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Bioactive Compounds and Functional Benefits of the Foshou Fruit: A Review

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Abstract This study is an important approach to studying the functional properties of the Foshou, which can be used in other food product systems. Foshou (*Citrus medica* L. var. *sarcodactylis* Swingle) is a medicinal plant member of the Rutaceae family. Foshou is now a potential functional food because it provides the human diet with micro and macronutrients along with a large pool of bioactive compounds, very much relevant to improving health and reducing the risk of several diseases. A huge number of benefits that Foshou possesses include Anti-helmintic, Anti-cancer, Anti-dyspepsia, Anti-oxidant Anti-microbial, Anti-inflammatory and Hypoglycaemic properties. Initial studies have found that the various components of Foshou show a variety of functional effects. These findings are extremely encouraging hence referring to the necessity of studying this plant extensively to confirm these findings and also reveal other functional effects. This study helps an overview of the bioactive compounds and functional benefits of this fruit and has potential functional benefits efficacy.

Keywords: *Citrus medica L., Foshou, medicinal plant, bioactive compounds, functional benefits, functional food*

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1. Introduction

Foshou (Citrus medica L. var. sarcodactyl is Swingle) is a medicinal plant from the Rutaceae family. Ordinarily, it is more popularly named "Buddha Hand Citron", "Five finger orange" or "Longevity orange" in commercial vegetable markets [1]. The Scientific name is Citrus medica L. var. sarcodactylis (Hoola van Nooten) Swingle. Foshou Common English names Buddha-Hand Citron, Buddha's-Hand, Buddha's Fingers, Fingered Citron, Flesh-Finger Citron. Foshou have many Vernacular names shown in (Table 1) [2].

Foshou grows as a small tree or shrub, its fruit is elliptical, pale yellow, with detached segments encircled by the pericarp. The fruit's surface is coarse and the pericarp white to pale yellow. The core of the pericarp usually soft, thick without seeds and difficult to remove meanwhile. The color of the sarcocarp is nearly pellucid to pale milky yellow, it contains 10-15 segments, it has an acidic taste to slightly sweet, and fragrant. The flowering period is from April to May, and the Fruiting period from October to November [3].

Foshou has economic significance because it was and still being use as a traditional Chinese medicinal material, sweetmeats, and functional vegetables [4]. Traditionally, in the eastern countries people prefer to take dried Foshou fruits in herbal medicines as an adjuvant for the treatment of a wide range of chronic diseases like respiratory tract infections, asthma, and hypertension. Attributed many therapeutic properties to Foshou polysaccharides (FPs), FPs is one of the most significant active constituents in Foshou [5].

The maturation stages greatly influence the effect on the synthesis of essential oils obtained from the Foshou fruits [4]. The polysaccharides extracted from Foshou fruits are of special importance because of their effective bioactivities, such as antioxidant [6]. Diets rich in natural antioxidants and various extracts from Foshou fruits are linked to minimize the risk of chronic diseases like obesity and accumulation of fat [4].

There are many studies which reported the chemical compounds of Foshou [7], and the effect of Foshou as anti-helmintic [8], Anti-cancer [9], Anti-dyspepsia [10], Anti-inflammatory [11,12], Anti-microbial [13,14], Anti-oxidant [6,15] and Hypoglycaemic [4]. Food can be classified as functional if confirmed as having beneficial effects on one or more functions in the body, sufficient nutritional effects, in a way that is relevant to either state of welfare and health or lowering of the risk of a disease [16].

There has been no report in literature about Foshou as functional benefits. Furthermore, the correlation between

consumption of Foshou and the functional benefits has not reported. Therefore, we seek to provide this missing data in order to fill this knowledge divide. Hence, the objectives of this review were to determine the bioactive compounds and functional benefits of Foshou as a novel functional food.

Table 1. Vernacular names of Foshou.

Country	Names	Ref.
Chinese	Fo Shou, Fo Shou Gan, Fo Shou Kan, Fo Shou Pian, Fo Shou P'ien, Fu Shou (佛手)	[2,7]
French	Cédrat Digité, Cédrat Main De Bouddha, Sarcodactyle.	[2]
Malaysia	Jeruk Tangan, Limau Jari, Limau Kerat Lintang.	[2]
German	Buddha fi nger, Ge fingerte Zitrone.	[2]
Italian	Cedro A Mano Di Budda.	[2]
Vietnamese	Cây Phât Thu, Phật Thủ.	[2]
Finnish	Sormisukaattisitruuna.	[2]
Dutch	Hand Van Boeddha.	[2]
Iraq	Al-Abbas's Hand.	[13]
Danish	Buddha finger.	[2]
Indonesia	Jeruk Tangan.	[2]
Japanese	Bushukan.	[2]
Thai	Som Mue.	[2]

2. Edible Plant Parts and Uses

Foshou fruit is edible and has eaten in China for centuries. In the southern provinces of China, Taiwan, and Japan, it is generally used as functional vegetables and preserved as dessert. The fruit mostly has no pulp but composed fully of the edible fleshy peel and it can be used in its fresh state or use to made pickled, candy, and jam. This dessert is an aromatic and tasty snack that is ideal for the dyspepsia and sore throat. In Indonesia, Foshou is eaten completely although it has no or scanty pulp or use as lalab (salad) with rice [2].

3. Bioactive Compounds

Many researchers have examined the chemical structure of Foshou and have come to the conclusion that there are four main classes the bioactive compounds namely (essential oils, flavonoids, phenolic acids, and coumarins) [7].

3.1. Essential Oils

Utilization of essential oils (EOs) is gaining momentum as functional components in food because of the increasing attention of patrons in effect elements from natural resources and the increasing concern over potentially harmful of food additives [17]. The oil concentrations in is generally from 0.125 to 0.325 %. The major components of Foshou oils include alpha-pinene (0.70-3.40 %), (1.38-2.88 %) beta-pinene, gamma-terpinene (15.89-33.71 %) and D-limonene (37.96 to 57.10 %) [18]. It has revealed that the constituent chemical composition of EOs are different at the different stages of maturity (Table 2) [15].

Table 2. Chemical composition of essential oils from the Foshou at different stages of maturity

No.[a]	Constituent	RI	% of total volatiles		
			IM	INT	MAT
1	α-Thujone	928	4.29c	4.66b	5.09a
2	3-Carene	934	8.26b	8.15b	9.01a
3	α-Pinene	948	6.38b	7.61a	7.73a
4	β-Pinene	970	2.76b	2.64b	3.18a
5	Camphene	997	0.22a	0.26a	0.29a
6	Terpinolene	1018	2.14b	2.79a	2.78a
7	Limonene	1025	36.37a	32.07b	33.84ab
8	(*E*)-β-Ocimene	1036	0.55b	0.74ab	0.99a
9	*p*-Cymene	1042	2.48a	1.64b	2.27ab
10	γ-Terpinene	1047	22.44b	25.23a	22.88ab
11	1,3-Cyclopentadiene	1078	1.75b	2.30a	2.36a
12	Linalool	1082	0.17a	0.16a	0.18a
13	Citronellal	1126	0.11a	Nd	Nd
14	(−)-4-Terpineol	1137	0.69b	0.88a	0.81a
15	α-Terpineol	1143	1.17b	1.61a	1.44ab
16	β-Citronellol	1179	0.20a	Nd	Nd
17	Nerol	1215	1.53a	1.13ab	0.91b
18	Geraniol	1228	2.02a	1.48ab	1.18b
19	Neral	1232	1.14a	1.60a	1.04a
20	Geranial	1249	1.95ab	2.26a	1.42b
21	Geranyl acetate	1352	0.15a	Nd	Nd
22	β-Caryophyllene	1424	0.27c	0.36b	0.46a
23	Neryl acetate	1452	0.23a	Nd	Nd
24	β-Cadinene	1435	1.09a	0.98a	0.74b
25	α-Cedrene	1447	0.55b	0.61a	0.64a
26	Elixine	1492	0.16a	Nd	Nd
27	β-Ionone	1503	0.49a	0.20b	0.30ab
	Total		99.56	99.38	99.54

Source [15].
[a] Kovats retention index (RI) relative to *n*-alkanes (C_8–C_{22}) on DM-5MS column; IM: green colored immature stage, INT: yellow-green colored intermediate stage, MAT: yellow colored mature stage; nd: not identified; volatile compounds percentages in the same line with different letters (a–c) are significantly different at $p < 0.05$ (Duncan's test); the bold shows the higher percentages.

3.2. Flavonoids

Flavonoids include a polyphenolic compound group that is differentiated by a benzo-y-pyrone structure, which is ubiquitous in fruits and vegetables, Flavonoids are fundamental for health care of humans as radical scavengers, because of their higher pharmaceutical activity [19]. Research findings of separated flavonoids from Foshou indicated the presence of diosmetin, 3',5,6-trihydroxy-3′,4′,7-trimethoxyflavone; 3,5,6-trihydroxy-7,4′-dimethoxyflavone; 3,5,8-trihydroxy-3′,4′-dimethoxy flavone; 3,5,8-trihydroxy-7,4′-dimethoxy flavone; hesperidin; citflavanone and diosmin [7].

3.3. Coumarins

The Coumarins isolated from Foshou include: 7-hydroxy -6-methoxycoumarin (scopoletin), 6,7-dimethoxy coumarin (scoparone), 5,7-dimethoxy coumarin (limettin), aviprin, 7-hydroxycoumarin (umbelliferone), 7-methoxy-5-prenyloxycoumarin, 7-hydroxy-5-methoxy coumarin, and byak-angelicin [20], 6-hydroxy-7-methoxycoumarin, 5-hydroxy-7-methoxy-8-prenyloxycoumarin (sibiricol), and bergapten [21].

3.4. Phenolic Acids

The phenolic acids as other phenolic compounds are able to quench the reactive oxygen species and scavenge free radicals and therefore provide effective means for treating and preventing free radical-mediated diseases, usually citrus represents the main provenance of polyphenolic antioxidants. Significant quantities of citrus peel as by-product tailings in the processing industry remains unexploited sources which can be used as ingredients in functional food [22]. The phenolic acids found in Foshou are vanillic acid, ferulic acid, p-coumaric acid, and protocatechuic acid [7].

3.5. Others

Foshou contain unique bioactive compounds such as polysaccharides, obacunone, limonin, and 5-methoxyfurfural [7]. limonin is considered anticarcinogenic, the glucosidc derivative of limonin is virtually tasteless and water soluble, it having an anticarcinogenic effect, thereby, also supporting the potential use as a functional food [23]. In another discovery, Vikram, Jesudhasan, Jayaprakasha, Pillai and Patil [24] also indicated that the obacunone may play an active role as a novel antimicrobial agent, where results them study claim that, certain limonoids are inhibitory to the cell-to-cell communication, biofilm formation and expression of Enterohemorrhagic Escherichia coli (EHEC) type three secretion system (TTSS).

4. Functional Benefits

Functional food from a natural source is most often accepted hence as much as Foshou is concerned, it might be considerd as a 'functional food' because it is qualified enough to provide the human diet with a large pool of bioactive compounds, relevant in lessening the hazard of a number of diseases and improving health. In addition, other parts of Foshou that are copious in nutrients and bioactive complexes possibly utilized as active constituents in pharmaceutical and food industries. This section highlights the functional benefits of Foshou.

4.1. Anti-helmintic Activity

Helminths live in the gastrointestinal tract, various to animate in tissues or the maggots move to into tissues. Helminths damage the host when they give rise to blood loss, depriving him of food, intestinal or lymphatic obstruction, damage the organs and by secreting toxins. Helminthiasis is seldom being lethal, but they are the highest reason of morbidity [25].

Foshou has an anthelmintic activity where the Foshou petroleum ether extracts of leaves showing activity against earthworm where Kabra, Bairagi, Mandade and Wanare [8] estimated the in-vitro anthelmintic potency of the petroleum ether extract of Foshou leaves using Indian earthworms (*Pheretima posthumad*). In their study, they were able to identified the time of paralysis and the time of a death of the earthworm after exposure to different concentrations of ether extract of a Foshou, result that study indicated that the Foshou potentiate paralyze of worm and addition to paralyzing worm and lead to death shortly after. The shortest time of death and time of paralysis was 30.86 min at the dose (80 mg/ml) of petroleum ether extract.

4.2. Anti-cancer Activity

Evidence confirming from epidemiological, in vitro, in vivo, and clinical trial data indicates that a plant-based diet can reduce risk chronic disease, especially cancer [26]. From the stem bark of Foshou were extracted 23 compounds, Lonchocarpol A a flavanol has showed marginally cytotoxic activity against four human cancer cell lines: MCF-7 Hep2, Daoy, and Hela cell lines [9].

4.3. Anti-dyspepsia Activity

Dyspepsia is a common term used to describe abdominal pain centered in the epigastrium, occasionally combined with other gastrointestinal complaints [27]. Foshou is one of 15 components of the Xiayou decoction. It has therefore been realized that mental symptoms such as concern and dejection in the functional dyspepsia (FD) of patients were noticeably improved after treatment with Xiaoyu decoction and psychotherapy [10].

4.4. Anti-inflammatory Activity

The functional foods have dietary bioactive compounds, it useful against chronic inflammation [28]. Inflammation is an initial host immune reaction mediated by inflammatory cytokines interleukin- 1b [IL-1b], interleukin-6 [IL-6], tumor necrosis factor-a [TNF-a], and related inflammatory mediators, such as prostaglandin E2 (PGE2), and nitric oxide (NO) which are produced by cyclooxygenase (COX-2), and inducible nitric oxide synthase (iNOS) respectively [29].

Foshou is used in traditional Chinese medicine for the treatment of allergic response and inflammatory conditions, where the Anti-inflammatory elements separated from the root barks and stem of Foshou were found to be nordentatin, citrumedin-B, xanthyletin, lonchocarpol A and atalanto flavon which displayed potent nitric oxide (NO)-reducing activity in microglial cells (Table 3) [12]. FEOs impede LPS-stimulated inflammation by hindering the ERK, NF-jB and JNK pathways in macrophages, and demonstrate that FEOs possesses anti-inflammatory properties [11].

4.5. Anti-microbial Activity

Many plants possess antimicrobial activity, and possible natural preservatives, treatment of foodborne diseases and functional foods [30]. The EOs of Foshou fruit peel have been confirmed to exhibit effective antibacterial activities against the Escherichia coli, Enterobacter cloacae, Proteus mirabilis, Streptococcus spp., Pseudomonas aeruginosa, Klebsiella pneumoniae, Staphylococcus aureus, and Bacillus sp. (Table 4) [13].

FEOs also exhibited a significant antimicrobial activity against Bacillus subtilis and Staphylococcus aureus. Inhibitory concentration of 2,500 ppm is shown in (Table 5) [14]. It can be seen that Lonchocarpol A, showed in vitro inhibitory activity against vancomycin-resistant Enterococcus faecium and methicillin-resistant Staphylococcus aureus [31].

Table 3. Effects of Tested Compounds on Nitric Oxide (NO) Production and NADPH Oxidase (NOX) Activity in Murine Microglial Cells, and DPPH Free Radical Scavenging Activity[a)]

Compound	IC50 (μ M) in NO production	NOX	DPPH
Xanthyletin	5.4±1.6*	NA	NA
Nordentatin	10.2±0.3*	NA	53.6±0.2
Atalantoflavon	1.4±0.2*	NA	NA
Lonchocarpol A	2.5±0.4*	24.4±3.9*	NA
1-(10→19)*abeo*-7a -Acetoxy-10b -hydroxyisoobacunoic acid-3,10-lactone	23.4±1.4	NA	NA
Nomilin	32.8±6.5	NA	NA
Limonin	NA	NA	NA
Lupeol	24.0±2.4	NA	NA
5,7-Dimethoxycoumarin	16.7±0.8	NA	NA
Citrusin	44.0±5.7	NA	NA
NA Limonexic acid	39.5±6.3	NA	NA
C-Glycosylflavone-vitexin	20.2±3.9	35.5±1.6*	NA
Positive control	16.8±1.5	0.8±0.4	28.0±4.2
	(L-NAME)	(DPI)	(Trolox)

Source: [12]

[a)]NO production was measured in the presence of 1-50μM of test compound. L-NAME (a non-selective NOS inhibitor), DPI (a NOX inhibitor) and trolox (a Vit. E analogue) were included as positive controls. Data were calculated as 50% inhibitory concentration (IC50) and expressed as the mean±S.E.M. from 3-10 experiments performed on different days using microglial cells from different passages. *p< 0.05 as compared with L-NAME. N.A., value not available (not effective).

Table 4. The inhibitory activity of the EOs extracted from Foshou fruit peel against the tested bacteria as demonstrated by diameters of theinhibition zone (mm)*

Isolated bacteria	Zone of Inhibition* 100μl FEOs Hand fruit peel
Enterobacter cloacae	18
Escherichia coli	15
Klebsiella pneumonia	22
Proteus mirabilis	20
Pseudomonas aeruginosa	15
Bacillus sp.	20
Staphylococcus aureus	25
Streptococcus spp.	20

Source: [13].

* Zone of inhibition, including the diameter of the cup plate method (8.0 mm) .The recorded value is mean value of 3 replicates.

Table 5. Antimicrobial activity of essential oil from the fresh leaf of Foshou and the standard antibiotic

Concentration (ppm)	Inhibition zone, mm (mean ± S.E.M.)[a]			
	Gram-positive			Gram-negative
	S. aureus	*B. subtilis*	*M. luteus*	*E. coli*
20,000	11 ± 0.3	15 ± 0.8	11 ± 0.3	8 ± 0.7
5,000	9 ± 0.3	9 ± 0.6	7 ± 0.3	No inhibition
Tetracycline[b]	13 ± 2	16 ± 2	35 ± 3	26 ± 0.7

Source: [14].

[a] The diameter of inhibition zone included diameter of paper filter disc (6 mm).[b] Tetracycline (5,000 ppm) was used as a standard antibiotic.

4.6. Anti-oxidant Activity

A balance between free radicals and antioxidants is requisite for appropriate physiological function. If free radicals exceeded the body's ability to strike a balance them, occur afterward a situation known as oxidative stress. Free radicals negatively alter proteins, lipids and DNA leading to a number of human diseases. Therefore, the provision of external antioxidants will provide the necessary support against any excessive oxidation [32].

Consequently, Foshou can be utilized as an external source of antioxidants. The antioxidant activities in vitro of Foshou polysaccharides (FPs) against superoxide anion radicals, hydroxyl, and 1,1-diphenyl-2-picrylhydrazyl (DPPH) as revealed through research. FPs had shown anti-oxidant potential for use in healthcare, food or medicine,that was preliminarily identified by the free radical scavenging assay [15].

The antioxidant activities of FEOs decreased because of increasing maturity in the harvest season and accumulation of ketones and monoterpene hydrocarbons was observed during maturation process [6].

4.7. Hypoglycaemic Activity

Diabetes mellitus has become an epidemic that requires a joint effort in its management. Dietary therapy application in treatment Diabetic became one of the choices aimed at adjusting diabetes-induced hyperglycaemia. It has been revealed that major regulator of diabetes is the insulin hence any food that can enhance action and secretion of insulin will be useful in the medication of this disease [33].

Insulin secretion effect of Foshou was confirmed in Wistar DIO rats and Sprague-Dawley SPF rats by insulin-glucose tolerance tests (IGTT) and kinetic analysis of the hypoglycemic patterns of the intraperitoneal glucose tolerance (IPGTT). Foshou fruits have slimming effects synchronously with insulin secretagogue and will be very helpful for diabetics type 2 [4].

Recently, food plants focus on natural products as a possible source of safer antidiabetic therapy and more potent. Because of the properties of insulin secretion of Foshou can use it as a functional food for anti-diabetic, however, further study is requisite to appreciate its active components accountable for it mechanism of action[33].

5. Traditional Chinese Medicine Uses

Traditional Chinese medicine (TCM) is an experiential health care grounded on human knowledge dating back many thousands of years. Its various aspects include Chinese material medical, acupuncture, and moxibustion, among others [34].

Foshou rarely used alone in treatment of patients. More frequently, Foshou used alongside other herbs grounded on traditional Chinese medicine theory. Foshou used in TCM to adjust the Qi flow of the Liver and Stomach, and pain relief. It is also used to cure recession of Qi of the Liver and Stomach marked by distending pain in the chest and hypochondriac regions, stuffiness feeling in the stomach, poor appetite, and vomiting (Table 6) [35].

Table 6. Foshou uses to treatment of some diseases in TCM

Disease	Symptoms	Composition
Qi stagnation of the Liver	distending pain in the chest and stomach regions.	Foshou with Yujin (root tuber of Curcuma wenyujin), Baishao (root of Paeonia lactiflora), and/or Xiangfu (rhizome of Cyperus rotundus).
Qi stagnation of the stomach	stuffiness feeling in the stomach, poor appitite and vomiting.	Foshou with Doukou (fruit of Amomum kravanh), Banxia (tuber of Pinellia ternate), and Muxiang (root of Aucklandia lappa) to strengthen the action.
Qi stagnation of the damp phlegm accumulation	panting, cough, phlegm, and chest tightness.	Foshou with Banxia (tuber of Pinellia ternate), and Fuling (sclerotium of Poria cocos) to eliminate dampness and phlegm.

Source: [35].

6. Toxicity Data and Safety Evaluation

Foshou fruit safe to use, acute toxicity test using 1 mL of emulsion/100 gbw (equivalent to 2000 mg/kg of Foshou fruits) per os daily for 7 days was shown to be totally nontoxic. Were the safety tests in vivo the conducted in Sprague-Dawley- SPF rats. The parameters were included the survial rate, weights of (kidney, spleen and liver), body weight, tissue Hematoxylin serum biochemical test, and Eosin (HE) stains etc. The clinical serum biochemical tests included examination of blood urea nitrogen (BUN), serum alanine aminotransferase (sGPT), and serum aspartate aminotransferase (s-GOT) [4].

7. Conclusion

The aim of this review was to investigate the bioactive compounds and functional benefits of Foshou (Citrus medica L. var. sarcodactylis Swingle). In general, it has confirmed that Foshou has functional properties that has not tapped yet. It is therefore recommended further extensive research be conducted to find several methods of preparation Foshou and the installation–function relationship of the bioactive components in Foshou. This would seriously assist the usage of Foshou fruit as a functional food element several of health benefits to humans in future. Finally, Foshou is an unexplored functional food, we in this review examined the possibility using the Foshou as a functional food, and it might be exploited as a basic raw material to development novel low cost nutritious functional foods.

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