with a wide range of biological activities including antioxidant, antimicrobial, and anti-inflammatory. This comprehensive analysis provides valuable insights into the chemical composition of *Dillenia ovata* Wall. ex Hook.f. & Thomson bark, suggesting its potential pharmacological activities and therapeutic uses, as well as anticancer properties.

The study conducted by KeoS., Leng et al., 2018, investigated the ethanolic extractions of various plant parts from *Bryophyllum pinnatum* (Lam.) Oken (កបិលភ័ស/kabellapoahs), bark of *Dillenia ovata* Wall ex Hook.f. & Thomson (ភ្លូធំ/phlouthom), rhizomes of *Drynaria fortunei* (Kunze ex Mett.) J.Sm. (ប៉ប្រក់/braabrak), and bark of *Lophopetalum wallichii* Kurz (ពាន់តាឡឺ/puen ta lei). Researchers found several compounds such as alkaloids, phenolic, tannins, flavonoids, terpenoids, cardiac glycosides, saponins, and resins. Additionally, ethanol extraction from the whole plants of *Bryophyllum pinnatum* (Lam.) Oken, bark of *Dillenia ovata* Wall ex Hook.f. & Thomson, rhizomes of *Drynaria fortunei* (Kunze ex Mett.) J.Sm. contained steroids, while bark of *Lophopetalum Wallichii* Kurz possessed essential oils. The ethanolic extracts from these plants exhibited antioxidant activities *in vitro*. These findings suggest the potential pharmacological activities of the plant extracts, particularly their antioxidant properties. These properties could have significant implications for their utilization in traditional medicine and pharmaceutical applications. According to the study by Chhouk et al., 2018, it was demonstrated that extraction of *Dialium cochinchinense* Pierre (ក្រឡាញ់/krolang), *Cinnamomum cambodianum* Lecomte (ទេពិរូ/tepirou), *Gardenia angkorensis* Pit. (ដៃខ្លា/daiklar), *Cananga latifolia* Finet & Gagnep. (ឆ្កែស្រែង/chkaesreng), and *Oroxylum indicum* (L.) Kurz (ដើមស្រោមដារ/daemsroamdaaw) obtained via SC-CO2-

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Table 1. A partial list of the medicinal plants of Cambodia.

Scientific Name	Local Name	Use Parts	Traditional use	References
Alpinia oxymitra K.Schum	ក្រគី/krakei	Rhizomes	Antimicrobial	Houdkova et al., 2018
Ampelocissus martini Planch.	ទំពាំងបាយដូព្រៃ/tum peang baaychuu prey	Leaves and root	Liver disorder	Lee et al., 2017
Anacardium occidentale L.	ស្វាយចន្ទី/svay chanti	Bark	Oxidative stress	Keo et al., 2012
Andrographis paniculata (Burm.f.) Wall. ex Nees	ស្មៅប្រម៉ាត់មនុស្ស/smav bramat moa nuh	Leaves	Liver disorder	Chassagne et al., 2017
Annona muricata L.	ទៀបបារាំង/tieb barang	Leaves	Antimicrobial	Keo et al., 2017
Aquilaria crassna Pierr ex Lecomte	ចន្ទក្រឹស្ណា/chan kroessnaa	Wood	Tumor	Xia et al., 2019
Azadirachta indica A.Juss.	ស្ដៅ/sdav	Bark	Antimicrobial	Keo et al., 2017
Bauhinia bracteate (Benth.) Graham ex Baker	ខ្លែងពណ៌/kleyn poa	Bark, sapwood	Liver disorder	Lee et al., 2017
Bauhinia pulla Craib	ខ្លែងពណ៌/khleng por	Bark, sapwood	Oxidative stress	Keo et al., 2012, Lee et al., 2017
Bombax ceiba L.	រកា/roka	Bark	Liver disorder	Lee et al., 2017
Borassus flabellifer L.	ត្នោត/thnaot	Flower	Oxidative stress	Keo et al., 2012
Bryophyllum pinnatum (Lam.) Oken	កបិលភ័ស/kabel lapoahs	Whole plant	Antioxidant	Keo, 2018
Cananga latifolia Finet & Gagnep.	ឆ្កែស្រែង/chhkae sraen	Bark	Liver disorder/ antioxidant	Chassagne et al., 2017/ Chhouk et al., 2018
Cardiospermum halicacabum L.	អំបែងបែក/ambeng bek	Resin	Liver disorder	Lee et al., 2017
Cayratia trifolia (L.) Domin	វល្លិត្រដែត/voa tradet	Whole plant	Liver disorder	Lee et al., 2017
Chromolaena odorata (L.) R.M.King & H.Rob.	កន្ត្រានខេត្ត/kantraing khaet	Leaves	Diarrhea, cold/fever, stomachache, postpartum disorders	Chassagne et al., 2016
Cinnamomum cambodianum Lecomte	ទេពិរ/tepirou	Bark and leaves	Antioxidant	Chhouk et al., 2018
Cinnamomum caryophyllus (Lour.) S.Moore	ក្រវាញដើម/kravanh daem	Leaves and bark	Liver disorder	Lee et al., 2017
Citrus lucida (Scheff.) Mabb.	ក្រសាំង/krasang	Malaria	Antimicrobial	Houdkova et al., 2018
Coix lacryma-jobi L.	ស្គួយ/skuey	Stem, leaves	Oxidative stress	Keo et al., 2012
Costus speciosus (J.Koenig) Sm.	ក្រចុក/tro thok	Root, tuber	Diarrhea, food poisoning	Chea et al., 2007
Curcuma longa L.	រមៀត/rameut	Rhizomes	Antimicrobial	Keo et al., 2017
Cyperus rotundus L.	ស្មៅក្រវាញជ្រូក/smav kravvan chruuk	Whole plant	Liver disorder	Lee et al., 2017
Dasymaschalon lomentaceum Finet & Gagnep.	ជើងចាប/Cheung chap	Leaves and stem	Liver disorder	Lee et al., 2017
Dialium cochinchinense Pierre	ក្រឡាញ់/krolang	Leaves	Antioxidant	Chhouk et al., 2018

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Dillenia ovata Wall. ex Hook.f. & Thomson	ភ្លូធំ/phlou thom	Bark	Antioxidant, antimicrobial, anti-inflammatory, anticancer	Soeurn et al., 2018/ Keo, 2018,
Dipterocarpus obtusifolius Teijsm. Ex. Miq.	ត្បែង/tbeng	Sapwood	Oxidative stress	Keo et al., 2012
Diospyros nitida Merr.	ឈើភ្លើង/chheu phleung	Bark, sapwood	Oxidative stress	Keo et al., 2012
Dracaena cambodiana Pierre ex Gagnep.	អង្រែដែក/angra èda èk	Root	Cancer	Khay et al., 2012
Drynaria fortunei (Kunze ex Mett.) J.Sm	ប៉ប្រាក់/braabrak	Rhizomes	Antioxidant	Keo, 2018
Fagraea fragrans Roxb.	តាត្រាវ/Tatrav	Bark, leaves	Malaria	Jonville et al., 2008
Ficus benjamina L.	ជ្រៃក្រឹម/chrey krem	Leaves	Liver disorder	Lee et al., 2017
Flueggea virosa (Roxb. Ex Wild.) Royle	លាជផ្ទះ/liëch Phtuhs	Stem	Diarrhea, food poisoning	Chea et al., 2007
Gardenia angkorensis Pit.	ដៃខ្លា/daiklar	Fruit	Antioxidant	Chhouk et al., 2018
Gomphrena celosioides Mart.	ស្មៅត្រចៀកទន្សាយ/S maw trachiek tonsaeay	Whole plant	Liver disorder	Chassagne et al., 2017
Harrisonia perforate (Blanco) Merr.	ដើមទន្ត្រានព្រៃ/daem tuntrien prey	Bark	Cancer	Khay et al., 2012
Kalanchoe pinnata (Lam.) Pers.	កបិលភ័ស/kabel lapoahs	Leaves	Diarrhea, cold/fever, stomachache, postpartum disorders	Chassagne et al., 2016
Lophopetalum wallichii Kurz	ពាន់តាឡី/puen ta lei	Bark	Antioxidant	Keo, 2018/ Va et al., 2018
Mangifera duperreana Pierre	ស្វាយព្រៃ/svaay prey	Leaves	Liver disorder	Lee et al., 2017
Manihot esculenta Crantz	ដំឡងមី/damlong mee	Whole plant	Worm infection	Seng et al., 2007
Micromelum falcatum (Lour.) Tanaka	រលាយស្វង/romleay smorng	Leaves, stem, root	Anti-inflammatory	Kouloura et al., 2014
Morinda citrifolia L.	ញស្រុក/ñoo srok	Root, fruit, leaves	Liver disorder/ pain, injury	Lee et al., 2017/ Meng et al., 2017
Moringa oleifera Lam.	ម្រុំ/morum	Leaves	Antidiabetic	Tang et al., 2017
Nicotiana tabacum L.	ថ្នាំជក់/tnam choek	Leaves	Antimicrobial	Keo et al., 2017, Oeung et al., 2017
Oroxylum indicum (L.) Kurz	ដើមស្រោមដាវ/daem sroam daaw	Bark	Antioxidant	Chhouk et al., 2018
Oryza rufipogon Griff.	ស្រែង៉ែ/sraa nae	Stem	Oxidative stress	Keo et al., 2012
Pandanus humilis Lour.	រំចេកស្រុក/rumchaek srok	Leaves	Liver disorder	Lee et al., 2017
Passiflora foetida L.	សាវម៉ាវព្រៃ/saavmaav prey	Whole plant	Liver disorder	Chassagne et al., 2017
Peliosanthes weberi (L. Rodr.) N.Tanaka	ត្បាលដែក/thbal daek	Leaves	Liver disorder	Lee et al., 2017
Phyllanthus emblica L.	កន្ធួតព្រៃ/kantut prey	Fruit	Oxidative stress	Keo et al., 2012, Lee et al., 2017
Physalis minima L.	ប៉េងប៉ោះស្រោម/peng poa srom	leaves	Liver disorder	Chassagne et al., 2017
Plumeria acutifolia Poir.	ចំប៉ី/champy	Leaves	Skin infection	Ningsih, 2014
Quisqualis indica L.	ដើមសក់សេះ/daem sakset	Seed	Liver disorder	Lee et al., 2017

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Smilax glabra Roxb.	ប័ប្រើស/papraha	Rhizomes	Liver disorder	Lee et al., 2017, Chassagne et al., 2017
Stephania rotunda Lour.	កុមារពេជ្រ/koma Péch	Tuber	Malaria	Chea, Hout, et al., 2007
Tinospora crispa (L.) Hook.f. & Thomson	បណ្តូលពេជ្រ/bânndôôl péch	Stem	Liver disorder	Lee et al., 2017
Vernonia cinerea (L.) Less.	ស្មៅរុយ/smav ruy	Leaves, root	Cancer/antimicrobial	Khay et al., 2012/ Keo et al., 2017
Willughbeia cochinchinensis (Pierre) K.Schum	វល្លិគុយ/voa kuy	Root	Liver disorder	Lee et al., 2017
Zingiber montanum (J.Koening) Link ex A.Dietr.	ពន្លៃ/pun lai	Rhizomes	Diarrhea, cold/fever, stomachache, postpartum disorders/Antimicrobial	Chassagne et al., 2016/ Keo et al., 2017

H extraction were found to contain a significant quantity of total phenolic compounds, indicating potential antioxidant properties. Va et al., 2018, conducted a study on *Lophopetalum wallichii* Kurz (ពាន់តាឡឺ/puen ta lei), which revealed promising findings regarding its alkaloid, phenolic, tannin, flavonoid, terpenoids, cardiac glycosides, and saponins properties, as well as its various resins contents. In the study by Keo S., Chrin et al., 2018, various plants were utilized to address conditions such as post-partum issues, hemorrhoids, gastroenteritis, and syphilis, with respective frequencies of n=12 (14.12%), n=9 (10.59%), n=8 (9.41%), and n=8 (9.41%). The results showed that most of the 25 families belonged to *Fabaceae* (n=4, 24%), *Poaceae* (n=4, 16%), Lamiaceae (n=4, 16%), Zingiberaceae (n=4, 16%), Menispermaceae (n=3, 12%), Phyllanthaceae (n=3, 12%), and Sapindaceae (n=3, 12%). According to the study of Xia et al., 2019, five compounds, including one newly discovered 2-(2-phenylethyl) chromone (1), three naturally occurring 2-(2-phenylethenyl) chromones (3-2), and a well-known 2-(2-pheynylethyl) chromone (2), were isolated from ethanol extracts of agarwood sourced from *Aquilaria crassna* Pierr ex Lecomte (ចន្ទក្រឹស្នា/chankroessnaa). One compound exhibited acetylcholinesterase (AChE) inhibitory activity (inhibitory ratio: 35±2.19%) and demonstrated cytotoxicity effects against the K562 tumor cell line (IC50: 40.81±0.64 μM), while three compounds displayed cytotoxicity against the BEL-7402 tumor cell line (IC50: 44.18±0.34 μM).

DISCUSSION

Of the *in vitro* studies using phytochemical analysis eligible for consideration, 68.96% (20) of them displayed various results such as *anti-plasmodial* activities, *anti-microbial* activities, *anti-oxidant* properties, cytotoxic activities, *cytoprotectiv*e activities, *hepatoprotective* activities, *anti-diabetic* activities, and *anti-inflammatory* activities. The results of these studies support the conclusions from ethnobotanical and ethnopharmacological surveys. At the same time, 6.89% (2) of the eligible *in vivo* studies displayed anti-plasmodial and anti-diabetic activities (mice). Based on the studies regarding the noted *anti-plasmodial* activities, we can confirm the statements regarding therapeutic value made by traditional healers during ethnopharmacological surveys. However, toxicological and pharmacological

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evaluations should be conducted before the consideration of clinical trials and certainly before any conclusions can be drawn. It should be noted that *in vivo* studies on the anti-diabetic activities of *Moringa Oleifera* support the conclusions of previous studies. Interestingly, the dose of the *M. oleifera* sampled from Cambodia is much lower than what was used in these previous studies. Based on the 20.68% (6) of studies that were either surveys, qualitative analysis or ethnobotanical and ethnopharmacological in design, we can conclude that medical plant species potentially cure diseases including infected wounds using different methods reported in Cambodia. An ethnobotanical survey found that people mostly used medicinal plants for post-partum care (stimulating appetite, milk production, and blood circulation), gastroenteritis, gastritis, cold/fever, and malaria. In this regard, the most frequently listed plant families are Dipterocarpaceae, Fabaceae, Lamiaceae, Leguminosae, Phyllanthaceae Poaceae, Rubiaceae, and Zingiberacea. In this study, there were 41 families and 99 species utilized in the formation of traditional medication. The highest number of species from one family was 16 from Fabaceae. In addition, Leguminosae and Poaceae are were the most predominantly used species for the treatment of liver diseases by Khmer traditional healers. Because liver treatments derived from medicinal natural plants are often financially acceptable for local and indigenous people, Khmer traditional healers are continuing to contribute to the professional process by practicing their learned knowledge (Chassagne et al., 2017). Most of the studies focused on two minority groups: Bunong, and Kuy. These studies considered the most common diseases that occur in the community. 72 families of plants have been used by the Bunong to perform traditional health care and cure different diseases such as cold/fever, diarrhea, or stomachache. These ailments are described as the primary syndromes affecting their communities (Chassagne et al., 2016). The Kuy population has utilized 165 plant species to treat maladies such as postpartum conditions, cold/fever, urinary tract infections, and skin infections. They utilize various plant parts such as the bark, roots, or leaves (Garcia et al., 2020). Indigenous people have depended on traditional herbs instead of Western medicine for use in their health system for many generations. Instead of relying on Western medication for medical care, the indigenous people of Cambodia have relied on traditional herbs and plants. The efficacy statements made by traditional healers have been confirmed by ethnopharmacological surveys conducted over a 30 year period. However, evaluation of toxicological and pharmacological properties should be conducted before any consideration regarding clinical trials. Across Cambodia, there are currently only a limited number of ongoing studies being conducted regarding the pharmacology of traditional medicinal plants. Due to the limited *in vitro* and *in vivo* research focused on these plants, a vast number of potentially therapeutic substances, many of which are unique to Cambodia, are potentially being overlooked. Further research could provide a better understanding of potentially new bioactive substances that exhibit therapeutic activities.

CONCLUSION

Cambodian medicinal plants have an established history of proving themselves effective and safe. They can be used as complementary medication or even considered as suitable alternatives to Western medicine for treating a wide variety of diseases and disorders. All the medicinal plant species recorded and reported in this study

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have been prescribed to treat a diverse range of illnesses. In addition, using traditional medications to treat topical wounds has been practiced among local and indigenous people for many generations. Based on our review, the findings indicate the plant species of Fabaceae, Poaceae, Lamiaceae, Menispermaceae, Rubiaceae, and Sapindaceae were the most widely utilized species by the local people in the treatment of various illnesses. For many centuries, these families of plant species have been used in the formation of traditional medication to treat various diseases.
The results from this research will hopefully encourage more Cambodians to confidently consider using traditional medicines when needed. Also, we would encourage the government to allocate national budget funds for the research of Cambodian Traditional Medicine. Moreover, these results will be considered as valuable information that will help researchers conduct further studies with traditional medicinal plants. The health benefits associated with this research will be realized by future generations. Medicinal plants deserve further study in order to be developed as commercially available natural products. Their various biological activities also require further study for efficacy along with the consideration of safety for human health.

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DECLARATION OF CONFLICT OF INTEREST

No conflict of interest is associated with this study.

DECLARATION OF HONOR

We declare on our honor that our results are not fake and made up.

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