Efficacy and safety in consuming python bile: a literature study

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Abstract. In Indonesia, consuming python bile is quite popular to treat various health conditions, such as respiratory disorders, fever, aches, and increase immunity. However, scientific study as a basis for the use in this modern era still limited. This research is a literature study to determine the efficacy and safety of python bile consumption. Literature search was conducted in June 2020. Appropriate keywords were put in Google search engine, Google Scholar and PubMed. The results showed pythons bile have the main content of bile acids and bile salts type Tauropyrocholate (TPC), Taurocholate (TC), Taurodeoxycholate (TDC) that could inhibit bacteria growths. Other compounds are protein and antioxidants. Consumption of python’s bile can provide benefits like bile function itself, namely elimination of toxins, increase the absorption of fat-soluble vitamins and cholesterol. Python bile can be a source of bacteria and parasites transmission. High doses (>2 biles) and long term use are not recommended since the potential damage of liver and kidneys. Python bile has the potential for efficacy in accordance with its empirical claims. The consumption of healthy snake bile, in accordance with the dosage and not often is quite safe. This finding must still be strengthened with experimental study.

1. Introduction
Like plants, animals are also used for treatment since a long time ago. The use of animal body parts in traditional medicine has become a part of the culture in many countries, both as internal medicine and external (topical) medicine [1–4]. Body parts used, ranging from skin, bile, meat, oil/fat, nails, bones, feathers, horns, tails, and shells [2,5]. The type of animals also varies depends on the regional culture or country concerned, ranging from mammals, reptiles, insects, amphibians, fish, aves, and worms [1,3,6,7]. Claims of efficacy include treating asthma, cough, jaundice, typhoid fever, toothache, high blood pressure, headache, eye pain, diabetes, malaria fever, skin disease, allergies, hemorrhoid, fracture, wound healing, and increase stamina and body immunity [2,3,8,9].

In the modern era as it is today, there is an increase in researches in order to prove the efficacy and safety of the use of traditional medicine, including those from animal [10,11]. Ethnomedicine diversity is a source of new drug exploration that is expected to solve various health problem in the future [11]. In addition, the existence of scientific evidence will also increase public knowledge, provide a sense of security and trust in the use of the traditional medicine.

Snakes are one of the popular reptiles that have various health benefits [5,7,12]. The snakes that are usually used in Indonesia are cobras and pythons [3,7]. Pythons or ‘sanca’ have been known as domesticated snakes, their skin used as crafts, and some people eat the fried meat [7]. Although not as

famous as the cobra, python bile is widely used for medicine in China, Africa, India, and Indonesia [3–5, 7, 8]. Based on information from people who consume python bile, they use the python bile by swallowing it directly or drying it, then cut it into pieces and swallowed with water or put in an empty capsule and drunk. The python bile is believed to be able to overcome colds/ runny nose, malaria fever, fever, cough, short of breath, aches, and increase body immunity. Based on testimonials from users, the therapeutic effect will be felt approximately 10 minutes after consumption which is marked by the body becoming light, light breathing, dizziness disappears, the body temperature drops to normal, and the body's immunity increases.

Based on the broad utility of python bile, it has the potential to be developed as a drug [12]. On the other side, the exploitation of this type of snake can threaten the population [7]. Therefore, research is needed regarding the actual efficacy and safety of the python bile so that it can be used rationally in the community. This research is a literature study to provide scientific evidence of the efficacy and safety of python bile.

2. Methods
The research is a literature study. Literature search was conducted in June 2020 through the google search engine, google scholar, and PubMed. The keywords are ular piton, empedu, python snake, bile, ular sanca, as well additional words related to efficacy, safety, taxonomy, and bioactive compound. Articles that fall into inclusion criteria are articles in Indonesian or English originating from scientific journals, parts of books, or web pages from reliable sources that are relevant to the subject of the study. The year of publication is not limited.

3. Results
3.1. Nomenclature and habitat
Pythonidae or Pythons Family has 10 genera and 44 species that were found until 2015. Pythons are one of the snakes that have existed since ancient times. Pythons can be found in tropical and subtropical regions of the eastern hemisphere especially sub-Saharan Africa, Asia which is located below 30 degrees latitude, Indonesia, Philippines, Papua New Guinea, and Australia. Two species of them, Python regius and P. molurus can only be found in the northern hemisphere while 42 other species are scattered in the equatorial and subequatorial regions. Burmese python (Python bivittatus), which is one of the largest species of pythons in the world, was also found in Florida, America, and became a nuisance animal in the national park. Burmese python is also a species of python that is widely used in medicine. As a tropical country, various species of phyton can be found in Indonesia. Some phyton species are even given the name of the area in Indonesia where they are found, eg: Halmahera python, Papuan python, Biak whitelip python, Borneo python, and Sumatran python (Table 1) [13].

Table 1. List of currently recognized python species.

| Genus       | Species | Common name           | Reynolds et al 2014       |
|-------------|---------|-----------------------|---------------------------|
| Antaresia   | Children| Children’s Python     | Chondropython childreni   |
| Antaresia   | Maculosa| Spotted Python        | Chondropython maculosus   |
| Antaresia   | Perthensis| Pygmy Python         | Chondropython perthensis  |
| Antaresia   | Stimsoni| Large-blotched Python | Chondropython stimsoni    |
| Apodora     | Papuana | Papuan Python         | Lisalia papuanus          |
| Aspidites   | Melanoccephalus| Black-headed Python | Aspidites melanoccephalus |
| Aspidites   | Ramsayi | Woma                  | Aspidites ramsayi         |
| Bothrochilus| Boa     | Ringed Python         | Bothrochilus boa          |
| Leiopython  | Albertsii| Northern Whitelip Python | Bothrochilus albertsii    |
| Leiopython  | Biakensis| Biak Whitelip Python  | *                         |
| Leiopython  | Fredparkeri| Karimui Basin Whitelip | *                         |
| Leiopython  | Huonensis| Huon Peninsula Whitelip | *                        |
The body parts of the pythons used for medicine are not only bile but also skin, flesh, blood, and marrow. Based on the results of ethnomedicine studies in several regions of Indonesia, there are known several species of pythons used as medicine (Table 2).

### 3.2. Morphology and chemical content of python bile

In the medical world, bile is a liquid produced by the liver. This fluid is usually green and contained in the gallbladder [8]. Based on ultrasound imaging conducted by Amira and Mokhamad in 2017, healthy pythons from 3 species: reticulated pythons (Malayopython reticulatus), python bodo (P. molurus, P. bivittatus), and healthy pythons (P. regius) have oval to rounded shaped anechoic gallbladder that is separated from the liver organ. The gallbladder walls were hyperechoic filling almost the entire body cavity. The size of the bile gland based on the number of ventral scales of the three pythons is 7-9 scales with the position of the organ in the middle of the body length in a varying range of ventral scale numbers [17].

In principle, the liquid bile of an organism is composed of [8]: 1. Bile acids as the main component which in most animals are mediated by amino acids: taurine or glycerin type to form soluble detergent- like Na+ or K+ salts. This bile salts are resistant to forming insoluble salts with Ca2+. Sterols as a result of the main catabolism of cholesterol are also found in bile. Each organism has several different types of bile acids and bile salts. 2. Bile pigment (bilirubin, biliverdin, or both) which
is the final product of solving heme in the form of mono or hetero conjugation with glucoronic acid, sometimes with glucose and xylose or taurine. 3. Unesterified cholesterol-containing traces of plants (phyto) and shellfish (konko) sterols. 4. phospholipids, not found in reptile bile. 5. Small amounts of protein, especially glycoproteins, various mineral salts, and antioxidants namely glutathione, vitamin E, and melatonin (n-acetyl-5-methoxytryptamine).

Table 2. Utilization of python for medicine in Indonesia.

| Species name | Local name | Part of the body | How to use | Claim efficacy | Area/ location |
|--------------|------------|------------------|------------|----------------|----------------|
| Python reticulatus | Piton | Skin | Oil from dried skin is applied to the affected body part | Cure skin diseases, prickly heat, burns, and allergies. | Painan (Sumatera Barat) [3] |
| Python reticulatus | Piton | Flesh and skin | Not explained | Smooth skin, heal burns, eczema, ulcers, pimples, and remove black spots. | Pasaman (Sumatera Barat) [3] |
| Python reticulatus | Piton | Bile | Not explained | Cure various diseases | Kalimantan Barat [14] |
| Python reticulatus | Sanca | 1. Fresh blood, bile, and marrow | Orally (be drunk) | Cure skin disease, impotence, diabetes, liver, poor vision, heart disease, asthma, and blood pressure | DKI Jakarta [7] |
| - | Ular piton | Bile | Be drunk /Swallowed | Reducing toxins in the body and cure asthma | Sulawesi Barat [15] |
| - | Ular sawo | Bile | Be eaten | Malaria fever | Riau (anak dalam tribe) [16] |

In the vertebrate group, including reptiles, the bile liquid contain steroid-conjugated bile acids as soluble salts [8]. According to Yeh et al., the main structure of bile acids in snakes consists of bitocholic acid, pytocholic acid, and 23R-hydroxycholic acid [18]. Based on the review conducted by Wang et al., pythons (P. morulus, P. bivittatus) mainly have the composition of bile acids and bile salts type tauropythocholate (TPC), taurocholate (TC), taurodeoxycholate (TDC) (figure 1) and bile pigments type biliverdin, bilirubin monoglucuronide (BMG), unconjugated bilirubin (UCB) [8].

Figure 1. Python bile acids and bile salts molecules, a. Sodium taurodeoxycholate (C26H44NaO6S) [19], b. Taurodeoxycholic acid C26H44NO6S- [20], c. Sodium taurocholate (C26H44NaO7S) [21], d. Taurocholic acid (C26H45NO7S) [22].
3.3. Rationalization of efficacy

Scientific paper about experimental tests of the efficacy and mechanism of snake bile to overcome health problems in national scientific journals has not yet found. But, there are papers about surveys of the use of snake bile to overcome health problems in the community. Some scientific articles from Chinese researchers discuss this. The mechanism of action of snake bile for treatment is indeed not much explained in detail. The scientific article is more towards the basics of its empiric use for thousands of years.

There are about 20 patented products that contain bile in China [12]. The use of dog, ox and common carp bile in TCM started since Zhou dynasty about 500 years BC. There are 44 bile from animals and humans that were used in TCM [8]. Bears bile, snakes bile, and cow-bezoar (gallstones) (naturally occurred), is a prestigious traditional medicine with high prices in China [6]. Python bile in TCM was used to treat gum inflammation, gum atrophy, dental caries, coughing, biliary colic, malnutrition, hemorrhoids, dysentery, skin diseases, infectious diseases, eye atrophy, fever in children and improving vision [8].

There are 3 snake families that use the most in China and Taiwan, namely Elapidae, Colubridae, and Viperidae. Research on the bile acid content of 17 species included in the 3 families above including famous Bungarus fasciatus, Naja naja (N. Naja), Dinodon rufzonatum, Elaphe taeniura, Enhydris chinensis, and Protobothrops mucrosquamatus showed there are 3 main ingredients of bile acids, namely tauro-3α, 12α-dihydroxy-7-oxo-5β-cholenoic acid (T1), tauro-3α, 7α, 12α, 23R-tetrahydroxy-5β-cholenoic acid (T2), taurocholic acid (TCA). The three bile acids are determined as markers that determine the quality of snake bile [12].

Bile acids in the organism’s body have the function of breaking down fat into fatty acids in the digestive tract so that it can be absorbed by the body, helping the absorption of fat-soluble vitamins and eliminating toxins [23]. Edible bile is thought to have the same function, so it can be a promising therapeutic agent for increasing vitamin absorption, improving biliary cholesterol saturation, treating gallstones, and improving symptoms cause by cholestatic liver disease[6]. This can explain the claim of the efficacy of python bile to increase body immunity by increasing fitness because of the absorption of fat-soluble vitamins and better fat metabolism.

Bile acids have steroid content [6]. Steroid hormones and bile acids are both formed from the breakdown of cholesterol. Research by Yasukawa et al. in 2009 against 55 derivatives of bile acids including deoxycholic acid showed topical anti-inflammatory activity which was indicated by inhibition of edema in rat ears smeared with the 12-O-tetradecanoylphorbol-13-acetate (TPA) inflammatory agent. The most potent types of bile acids are Chenodeoxycholic acid, methyl 3a, 7a, 15a-trihydroxy-5b-cholan-24-oate and methyl 3a, 7a, 15b-trihydroxy-5b-cholan-24-oate. This effect can even be compared with hydrocortisone [9].

Bile salts are potent antibacterial agent and an important component to protect the small intestine from invasive microorganisms. In vitro experiment showed that cholic and deoxycholic bile salts at concentrations of 20 and 1 mm had the ability to kill the Staphylococcus aureus bacteria by increased damage and leakage in the cell membrane, causing the contents in the bacteria cells to come out [24]. Another invitro experiment conducted by Sung et al have demonstrated that hydrophobic bile salts such as sodium taurodeoxycholate had more potent inhibition on the growth of two common biliary pathogens Escherichia coli and Enterococcus fecalis when compared with hydrophilic bile salts (sodium taurocholate) [25]. Besides, all parts of the snake, including its bile, are a source of protein and contain antioxidants [8,26]. This can be the initial basis for claims of the efficacy of python bile for colds/runny nose, malaria, fever, heat, cough, shortness of breath caused by respiratory tracts allergy or infection (such as: asthma, bronchitis), aches.
3.4. Safety

The composition of bile acids is different between each species and this determines the efficacy and safety. N. naja from the Elapidae family is a type of cobra mainly contains bile acids type cholic acid, and chenodeoxycholic acid. Consumption of more than 5 bile from N. naja was reported to cause poisoning which is characterized by kidney and liver damage. The common dose of N. naja bile is equivalent to the bile of a snake (weight of 2-3 grams). Administration of 2-3 times the above dose in rat triggered kidney and liver dysfunction. Administration for 19 consecutive days caused an increase in Serum Glutamic Oxaloacetic Transaminase (SGOT), Serum Glutamic Pyruvic Transaminase (SGPT), Alkaline Phosphatase (ALP), plasma urea nitrogen and creatinine especially in 3 times dose. Whereas Hemoglobin (HB), hematocrit and red blood cell were also increased. The ratio of kidney and liver weight compared to body weight increased. On the other side, the weight of rats was lower than control group. Histopathological results showed necrosis and swelling of hepatocytes, degeneration, and enlargement of renal tubular/peritubular tissue. A decrease in the concentration of Na+, K+ and Ca++ ions were also found. Based on this research, chenodeoxycholic acid was identified as a compound causing toxicity. Chenodeoxycholic acid toxicity is below cyprinol sulfate which is the main component of grass carp bile acids. Cyprinol sulfate can cause acute toxicity leading to death, while chenodeoxycholic causes toxicity when consumed regularly and buildup occurs in the body [18].

Until the time this article was written, the authors found no death case report due to consumption of python bile. This may be because, chenodeoxycholic and cyprinol sulfate are not the major component of python bile acids [8].

Consumption of python body parts can also increase transmission of diseases originating in animals, such as [26–28]:

3.4.1. Bacteria. *Salmonella spp* is the most common group of bacteria found in reptiles including snakes. Other types of bacteria that can be transmitted to humans are *non-tuberculosis mycobacteria, chlamydia, leptospire, Escherichia coli, Klebsiella sp, Campylobacter spp, Campylobacter spp.*, *Yersinia spp*.  

3.4.2. Parasites. Protists and related microorganisms eucaryotic: *Cryptosporidium parvum, Cryptosporidium muris, Toxoplasma gondii, Cyclospora cayetanensis*. Metazoa: *Cestoda (Spirometra spp), Acanthocephalan, Nematoda (Trichinella spp), Leeches, Pentastomides, and Arthropods*.  

Pythons that contain bacteria or parasites in their bodies can show symptoms of illness, although most are only as a carrier. Snakes infected with non-tuberculosis mycobacteria usually look thin and lack appetite [27]. Chlamydia abortus and C. pneumoniae can cause airway disorders in Burmese pythons (P. molurus, P. bivittatus). Salmonella-infected snakes experience diarrhea and expel the bacteria in their feces [28].

4. Discussion

The python is one of the reptiles on the CITES list. The animal export trading is limited and regulated in the Regulation of the Minister of Trade of the Republic of Indonesia Number 122 of 2018 [29]. According to the 2008 Red List, pythons and bulls are in the vulnerable category because the adult population in nature is less than 10 000 and has a 10% chance of extinction within 100 years [7]. The alternative is to breed pythons for medicinal purposes so that the snake's health is more secure, does not become a carrier for parasitic diseases, and its survival in nature is maintained.

The empirical evidence of python bile efficacy, in Indonesia and especially in TCM for hundreds of years and still establish until now cannot be ignored. In vitro experiments prove the anti-inflammatory and antibacterial effect of bile acids and bile salts. Although, these results still have to be corroborated by evidence of preclinical trials and clinical trials. The instant effect that is felt after 10 minutes of consuming python bile is probably due to the content of bile acids/bile salts which immediately works when it enters the small intestine. However, how much this content is in dry bile compared to fresh
bile still has to be proven by experimental research. In China, the quality of traded dry bile is still an interesting issue.

Snake bile in medicine must be used wisely because consumption in large doses and over a long period of time can cause liver and kidney damage. Consumption of snake bile can also increase the risk of contracting bacteria and parasites.

5. Conclusion and suggestion
Based on this study, python snake bile contains bile acids, bile salts, proteins, antioxidants (glutathione, vitamin E, melatonin), which have the potential to become anti-inflammatory, antibacterial, improve fitness (increase absorption of vitamins), and treat digestive diseases due to bile (glutathione, vitamin E, melatonin), which have t

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