Pharmacological Activities and Phytochemical Compounds: Overview of Pouteria Genus

Sani Nurlaela Fitriansyah1,2,*, Irdi Fidrianny1, Rika Hartati1

ABSTRACT
Species of Pouteria are widely spread in various countries. Pouteria is one of the genus that have diverse pharmacological activities. This review includes an overview of the species from Pouteria, phytochemical methods used in isolation of compounds from Pouteria, and their pharmacological activities. The trends in the pharmacological activity of Pouteria is antioxidant activity, anti-diabetic and antimicrobial activities. However, information on its use as a traditional medicine from Pouteria was poor. Chemical compounds that have been widely isolated from Pouteria genus included phenolic acid, other phenolics non flavonoid, flavonoids, and terpenoids derivative. The most widely reported chemical compounds from Pouteria are terpenoid derivatives. Further research is needed for the mechanism of action based on the pharmacological activities of chemical compounds.

Key words: Pouteria genus, Pharmacological activities, Phytochemical compound.

INTRODUCTION
Pouteria genus in one of the 53 genus, Sapotaceae family, which has 325 species and distributed in tropical and subtropical region. Some species of Pouteria were used as traditional medicine. The experiment of pharmacological activities can be based on a report the use of these plants as traditional medicine and chemical content. Information regarding pharmacological activities and phytochemical compounds of Pouteria genus were needed for developing Pouteria genus uses in pharmacy industries. Therefore, this article reported information concerning pharmacological activities, phytochemical method and chemical compounds of Pouteria genus.

METHOD
The data was collected through PubMed. There are 71 journals in PubMed with keyword Pouteria. Journals that used as literature for this review are classified based on international journals indexed by Scopus, quartile 1-4.

RESULTS
The uses of Pouteria genus as traditional medicine can be shown in Table 1. Several species of Pouteria genus were used as food material. The fruits of Pouteria was often consumed directly and used as an additional ingredient in food such as in pudding. In traditional medicine, P. ramiflora as anti-hipperlipidemic, P. campechiana, was used for heart disease, liver, epilepsy, stomach diseases, and skin disruption. Other species of Pouteria genus was applied for inflammation, diabetes, indigestion, diarrhea, nausea, throw up and relieve back pain. Based on the taxonomy of Pouteria, the most studied species is P. campechiana, and it can be seen the order and total species studies in term of pharmacological activity and the compounds isolated in Figure 1.

Phytochemical Compounds of Pouteria Genus
Secondary metabolites in plants are generally produced through the pathway of shikimic and acetic acid. Secondary metabolites from shikimic pathway are phenylpropanoid, simple phenolic compound and polyphenols including flavonoids. Whereas from the acetic acid pathway it is derivative of terpenoids, sterols and derivative of volatile compounds. In this review, information regarding phytochemical compounds of Pouteria genus up to 2019, was presented in Table 2 and Figure 2. Flavonoid, phenolic compounds and terpenoids were secondary metabolite isolated from Pouteria genus.

Other terpenoid compounds that have isolated included α-amyrin and lupeol. These compounds were found in P. torta fruits and flower and P. cainito fruits. Alpha-amyrin acetate and β-amyrin were presented from stem bark extract of P. tomentosa, P. torta and P. gardneri leaves extract. Beta-amyrin acetate and betulinic acid were isolated from methanol leaves extract of P. torta and P. tomentosa. Ursolic acid was reported from several species of Pouteria, included P. venosa extract, P. gardneri extract and P. tomentosa extract. Taraxerol was reported in P. cainito extract and P. venosa extract. While carotenoids were found in P. cambodiana. The other phenolic groups which were isolated from Pouteria, included gallic acid, (+)-gallocatechin, (-)-catechin, (-)-epicatechin, (+)-catechin-3-O-gallate epicatechin, and myricitrin from P. campechiana, P. sapota and P. viridis extracts. Myricitrin have been also isolated from P. torta extract. Stilbenes and protocatechuic acid have...
Table 1: The use of Pouteria genus as traditional medicine.

| Species                        | Part of                  | Uses as traditional medicine                                           | Ref. |
|--------------------------------|--------------------------|-------------------------------------------------------------------------|------|
| *Pouteria caimito*             | Leaves, Flesh of fruit   | for antimalaria, reduce pain, and wound healing                        | 14   |
|                                | Latex                    | to relieve cough, bronchitis, and other lung disorders as a laxative   | 15   |
| *Pouteria cambodiana* (Pierre ex Dubard) Baehni | Stem bark, Other parts | decoction of stem bark to facilitate breast milk                        | 16   |
|                                |                         | for nausea, vomiting, fever and relieve back pain                      | 8,9  |
| *Pouteria ramiflora* (Mart.) Radlk | Fruits and root, Stem bark | as anthelmintic, dysentery, and inflammation                           | 15, 10, 17 |
| *Pouteria campechiana* (Kunth) Baehni | Peel of fruits, Leaves | antipyretic and for healing injured skin                              |      |
|                                |                         | fever reducing medication                                              |      |
|                                |                         | decoction of leaves for diarrhea                                       |      |
| *Pouteria sapota* (Jacq.) H. E. Moore & Stern | Seed and seed oil | to reduce pain in the ear, to treat kidney stones, rheumatism, and digestive disorder | 18   |

Figure 1: Total species studies in term of pharmacological activity and the compounds isolated.

Figure 2: Compounds that have been isolated from Pouteria based on secondary metabolite.
Table 2: Phytochemical compounds of Pouteria up to 2019.

| Phytochemical compounds | Species          | Part used            | Extraction method         | Solvent          | Ref. |
|-------------------------|------------------|----------------------|---------------------------|------------------|------|
| **Flavonoid**           |                  |                      |                           |                  |      |
| Myricetin               | *P. campechiana*  | Leaves and seed      | Maceration                | EtOH 70%         | 27   |
|                        | *P. torta*       | Leaves               | Percolation               | EtOH-Water (7:3) | 28   |
| Myricetin-3-O-β-galactoside | *P. campechiana* | Leaves and seed      | Maceration                | EtOH 70%         | 27   |
| Myricetin-3-O-α-L-rhamnoside | *P. campechiana* | Leaves; Seed         | Maceration                | EtOH 70%         | 27   |
| **Quercetin**           |                  |                      |                           |                  |      |
| Quercetin-3-O-α-L-rhamnopyranoside | *P. campechiana* | Leaves               | Maceration                | Methanol         | 30   |
| **Phenolic compound**   |                  |                      |                           |                  |      |
| Gallat acid             | *P. campechiana*  | Leaves and Seed      | Maceration                | Ethanol 70%      | 27   |
| **Terpenoid**           |                  |                      |                           |                  |      |
| a. Neoxanthin;          | *P. sapota*      | Ripe Fruit           | Homogenized with acetone  | Acetone          | 31   |
| (9’Z)-Neoxanthin        |                  |                      |                           |                  |      |
| c. Capsoneoxanthin      |                  |                      |                           |                  |      |
| a. α- and β- amyrin     | *P. gardneri*    | Leaves               | Maceration                | n-Hexane         | 32   |
| b. Lupeol               |                  |                      |                           |                  |      |
| c. α- amyrin acetate    |                  |                      |                           |                  |      |
| d. 9-taxarastanol acetate |              |                      |                           |                  |      |
| a. ursolic              | *P. gardneri*    | Leaves               | Maceration                | Ethanol          |      |
| b. oleanol acid         |                  |                      |                           |                  |      |
| Monoterpenes (a-Pinene) | *P. elegans*     | Ripe fruits          | HS-SPME technique         |                 | 33   |
| a. sapotexanthin, 5,6-epoxide |              |                      |                           |                  |      |
| b. sapotexanthin, 5,8-epoxide |            |                      |                           |                  |      |
| c. cryptocapsin         | *P. sapota*      | Ripe fruits          | Homogenized in mortar     | Acetone          | 34   |
| d. capsanthin, 5,6-epoxide |              |                      |                           |                  |      |
| a. Friedelin            | *P. ramiflora*   | Leaves               | Maceration                | n-Hexane         | 35   |
| b. Epi-friedelanol      |                  |                      |                           |                  |      |
| Taraxerol               | *P. venosa*      | Leaves; bark; stem bark | Maceration              | Ethanol          | 11   |
| a. Spinasterol;         | *P. cambodiana*  | Stem bark            | Maceration                | Ethyl acetate    | 36   |
| b. Three triterpenes fatty acid ester |  |                      |                           |                  |      |
| c. Spinasterol;         | *P. cambodiana*  | Stem bark            | Maceration                | Ethyl acetate    | 36   |
| d. Spinasterol          |                  |                      |                           |                  |      |
| Cryptocapsin            | *P. sapota*      | Fruits               | Homogenized with NaHCO₃   | Acetone          | 37   |
| a. Cryptocapsin, 5,6-epoxide |              |                      |                           |                  |      |
| b. 3’-deoxycapsanthin   | *P. sapota*      | Fruits               | Homogenized with NaHCO₃   | Acetone          | 38   |
| c. 3’-deoxycapsorubin   | *P. sapota*      | Fruit                | Homogenized with NaHCO₃   | Acetone          | 39   |
| b. 3,3’-dideoxycapsorubin |            |                      |                           |                  |      |
| Sapotexanthin (all-E,5’R)-β,x-caroten-6’-one | *P. sapota* | Fruit                | Homogenized with NaHCO₃   | Acetone          | 40   |

been isolated from *P. cambodiana* extract.\textsuperscript{13,16} Besides that, four of dihydroflavonols (dihydrokaemferol glycosides) were isolated from methanol-water (80:20) extract of *P. obovate*.\textsuperscript{25}

**Pharmacological activities**

The pharmacological activities research of Pouteria varied widely. The pharmacological activity trends under study can be seen in the Figure 3 and in Table 3.

**Antioxidant activity**

Antioxidant activity was the most reported from Pouteria genus. Some extracts and fractions of Pouteria active as antioxidant. Many species of Pouteria have antioxidant activities included methanol extract of stem bark *P. cambodiana* with IC₅₀ against DPPH 0.24 mg/ml,\textsuperscript{36} acetone extract, methanol and acetone fractions of *P. campechiana* fruit,\textsuperscript{3} ethanol and water extracts of *P. campechiana* fruits with different level maturity of 4, 8, 12, 16, 20 and 24 weeks as antioxidant against DPPH,
Table 3: Pharmacological activities of *Pouteria* genus.

| Species          | Part Used | Pharmacological activities                                                                 | Ref.               |
|------------------|-----------|-------------------------------------------------------------------------------------------|--------------------|
|                  | R | RB | F  | S  | St | StB | L            |
| *P. torta*       | + |     | +  | +  | +  |      | 4; 12; 28; 51; 53; 54; 55 |
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FRAP and ABTS with variation inhibition.\textsuperscript{4} Besides that, leaves extract of \textit{P. ramiflora} and \textit{P. venosa},\textsuperscript{11} \textit{P. viridis} fruits extract\textsuperscript{1} and \textit{P. splendens} leaves\textsuperscript{4} had antioxidant activity. Antioxidant activity of \textit{P. caimito} leaves extract had the smallest IC\textsubscript{50} of 36.1 µg/ml compared to n-hexane and ethanol extracts.\textsuperscript{14} The phenolic group can contribute to antioxidant activity. Phenolic compound of methanol-acetic acid (85:15) fruit extract of \textit{P. sapota} showed antioxidant activity.\textsuperscript{20} Beside the phenolic group, the carotenoid group can also contribute to antioxidant activity. Ethanol extracts of \textit{P. campechiana} fruits that were stored for 2, 4, 6, 8, 10 and 12 days gave increasing in total carotenoid content and followed by increasing in antioxidant activity.\textsuperscript{43}

Other pharmacological activities

Methanol extracts of \textit{Pouteria cambodiana} stem bark\textsuperscript{39} and \textit{P. campechiana} leaves\textsuperscript{46} was reported to have immunomodulatory activity. \textit{P. gardnerii}, \textit{P. ramiflora} dan \textit{P. torta} extracts did not show active against \textit{Aedes aegypti}, \textit{Rhodnius maxalis} and \textit{Dipetalogaster maxilis}.\textsuperscript{39,40} N-hexane-ethyl acetate (1:1) fraction of \textit{P. venosa} active against \textit{A. aegypti}.\textsuperscript{41} \textit{P. ramiflora} water extract and fraction of the ethanol extract of \textit{P. torta} leaves\textsuperscript{42} and methanol extract of \textit{P. torta} leaves\textsuperscript{42} revealed to possess toxicity effect towards \textit{Artemia salina}. While stem bark, lignum and root of \textit{P. guianensis} have no toxicity effect towards \textit{Artemia franciscana}.\textsuperscript{40,46} Pouterin compound from \textit{P. torta} showed insecticidal effect against \textit{Callosobruchus maculatus}, also has the ability to agglomerate erythrocytes in humans, rabbits and mice.\textsuperscript{40} The other researches stated that stem extract of \textit{P. sapota} active as antiplasmodium\textsuperscript{40} and leaves extract of \textit{P. venosa} as antimalarial.\textsuperscript{40} Hydroethanol of stem and stem bark extracts of \textit{P. guianensis} active as anti-termite against Nasutitermes sp.\textsuperscript{46}

Wood root extract of \textit{P. torta} have cytotoxicity effect against HCT-8 (human colon carcinoma) with IC\textsubscript{50} 37.9 µg/ml, HL-60 (leukemia) with IC\textsubscript{50} 31.7 µg/ml, SF-295 (Brain) with IC\textsubscript{50} 30.2 µg/ml and MDA-MB-435 (melanoma) with IC\textsubscript{50} 21 µg/ml.\textsuperscript{46} Methanol leaves extract of \textit{P. viridis} active as anti-HIV.\textsuperscript{46} N-hexane leaves extract of \textit{P. torta} active as antagonist estrogen at estrogen beta (ER\textsubscript{β}) receptor.\textsuperscript{41}

\textit{P. gardnerii}, \textit{P. ramiflora}, \textit{P. torta}, and \textit{P. caimito} have been tested for as inhibitor tyrosinase. Water leaves extract of \textit{P. torta} and \textit{P. caimito} active as an inhibitor of tyrosinase with IC\textsubscript{50} 30.1 µg/ml and MDA-MB-435 (melanoma).\textsuperscript{46} Ethanol leaves extract of \textit{P. ramiflora} and \textit{P. torta} showed IC\textsubscript{50} 249.83 µg/ml and 104.34 µg/ml.\textsuperscript{42}

\section*{DISCUSSION}

Pouteria is a genus that has many types. The plant part of the Pouteria species can be used as food ingredients and have pharmacological activities. The part of the plant which often used as food material is a fruit. A peel of fruit, leaves, and stem bark were reported to have more potential in term of pharmacological activity.

Phytochemical compound in plants is generally produced through the pathway of shikimic and acetic acid. Phytochemical compounds are important components in plants. It can be isolated from the initial extraction step. The extraction method and solvent used will affect the resulting.\textsuperscript{73} The extraction method can be influenced by the type and amount of phytochemical compounds which was isolated. In addition, factors of kinship in the taxonomy of a plant can affect the type of chemical compounds. Among the types of Pouteria have a kinship, namely one genus. Therefore, several types of Pouteria have the same chemical compounds.

Trends in pharmacological activity of Pouteria are antioxidant and antimicrobial activity. The pharmacological activity of a plant can be caused by the presence of chemical compounds. The type of chemical compound and the concentration of chemical compounds in a plant can affect the type of pharmacological activity or the strength of the pharmacological activity. Antioxidant activity can be caused by the presence of the compounds from polyphenol group. Phenolic acids and flavonoids greatly contribute to antioxidant activity. The position of the OH group and the presence of double bonds on carbon atom no 2 and no 3 on flavonoids can affect the intensity of antioxidant activity. Antimicrobial activity can also be caused by the presence of compounds belonging to the polyphenol group and terpenoid derivatives. In Pouteria, many chemical compounds that have been isolated are phenol and polyphenol group and terpenoid derivatives.

\section*{CONCLUSIONS}

Based on the literature, species of Pouteria which have presented to came from subtropical and tropical areas such as in North America, Central America, and Asia. \textit{Pouteria campechiana} is the species most studied. Some pharmacological activities and phytochemical compounds of Pouteria genus have been widely stated. Extracts of Pouteria genus were demonstrated to have some pharmacological activities, however information concerning treatment the skin and other pharmacological activity of fraction and chemical compound of Pouteria genus was less. In addition, so far information on the mechanism of chemical compound from Pouteria genus guided by pharmacological activities has not been found.

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Graphical Abstract

About Authors

Sani Nurlaela Fitriansyah: Doctoral student in ITB and a lecture in Department of Pharmaceutical Biology, Indonesian School of Pharmacy, Bandung Indonesia. Develop work in pharmacognosy of natural material.

Irda Fidrianny is Professor in Department of Pharmaceutical Biology, School of Pharmacy, Institute Technology of Bandung. Develop work in phytochemical and standardization of natural materials.

Rika Hartati is Doctoral in Department of Pharmaceutical Biology, School of Pharmacy, Institute Technology of Bandung. Develop work in pharmacognosy and phytochemical of natural materials.

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