World Health Organization (WHO) reported that 88% of its member or 61 countries acknowledge the use of traditional and complementary medicines. *Persicaria odorata* is being used as traditional herbs to treat fever, nausea and promoting hair growth. Besides, it is used as an anti-inflammatory agent in Vietnam to relieve swelling and treat wounds, sores, and ulcers. This review aims to evaluate the phytochemical and pharmacological status of *P. odorata*. *P. odorata* is a plant with a high content of phenols and flavonoids. Among the essential chemical constituents in the *P. odorata* are methyl gallate, (+)-catechin, eupatoriocromene, n-dodecanal, polygonumins A, α-humulene and anthraquinone. *P. odorata* also exerts many pharmacological effects such as antioxidant, anti-inflammatory, antibacterial and anticancer effects. The commonly used part of *P. odorata* for extraction are leaves followed by the aerial part, rhizomes and stems. Nevertheless, more studies are needed to identify the efficacy and toxicity of *P. odorata*. New drugs could be developed from the active compounds of *P. odorata* in the future.
Keywords: Persicaria odorata; Polygonum odoratum; kesum, pharmacological study; phytochemical study.

LIST OF ABBREVIATIONS

| Abbreviation | Meaning |
|--------------|---------|
| 1H- and 13C-NMR | Nuclear magnetic resonance spectroscopy |
| ABTS | 2,2'-azino-bis (3-ethylbenzothiazoline-6-sulfonic acid) |
| CC<sub>50</sub> | Cytotoxic activity concentration |
| COX-1 | Cyclooxygenase-1 |
| COX-2 | Cyclooxygenase-2 |
| DPPH | 1,1-diphenyl-2-picrylhydrazyl |
| EDX | Energy dispersive X-ray spectroscopy |
| FESEM | Field emission scanning electron microscope |
| FTIR | Fourier transform infrared |
| GAE | Gallic acid equivalent |
| GC-MS | Gas Chromatography-Mass Spectrometer |
| GPx-1 | Glutathione peroxidase-1 |
| GRe | Glutathione reductase |
| HPLC | High performance liquid chromatography |
| IL-6 | Interleukin-6 |
| IL-10 | Interleukin 10 |
| MBC | Minimum bactericidal concentration |
| MIC | Minimum inhibitory concentration |
| Mn-SOD | Manganese superoxide dismutase |
| MRSA | Methicillin-resistant Staphylococcus aureus |
| PO-AgNPs | Silver nanoparticles synthesised from P. odorata leaves extract |
| QE | Quercetin equivalent |
| SAR | Structure and activity relationship |
| sPLA2 | Secretory phospholipase-A2 |
| TLC | Thin-layer chromatography |
| UV-Vis | Ultraviolet-visible |
| XRD | X-ray diffraction |

1. INTRODUCTION

The use of traditional herbs in treatment is still prevalent in many countries due to the plants availability, low cost and effectiveness [1]. US Food and Drug Administration (FDA) also approved many botanical drugs in the market [2]. World Health Organization (WHO) also reported that 88% of its member or 61 countries acknowledge the use of traditional and complementary medicines [3]. In 2019, US$ 83 billion was estimated for the global market size of herbal medicines and is expected to increase up to US$ 550 billion by 2030 [4]. In Malaysia, the Sabah Natives were the highest user of traditional and complementary medicines from 2012 to 2018, followed by Malay users [5].

**Persicaria odorata** (Lour.) Sojak (Polygonum odoratum) is a green plant that belongs to the family Polygonaceae [6]. It also has many names including Persicaria minor (Polygonum minus), Vietnamese coriander and Vietnamese mint [6,7]. In Malaysia, the common names of leaves *P. odorata* are known as Daun kesum or Daun laksa. Other common names for *P. odorata* are *phak phai* in Thailand, *rau rdm* in Vietnam and *lakh* in Hindi [6]. *P. odorata* also a native species widely available in South-eastern Asia country including Vietnam, Singapore and Thailand [6]. The optimal condition for *P. odorata* to grow is at a warm temperature and moist soil. *P. odorata* can grow until 15 to 30 cm in a stable condition [8]. The leaves colour of *P. odorata* are dark green and the shape is intermediate between the lance and egg-shaped (Fig. 1). It has a grooved stem about 2 to 3 mm wide [9].

*P. odorata* has a unique pungent smell that can make the dishes have a unique taste [10]. It is widely used in Malaysia as a garnish in cooking such as *laksa, Asam pedas* and curry. It can also be taken raw with local cuisines such as *Nasi ulam* and *Nasi kerabu*. In Vietnam, the leaves of *P. odorata* are consumed fresh such as in the lotus shoot salad and chicken salad [11]. Besides, the leaves of *P. odorata* are used as traditional herbs to treat fever, nausea and promoting hair growth. It is also used as an anti-inflammatory agent in Vietnam to relieve swelling and inflammation and treat wounds, sores and ulcers [12]. *P. odorata* is also being taken by the Chinese Buddhist to reduce sexual desire [13]. Other than that, *P. odorata* has many pharmacological effects such as anticancer, antibacterial, anti-inflammatory, anti-fungal and antioxidant [14–17].

Various active compounds were reported in the *P. odorata* extraction such as flavonoids and phenolic compounds [12]. Among the compounds that are reported to produce the
pungent of *P. odorata* are (Z)-3-hexenal, (Z)-3-hexen-1-ol, decanal and dodecanal [18]. In addition, the extraction method also influences the phytochemical found in the plant extracts [1]. Among the solvents used in extraction method of *P. odorata* were water, methanol and dichloromethane [19]. As there are many pharmacological effects exerted from *P. odorata*, many researchers are interested in studying the phytochemical, potential therapeutic uses and mechanism of action of *P. odorata*. The objective of this study is to update information about phytochemical and pharmacological effects of *P. odorata*. The review includes studies conducted on the antioxidant, anti-inflammatory, anticancer and antibacterial activities of the plant that have been documented up to April 2021.

2. PHYTOCHEMICAL ANALYSIS OF PERSICARIA ODORATA

Many chemical constituents are found in *Persicaria odorata* that are beneficial to many daily uses, including cooking and therapeutic effects. A recent study by Nguyen et al. [20] found that *P. odorata* leaves contain various compounds such as alkaloids, anthraquinones, coumarin, flavonoids, reducing compounds, saponin, tannins and triterpenoid. Saad et al. [5] screened the phytochemical of methanol extracts of *P. odorata* leaves and discovered tannins, phenols, sulphate and nitrates that were obtained by ultrasonication extraction method. Although most previous research used the leaves part of the *P. odorata*, a few studies used the rhizomes, stems and aerial parts of the plant. In a research by Deng et al. [21], the results showed saponin, flavonoid and sugar in the rhizomes of *P. odorata*. These findings matched with a review report by Khan and Rauf [22], who concluded that homoisoflavanone, triterpenoids and steroidal saponins could be extracted from the rhizomes of *P. odorata*. Other than that, other chemical constituents reported by the previous study are also shown in (Table 1).

![Fig. 1. Morphology of *Persicaria odorata* plant](image-url)
Table 1. Phytochemical constituents from different parts of *P. odorata*

| Part Used            | Chemical constituents                                                                 | Ref. |
|----------------------|---------------------------------------------------------------------------------------|------|
| Aerial parts         | Terpenoids, sterols, steroids, phenols, coumarins and other unidentified organic compounds. | [25] |
|                      | Carboxyls, alcohols, sesquiterpenes, oxidised sesquiterpenes, monoterpenes, oxidised monoterpenes, oxidised diterpenes and α-humulene. | [28] |
| Fresh and dried leaves | Phenolics content: methyl gallate, (+)-catechin, sinapic acid hexoside, (epi)catechin gallate, quercetin 3-O-β-D-glucuronide, quercetin 3-O-β-D-rihamnoside, tetrahydroxyflavonol derivative, quercetin sulfate and kaempferol sulfate. | [11] |
|                      | Eupatoriocromene, dodecanal, alphacaryophyllene, beta-caryophyllene and decanal.      | [27] |
| Leaves               | Alkaloids, anthraquinone, coumarins, flavonoids, reducing compounds, saponins, tannins and triterpenoids. | [20] |
|                      | Tannins, phenols, sulphate and nitrates.                                              | [33] |
|                      | Moisture, ash, crude protein, crude fat, crude fibre, calcium, phosphorus, saponins, tannins, total phenols, flavonoids and alkaloids | [32] |
|                      | Terpenoids, flavonoids, tannins, phenolic compounds, carbohydrates, mucilages, proteins and amino acids. | [12] |
|                      | Decanal, β-citral, α-citral, dodecanal, caryophyllene, euparone, drimenol and alkene. | [29] |
|                      | Aldehyde compounds: alkanals, anisaldehyde, methyl vanillin and polygodial. Alkanols compounds: dodecanol, decanol, undecanol, drimenol, bisabolol and neoiso-menthol. | [30] |
|                      | Protein and polysaccharides.                                                           | [7]  |
| Leaves and stems     | Phenolics and flavonoids.                                                              | [19] |
| Rhizomes             | Phenolic acids: gallic acid and chlorogenic acid. Flavonoid: quercetin.                | [24] |
|                      | Saponin, flavonoid and sugar.                                                          | [21] |
|                      | Homoisoflavanone, triterpenoids and steroidal saponins.                                | [22] |
| Stems                | Polygonumins A.                                                                       | [31] |

Chansiw et al. [19] used the leaves and stems part of the *P. odorata* in their research and found no apparent difference in the percentage yield between leaf and stems extract. However, the total phenolic content (TPC) and total flavonoid content (TFC) are higher in the leaf extract than in the stems extract. This study found that TPC and TFC are highest in methanolic extract compared to dichloromethane and water extract. Methanol is a powerful extraction solvent that is recommended for obtaining high levels of phytochemical components [23]. Next, a recent study from Thongra-ar et al. [24] found that TPC in the leaves extracts are slightly higher than stems extracts, respectively 22.89 ± 9.16 and 22.27 ± 8.77 g gallic acid equivalent/ 100 g extract (g GAE/ 100 g extract). Furthermore, the TFC in the leaves extracts are also higher than stems extracts, which were 7.20 ± 3.61 and 4.06 ± 1.73 g quercetin equivalent/ 100 g extract (g QE/ 100 g extract) respectively, by using 75% ethanol. Yanpirat et al. [25] revealed the presence of terpenoids, sterols, steroids, phenols, coumarins and other unidentified organic compounds at the aerial parts of *P. odorata* by using a Thin-layer chromatography (TLC) plate. TLC analysis revealed a variety of colors of phytochemical compounds depending on the Rf values [26].

Some studies reported the different yields and constituents between fresh and dry leaves of *P. odorata*. Pawłowska et al. [11] aimed to find a significant difference between the major constituents of the phenolic contents found in the fresh and dry leaves. The study identified that the fresh leaves have a less variability group of compounds than dry leaves. Besides, Sasongko et al. [27] found that since certain volatile compounds from dry leaves were vaporised during the drying process, causing the yield of essential oil from dry leaves was lower than fresh leaves. According to this study, the main volatile compounds found in the fresh leaves and dried leaves are eupatoriocromene (21.71% and 20.94%), dodecanal (19.96% and 18.72%), alpha caryophyllene (12.57% and 11.62%), beta-caryophyllene (11.07 % and 11.40%) and
higher polysaccharide contents than aqueous
the plant. However, 100% aqueous extract has
proteins compared to 100% aqueous extract of
ethanol. This study also discovered that carbonyls and alcohols account for 68.8% of essential oil composition, mostly
decanal (C10) and dodecanal (C12).
Furthermore, the sesquiterpenes account for
11.5%, oxidised sesquiterpenes was 5.7%, along
with monoterpenes, oxidised monoterpenes and
oxidised diterpenes that are less than 1% of the
essential oil composition. This study also found abundance of α-humulene (4.5%) in the essential
oil of P. odorata that responsible for the anti-
inflammatory and antibacterial effects of the
plant. The findings were similar to the study by
Ridzuan et al. [29], who discovered the decanal
and dodecanal were the main compounds in the
essential oil of P. odorata besides β-citral, α-
citral, carophyllene, euparone, drimenol and
alkene, when using Gas Chromatography-Mass
Spectrometer (GC-MS). Fujita et al. [30] also
used GC-MS to analyse the essential oil of fresh
P. odorata leaves extracted by steam distillation,
revealed 25 volatile compounds with 78% were
aldehyde compounds, which the most frequent
are dodecanal (55.5%) and decanal (11.6%).
Other aldehyde compounds which were noticed
in this study were alkanals, anisaldehyde, methyl
vanillin and polygaloid. This study also found
alkanols compounds, including dodecanol,
deanol, undecanol, drimenol, bisabolol and
eoiso-menthol. On top of that, several phenolics
compounds were reported in the experiment by
Pawlowska et al. [11] using high-performance
liquid chromatography coupled with diode-array
detection and electrospray ionization tandem
mass spectrometry (HPLC-DAD-MS²)
analysation of the methanolic-aqueous extracts
of P. odorata. The major compounds identified
were methyl gallate, (+)-catechin, quercetin 3-O-
β-D-glucuronide, tetrahydroxyflavonol derivative
and kaempferol sulfate.

According to Abubakar et al. [7], aqueous-
ethanol is a better solvent for total protein
extraction of P. odorata because aqueous-
ethanol extract showed higher contents of
proteins compared to 100% aqueous extract of
the plant. However, 100% aqueous extract has
higher polysaccharide contents than aqueous-
ethanol extract, proving that aqueous extract is
more suitable for total polysaccharide extraction.
Next, Ahmad et al. [31] found a new compound
with anticancer and antiviral effects, known as
polygonums A, from the stems of P. odorata.
The molecular formula is C_{52}H_{90}O_{21}. This study
found many functional groups in the
polygonums A, including aliphatic carbon,
aromatic and carbonyl. Unlike vanicoside A,
polygonums A consists of four phenylpropanoid
units and a sucrose unit. Next, Sim et al. [32]
identified moisture (88.64%), ash (1.83%), crude
protein (3.5%), crude fat (0.83%), crude fibre
(10.66%), calcium (0.47%) and phosphorus
(0.12%), together with the presence of secondary
metabolites which were saponins, tannins, total
phenols, flavonoids and alkaloids in the dried
leaves of P. odorata. In 2016, Dash and Zakaria
[12] also explored the existence of terpenoids,
flavonoids, tannins and phenolic compounds,
along with carbohydrates, mucilages, proteins
and amino acids, in the liquid extract of P.
odorata under visible light and UV at 366 and
254 nm, respectively. This study used dried
leaves of P. odorata extracted with four different
solvent, which are petroleum ether, chloroform,
methanol and distilled water.

3. PHARMACOLOGICAL ACTIVITIES OF
PERSICARIA ODORATA

Persicaria odorata is a natural plant that has
been used for daily application and medicinal
purposes. Since the plant is widely available in
Southeast Asia, it has piqued the interest of
researchers who want to learn more about its
therapeutic properties. Although there are a few
assumptions about the ability of P. odorata to be
used in conjunction with current therapy, the
claims should be accompanied by sufficient
evidence. Among the pharmacological activities
of P. odorata found in the research are
antioxidants, anti-inflammatory, antibacterial
and anticancer effects.

3.1 Antioxidant Effects

An antioxidant is a substance that is able to trap
reactive oxygen species (ROS) [34]. Among the
definition of antioxidants are the compounds that
reduce the redox state and scavenge ROS by act
as a redox couple in the cells [35]. The
antioxidant therapeutic agent can prevent and
block the effects of oxidative stress [36]. The
effectiveness of antioxidant therapy depends on
antioxidant usage at the early stages of
pathology, suitable concentration use depending
on the damaged area, sufficient retention time, safety, beneficial interactions with body systems and absence of toxic product accumulation [37]. Neutralisation of active oxygen species at the beginning stages of their production can effectively block the damage induced by oxidative stress [38]. The antioxidant activity commonly is determined by using half-maximal inhibitory concentration (IC$_{50}$) on reagents such as DPPH (1,1-diphenyl-2-picrylhydrazy) and ABTS (2,2'-azino-bis (3-ethylbenzothiazoline-6-sulfonic acid)) [39]. The lower IC$_{50}$ value indicates higher antioxidant activities [40].

Nguyen et al. [20] found a positive relationship between the TPC and antioxidants activity in the ethanol and aqueous extraction of P. odorata. The IC$_{50}$ were 311.26 ± 3.06 μg/mL and 167.66 ± 6.67 μg/mL on DPPH and ABTS assay, respectively. These proved that the ethanolic leaf extract P. odorata has a vigorous antioxidant activity. The TPC and TFC of ethanolic extract from leaves of P. odorata were 58.56 ± 3.86 μg GAE/mg and 70.65 ± 4.14 μg QE/mg respectively, that are higher than the aqueous extract. Flavonoids, phenolic acids and tannins are among the antioxidants available in natural plant extracts that can help to prevent pathogenesis by overcoming the damaging effects [19].

A study from Chansiw et al. [19] used three different solvents, which were 95% methanol, dichloromethane and water, to determine the antioxidant effects of leaves and stems extracts of P. odorata. This study found that the methanolic extract of leaves and stems showed more potent antioxidant activity than dichloromethane and water extracts. The DPPH and ABTS radical scavenging activities of methanolic extract of P. odorata leaves and stems increased in a concentration-dependent manner. According to this study, high levels of TPC may relate to the antioxidant activities. The methanolic extract showed the highest TPC, while the lowest was in the dichloromethane extract.

![Fig. 2. Structures of some of the essential chemical constituents found in P. odorata [11,27,30-33]](image)
| Activity          | Part of plant | Type of extract | Summary of findings                                                                                                                                                                                                 | Reference |
|------------------|---------------|-----------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------|
| **Antioxidant**  | Leaves        | Ethanol         | The extraction of *P. odorata* showed high antioxidant activity with DPPH and ABTS assays.                                                                                                                                 | [20]      |
|                  |               | Leaves and stems | Methanolic leaf extract of *P. odorata* had the highest concentration of phenolic compounds and had the most potent antioxidant activity.                                                                                                                                       | [19]      |
|                  | Leaves        | Ethanol         | The extraction of *P. odorata* increase the mRNA expression of antioxidant genes. Besides, the IC$_{50}$ for leaves and stems of *P. odorata* were 7.74±0.47 and 7.91±0.43 μg/mL, respectively, in the DPPH scavenging activities. | [24]      |
|                  | Leaves        | Methanol        | The extraction of *P. odorata* has scavenging activity on the DPPH reagent. It also has the highest electrical current conductivity compared to the other nine herbal extracts.                                                                                                     | [41]      |
| **Anti-inflammatory** | Aerial part | Water           | Ethanolic extract showed the highest effect in reducing IL-6 secretion with IC$_{50} = 25$ μg/mL. The two main fractions that contributed to the anti-inflammatory activity of *P. odorata* ethanol extract were scutellarein-7-glucoside and quercitrin. | [44]      |
|                  |               | Ethanol and water |                                                                                                         |           |
|                  |               | Ethanol         |                                                                                                         |           |
|                  | Leaves        | Methanol        | The extract of *P. odorata* reduces nitric oxide production in RAW 264.7 cells induced by LPS.                                                                                                                        | [19]      |
|                  |               | Dichloromethane Water |                                                                                                         |           |
|                  | Aerial parts  | Ethanol         | The ethanolic extract of *P. odorata* was found to inhibit COX-1, COX-2 and 5-LOX activity via in-vitro test. Meanwhile, the aqueous extract of *P. odorata* was found to significantly reduce the inflammatory effects of rat paw oedema after 4 hours of administration of λ-carrageenan. | [46]      |
| Antibacterial    | Fresh-leaves  | Aqueous         | The aqueous-ethanol extract of *P. odorata* was more potent than the aqueous extract for the antibacterial activity against *S. aureus, E. faecalis* and *E. coli*. However, both extractions do not have effects on *P. aeruginosa*. | [7]       |
|                  |               | Aqueous and ethanol |                                                                                                         |           |
| Activity | Part of plant | Type of extract | Summary of findings | Reference |
|----------|---------------|-----------------|---------------------|-----------|
| Aerial parts of dried leaves | Aqueous | The essential oil of *P. odorata* showed antibacterial activity in the form of vapour and liquid phase against *E. faecalis*, *S. pyogenes*, *B. subtilis*, *E. coli*, *P. aeruginosa* and *K. pneumoniae*. The vapour phase of essential oil *P. odorata* showed twice effectiveness against *E. coli* compared to the liquid phase. | [28] |
| Leaves | Aqueous | PO-AgNPs showed inhibition against tested MRSA, *S. aureus*, *S. epidermidis* and potent inhibition against *P. aeruginosa*. | [48] |
| Anticancer | Stems | Methanol | The newly isolated compound from *P. odorata* known as polygonuminus A is a potential anticancer compound against K562 (Human Leukaemia Cell Line), MCF7 (Human breast adenocarcinoma cell line) and HCT116 (Colorectal cancer cells). Besides, the most effective cytotoxicity effects were found against K562 cells. | [31] |
| Aerial part | Ethanol | *P. odorata* extract showed CC50 value of 775 μg/mL against HT-29 (human colon adenocarcinoma) and 1665 μg/mL against HepG2 cells (human hepatocellular carcinoma). | [64] |
| Aerial part | Methanol | *P. odorata* showed anticancer effects against oral squamous cell carcinoma by suppressing the Akt/mTOR pathway. | [6] |

Meanwhile, in 2021, Thongra-ar et al. [24] discovered that the ethanolic extracts from the leaves and stems of *P. odorata* have antioxidant effects, by preventing the formation of intracellular reactive oxygen species (ROS) caused by hydrogen peroxide (H₂O₂) in the human embryonic kidney-293 (HEK-293) cells. The DPPH scavenging activities were also tested using the extraction and found IC₅₀ for leaves and stems of *P. odorata* were 7.74±0.47 and 7.91±0.43 μg/mL, respectively. The mRNA expression of antioxidant genes such as manganese superoxide dismutase (Mn-SOD), glutathione peroxidase-1 (GPx-1), catalase and glutathione reductase (GRe) in the cells were also increased, when treated with leaves and stems of *P. odorata* extracts. However, the leaves extract demonstrated superior efficacy in inducing mRNA expressions than the extract of the stem. Both extractions contained phenolic, such as gallic acid and chlorogenic acid, along with flavonoid such as quercetin.

Another study from Saad et al. [41] found that the Minimal Inhibitory Concentration of herbal extracts by half amount (MIC₅₀) of the methanolic extract of dried leaves *P. odorata* was 0.07 ± 0.01 mg/mL and the scavenging activity on DPPH reagent was more than 70%. Tannins, phenol, sulphate and nitrate were found in the *P. odorata*. Besides, electrical current conductivity was used as a new approach to identify the antioxidants properties in the ten selected herbal extracts, which were *P. odorata*, *Strobilanthes*
crispa, Pereskiia saccarosa, Ehretia laevis, Plectranthus amboinicus, Orthosiphon staminous, Andrographis paniculate, Clincacanthus nutans, Murraya koenigi and Frankincense. The results showed that P. odorata extract had the highest electrical current conductivity of about 0.116Ω·cm compared to other herbal extracts. This study concluded that a good amount of antioxidant property could be reflected with a good amount of electrical current conductivity. All the ten selected herbal extracts showed an excellent antioxidant property.

### 3.2 Anti-inflammatory Effects

Inflammation is a natural host defence mechanism against pathogen invasion that is crucial to the body. Nevertheless, inflammation can also harm body cells by releasing various membrane components that trigger the inflammatory response. Many diseases are related to the overproduction of pro-inflammatory cytokines. It can cause systemic inflammatory response syndrome, extensive tissue injury and septic shock [42]. As a result, several researchers have investigated the anti-inflammatory properties of medicinal plants. The presence of anti-inflammatory activity can be identified by the ability reducing the secretion of pro-inflammatory cytokines such as IL-6 and TNF-α or increasing the anti-inflammatory cytokine IL-10 [42,43].

The anti-inflammatory activity of P. odorata aerial extracts was discovered by Onkolog et al. [44] in 2016. This analysis used three different solvents for extraction: water, 50% ethanol in water and ethanol. The results showed that, by adding either 100% or 50% ethanol extract of P. odorata at a concentration of 100 g/mL to LPS-induced RAW 264.7 cells, the secretion of IL-6 was significantly reduced. However, the ethanolic extract has the most excellent effect and significant inhibition of IL-6 secretion in a dose-dependent manner, with an IC50 of 25 µg/mL. This study also used nuclear magnetic resonance spectroscopy (1H- and 13C-NMR) and high performance liquid chromatography (HPLC) to identify the main fraction of the ethanolic extract that reduced IL-6 and TNF-α production. Scutellarein-7-glucoside (IC50=102 µM) and querctinin (IC50=77 µM) are the two essential fractions that contributed to nearly half of the anti-inflammatory activity of P. odorata ethanolic extract, by reducing IL-6 secretion. Gut microbiota can hydrolyse scutellarein-7-glucoside and querctinin into more active aglycones scutellarein and querctinin in the human gut [44].

Aglycone quercetin is the flavonoids found in many fruits and plants and has been shown to have anti-inflammatory, antioxidant and antitumor effects [45].

Another research by Chansiw et al. [19] discovered that P. odorata has an anti-inflammatory effect by measuring the nitric oxide in RAW 264.7 cells induced by LPS. In a concentration-dependent manner, they discovered that leaves extracts were more potent than stems extracts. This study used three different types of extracts, which are water, dichloromethane and methanol. The dichloromethane extract of P. odorata leaves and stems showed the highest inhibitory effect of nitric oxide production, with IC50 = 53.75 + 0.75 µg/mL and IC50 = 147.50 + 1.44 µg/mL, respectively. The anti-inflammatory agents contained in the dichloromethane extracts were still unknown. Only E-15-heptadecenal and 3,7,11,15-tetramethyl-2-hexadecen-1-ol were contained in the methanol extracts, which may be linked to the anti-inflammatory effects of P. odorata.

Next, an in-vitro and in-vivo study of anti-inflammatory effects of P. odorata was conducted by George et al. [46]. This study used ethanolic extract of P. odorata in in-vitro test. The anti-inflammatory effects were identified by the ability of the extract to inhibit enzymes that mediated the inflammatory response, which are cycloxygenase-1 (COX-1), cyclooxygenase-2 (COX-2), lipoxigenase (5-LOX) and secretory phospholipase-A2 (sPLA2). These essential enzymes are crucial in forming pro-inflammatory mediators such as arachidonic acid (AA), which are responsible for many metabolic pathways [46]. In excess, AA will cause severe inflammation such as joint damage. The in-vitro study results showed that P. odorata inhibited COX-1 and 5-LOX enzymes at 100 µg/mL. However, no inhibitory effect of P. odorata against sPLA2 and only 25% inhibition towards COX-2 at the same dose. The ability of P. odorata in inhibition of 5-LOX and COX enzymes makes it a potential anti-inflammatory drug.

Meanwhile, for the in-vivo test from the same study by George et al. [46], this experiment tested the anti-inflammatory effects of aqueous extract of P. odorata by its ability to inhibit the A-carrageenan-induced paw oedema in the rat model. The purpose of using aqueous extract instead of ethanolic extract was to mimic the human consumption of P. odorata that is
commonly used in cooking. The study results found that $P. \text{odorata}$ significantly $(p<0.01)$ reduced the $\lambda$-carrageenan-induced paw oedema after 4 hours of administration of carrageenan at dose 100 mg/kg and 300 mg/kg. The maximum anti-inflammatory effects can be seen after 4 hours, possibly because the anti-inflammatory mediators were assumed to be highly released at this time. The presence of flavonoids could contribute to the anti-inflammatory effects of $P. \text{odorata}$ because flavonoids were found to exhibit anti-inflammatory effects [47].

### 3.3 Antibacterial Effects

$P. \text{odorata}$ showed a broad-spectrum of antibacterial effects against gram-positive bacteria and gram-negative bacteria. However, the antibacterial effects' effectiveness was also influenced by the active compounds' ability to penetrate the bacterial cell and damage the DNA [28]. Among the bioactive metabolites in the $P. \text{odorata}$ that contributed to the antibacterial effects are terpenoids, aldehydes and alcohols [10]. The solvent used for extraction of $P. \text{odorata}$ also affects the antibacterial activity of the plant [7]. Besides, the essential oils of $P. \text{odorata}$ also exhibit antibacterial effects, but the effectiveness depends on the vapour or liquid phase and target bacteria [28]. A recent study found that $P. \text{odorata}$ extract containing silver nanoparticles can improve its antibacterial activities and prevent antibiotic resistance [48].

Abubakar et al. [7] revealed that $P. \text{odorata}$ extract using 100% aqueous and 30% aqueous-ethanol solvents have antibacterial activity against $\text{Enterococcus faecalis}$, $\text{Escherichia coli}$ and $\text{Staphylococcus aureus}$, but no extract can inhibit $\text{Pseudomonas aeruginosa}$. The absence effect on $P. \text{aeruginosa}$ might be because of the unsuitable solvent used or the low dosage of extracts. The solubility of active metabolites also influenced by the type of solvent used in
positive bacteria that were susceptible to the agar and broth, respectively. The tested gram
essential oil was obtained by hydrodistillation. The antibacterial activity against six from eight
bacteria in the form of vapour and liquid extract. The tested bacteria in the essential oil of
P. odorata was more potent than aqueous ethanol extraction, followed by E. coli and E. faecalis. The antibacterial effects of aqueous-ethanol P. odorata extract were more potent than aqueous P. odorata extract. The highest concentration (200 mg/mL) of aqueous-ethanol P. odorata extract showed the highest zone of inhibition for S. aureus, E. coli and E. faecalis, with diameters of 19.50 mm, 18.00 mm and 19.33 mm, respectively. Meanwhile, for the aqueous extract the diameters were 16.60 mm, 16.45 mm and 15.70 mm, respectively. This study also identified the minimum inhibitory concentration (MIC) and minimum bactericidal concentration (MBC) of the extracts. MIC was used to identify the lowest concentration of the extract to prevent the visible growth of bacteria, while MBC is the minimum concentration that causes the death of bacteria. The results showed that the MIC of aqueous-ethanol P. odorata extract (50 mg/mL) for the S. aureus, E. coli and E. faecalis was outstanding compared to MIC of aqueous P. odorata extract (100 mg/mL). The value of MBC was found to be the same as the MIC value for both extracts except for aqueous-ethanol extract against E. coli as the MBC (100 mg/mL) was higher than MIC (50 mg/mL).

Meanwhile, in 2020, Řebíčková et al. [28] discovered that the vapour phase of P. odorata (MIC = 512 µg/mL) showed twice effectiveness against E. coli compared to the liquid phase (MIC = 1024 µg/mL). The antibacterial effects of essential oil of P. odorata against bacteria are contributed by the abundance of α-humulene, an active compound that responsible for anti-inflammatory and antibacterial effects in many plants [50]. This study also concluded that the gram-positive bacteria were more susceptible to the essential oil of P. odorata than gram-negative bacteria as the MIC were 512 µg/mL and 1024 µg/mL, respectively. The possible reason is that the peptidoglycan of the gram-positive bacteria is easier to be broken down by the active compound, which subsequently helps the essential oil penetrate the cells and damage the DNA [28]. Moreover, the gram-negative bacteria are more resistant than gram-positive bacteria to the active compounds, might because their cell wall is more complex [51]. Anyhow, the internal use of essential oil of P. odorata must be used with caution as they may cause allergic or irritation due to the presence of cis-caryophyllene [52].

Next, a recent study in 2021 by Aminullah et al. [48], found the antibacterial activity of silver nanoparticles synthesised from P. odorata leaves extract (PO-AgNPs). Previously, there are findings on the broad-spectrum antibacterial effects from other green plants synthesised silver nanoparticles that can be used as an option for antibacterial resistance [53,54]. The nanoparticle
size help to disrupt the membrane of bacteria by increasing the attachment on the cell wall, then causing cell death [48]. This study synthesised PO-AgNPs by adding 1 ml of 2% (w/v) of the P. odorata leaves extract into 10 ml of 1 mM of AgNO₃. The formation of PO-AgNPs can be seen by changing colour from yellowish to dark brown. The physicochemical properties of PO-AgNPs were conducted using various tests: Ultraviolet-visible (UV-Vis) spectrophotometer, Fourier transform infrared (FTIR) spectroscopy analysis, X-ray diffraction (XRD) analysis and energy dispersive X-ray spectroscopy (EDX). Besides, field emission scanning electron microscope (FESEM) was used to identify the morphology and shape of the PO-AgNPs. In order to test the antibacterial activity of PO-AgNPs, the standard disc diffusion technique and time-kill assay were conducted.

The results of the same study [48], found that PO-AgNPs showed antibacterial activity against Methicillin-resistant Staphylococcus aureus (MRSA), S. aureus, S. epidermidis and P. aeruginosa. The activity increases when the amount of PO-AgNPs increases from 10 to 200 μg, indicated by increasing of the inhibition zone. The time-kill assays also possessed the ability of PO-AgNPs to inhibit bacterial growth as the number of viable cells decreases within 24 hours. Besides, PO-AgNPs showed a potent inhibition in the P. aeruginosa. The zone of inhibition against P. aeruginosa at 200 μg of PO-AgNPs was 13 mm, which was higher than 30 μg of chloramphenicol which was 9 mm. Chloramphenicol was being used as a positive control in this study. The strong antibacterial effects of PO-AgNPs could happen because P. aeruginosa has a thin peptidoglycan layer that enables more interaction between the bacteria and PO-AgNPs [48].

### 3.4 Anticancer Effects

According to World Health Organization (WHO), Malaysia recorded 43,837 total cancer cases and 26,395 cancer deaths in 2018. Among the top five most common cancer cases reported were breast cancer, cervix cancer, colorectum cancer, leukaemia and liver cancer [55]. Cancer also causes nearly 10 million deaths in 2020 worldwide [56]. Nowadays, chemotherapy is being used to treat many types of cancer. However, it is also associated with severe side effects such as fatigue, diarrhoea, nausea, febrile neutropenia and rash [57]. Chemotherapy drugs are also expensive and subsequently increase the cost of cancer treatment. For example, the cost per patient for colorectal cancer in Malaysia is from RM13 672 for stage I to RM27 972 for Stage IV [58]. Cost can limit the ability to access anticancer drugs [59]. Hence, the researchers keep finding to identify the potential plants and active compounds that can help to reduce the cancer burden, especially in terms of side effects and cost.

A study by Ahmad et al. [31] identified the anticancer effects from a new compound that was isolated from the stems of P. odorata, known as polygonumins A. The P. odorata was extracted by using methanol. The polygonumins A structure was identified using Frontier Perkin-Elmer FTIR/NIR spectrophotometer and Bruker NMR 600 MHz Cryo-Probe instrument. The cancer cell lines used in this experiment were K562 (human leukaemia cell line), C33A (cervical cancer cell line), HCT116 (colorectal cancer cell line), A549 (human lung adenocarcinoma epithelial cell line), H1299 (human non-small cell lung cancer cell line) and MCF7 (human breast adenocarcinoma cell line). This experiment identified the antiproliferative of polygonumins A from the methanolic extract of P. odorata against the cancer cell lines by using the MTT proliferation assay. The results found that polygonumins A at 24 hour treatment has cytotoxicity against all cancer cell lines except for A549. However, as the set value for the potential anticancer compounds is 4 μg/mL [60], polygonumins A can be recognised as a potential anticancer compound against three cancer cell line, which were HCT116, MCF7 and K652 because the IC₅₀ were 3.24 μg/mL, 2.87 μg/mL and 2.25 μg/mL, respectively. The positive control in this study was doxorubicin. It is a chemotherapy drug that blocks the topoisomerase II, to reduce or stop the growth of cancer cells [61].

Based on the results, polygonumins A can be a potential anticancer compound for colorectal cancer, human breast cancer and human leukaemia. Additionally, the most effective cytotoxicity effects were found against K562 that represents the human leukaemia cell line. The IC₅₀ of polygonumins A (2.25 μg/mL) against K562 was lower than doxorubicin (2.97 μg/mL). The result showed the potential of polygonumins A to be used to treat human leukaemia. Besides, leukaemia cells were more sensitive to chemotherapy than other cancer cells [62]. The mechanism of action of polygonumins A was not fully understood. However, the presence of the sugar moiety in the compound might contribute
to the anticancer effects. Several compounds that possessed anticancer effects, such as CCL-34 also contained sugar moieties based on the structure and activity relationship (SAR) analysis [63].

Another study found the anticancer effects of *P. odorata* against colon and liver cancer cell lines was by Putthawan et al. [64]. This study extracted the aerial part of *P. odorata* by using 80% ethanol. Then, cytotoxicity effects on the cell proliferation of HT-29 (human colon adenocarcinoma) and HepG2 cells (human hepatocellular carcinoma) were identified by using MTT proliferation assay. Besides, this study also conducted a morphological analysis of the HT-29 and HepG2 cells by using a light microscope at 200x magnification. The analysis on the DNA fragmentation was done by using agarose gel electrophoresis, conducted at 100 v at 30 min. Apart from *P. odorata*, this study also evaluated other seven plants with high polyphenol and antioxidant properties, which are *Camellia sinensis, Careya sphaerica, Cratoxylum formosum, Eleutherococcus trifoliatus, Ficus auriculata, Schima wallichii and Vaccinium sprengeli*.

However, out of eight plants, only two plants were found to have strong anticancer effects against HT-29 and HepG2 cancer cell lines, which were *P. odorata* and *S. wallichii*. The positive control used in the cytotoxicity test was mitomycin C. The results of the cytotoxicity activity showed that *P. odorata* (66.86%) extract at 2,000 μg/mL has higher cytotoxicity effect than mitomycin C (17.32%) at 50 μg/mL against HT-29. Even so, the cytotoxicity effects of *P. odorata* extract (68.94%) against HepG2 was lower than mitomycin C (81.35%). When the concentration of the extracts increased, the cytotoxicity effect of *P. odorata* also increased. On top of that, the only tested plant that has higher cytotoxic effects than *P. odorata* in both cell lines was *S. wallichii* extract. Furthermore, the cytotoxic activity concentration (CC_{50}) of *P. odorata* extract against HT-29 was 775 μg/mL and HepG2 cells was 1665 μg/mL.

Next, the same study also found that *P. odorata* caused morphological changes in the HT-29 and HepG2 cells, depending on the concentration. At 500 μg/mL, the cancer cells showed the characteristics of apoptosis. The cancer cells were found to shrink, has denser cytoplasm and the shape was more tightly packed. At 4000 μg/mL, the cancer cells lost the cell adhesion, forming the membrane blebbing and decreasing the cell density. In addition, a smear pattern was observed in the DNA ladder test, that does not happen to control cells. These results indicates that HT-29 and HepG2 cancer cell lines undergo DNA fragmentations when treated with *P. odorata* extract. *P. odorata* extract was more effective than *S. wallichii* to cause DNA fragmentation of HepG2, but less effective than mitomycin C. The ability of *P. odorata* to induce apoptosis in the cancer cell lines is believed due to high polyphenol concentration in the extract because polyphenol was found to induce apoptotic properties [65]. Besides, flavonoid may also contribute to the anticancer effects of *P. odorata* [66].

Interestingly, many recent studies discover the potential of *P. odorata* as anti-oral cancer [6,67,68]. One of the studies is by Khwairakpam et al. [66]. This research identified the ability of *P. odorata* to inhibit cell proliferation, survival and migration against oral squamous cell carcinoma (OSCC) through the suppression of the Akt/mTOR pathway. This study used different type of OSCC cell lines which are SAS, HSC-3, and SCC-9. The normal cell line used was HaCaT (human keratinocyte). The results showed that the methanolic extract of *P. odorata* exhibit higher anti-proliferation against SAS cancer cells (IC_{50}=75 μg/mL) compared to HaCaT normal cells (IC_{50}=100 μg/mL). However, the antiproliferative effects for HSC-3 and SCC-9 were lower than HaCaT. Next, *P. odorata* has a higher cytotoxicity effect against SAS cell line (60-80%) at a concentration-dependent manner (100-200 μg/mL) than against HSC-3 and SCC-9. The result indicates that *P. odorata* is suitable to prevent the replication of the SAS cancer cell line.

The same study [6] also found that *P. odorata* arrest the cell cycle at the G2/M phase. The G2/M phase checkpoint in the cell cycle is vital to prevent damaged cells from undergoing mitosis [69]. Besides, arrest the cancer cells at the G2/M phase will increase apoptosis of the cancer cells that lead to death [70]. At 200 μg/mL, *P. odorata* extract was found to induce 10% apoptosis in SAS cells. *P. odorata* extract also reduces the survival fraction and inhibits the migration of SAS cells. These effects increase when the concentration increases. These results proved that *P. odorata* extract could inhibit the cell division of SAS cells and prevent them from metastasis to other part of the body.
The study by Khwairakpam et al. [6] continued to analyze *P. odorata* through the western blot analysis. *P. odorata* was found to reduce the expression of the key proteins involved in cancer metabolism, which are survivin, cyclin-D1, COX2, VEGF-A, and MMP-9. *P. odorata* also exhibit the anticancer effects at a dose-dependent manner, by decreasing the expression of Akt1, phospho-Akt, m-TOR and phosphor-mTOR in SAS cells. This suggests that *P. odorata* can suppress the Akt/mTOR pathway in SAS cells. Among phytochemicals to be considered in the anticancer activity of *P. odorata* toward OSCC are glycosides, saponins, flavonoids, alkaloid and quinones [6]. Hence, *P. odorata* extract was found to be adequate to possess anticancer activity against OSCC cancer cells. Nevertheless, the summary of pharmacological activities of *P. odorata* is shown in (Table 2).

### 4. CONCLUSION

Plants are the source of many active metabolites that can help to improve current pharmacological treatment. Many plants are already being developed into a powerful drug in this era. Besides, many researchers are studying the plants to find a new potential active compound that can be developed into a new drug. Researchers and pharmaceutical companies can take the lead on *P. odorata* since it exerts many pharmacological effects such as antioxidant, anti-inflammatory, antibacterial and anticancer effects. However, more studies are needed to identify the efficacy and toxicity of *P. odorata*. New research also needs to find the most suitable extraction method of *P. odorata* to get the active compounds. A standardised guideline for the extraction methods needs to be documented. The current technologies can also be used to identify the synergistic effects of *P. odorata* in combination with other compounds. Hence, a potent drug with the most negligible side effects can be developed.

### DISCLAIMER

The products used for this research are commonly and predominantly use products in our area of research and country. There is absolutely no conflict of interest between the authors and producers of the products because we do not intend to use these products as an avenue for any litigation but for the advancement of knowledge. Also, the research was not funded by the producing company rather it was funded by personal efforts of the authors.

### CONSENT

It is not applicable.

### ETHICAL APPROVAL

It is not applicable.

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### COMPETING INTERESTS

Authors have declared that no competing interests exist.

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