



(REVIEW ARTICLE)



From ethnopharmacology to phyto medical potential of the different parts of mangosteen (*Garcinia Mangostana* L.)

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Abstract

Garcinia has a long history of medicinal use. Indeed, they are popular in Asia and Africa for their healing properties. All parts of this plant tree are used in folk medicine for many different health affections, including skin infections, wounds, and diarrhea. In this review, we present an overview of *G. mangostana*, this medicinal plant, which takes an important place in the worldwide pharmacopeia. Consisting of an overview of this plant and contribution to its valorization by various evidence of its medicinal potential both in traditional and conventional medicine showing of the curative capacities of each part of the plant tree. We showed off that, on the one hand, traditional uses of the different plant parts match with laboratory test results, although experiences mostly used isolated molecules or organic extracts. On the other hand, researches also demonstrated interesting new medicinal properties of the plant comparing to the traditional medicinal uses, which are limited to ancient practices. These facts present *G. mangostana* is a reliable plant for making an improved traditional medicine or an edible source of bioactive molecules extracted in leaf, stem bark, fruit hull, or whole fruit to develop news drugs with low toxicity.

Keywords: *Garcinia mangostana*; Monography; Ethnomedicine; Pharmacological Activities; Scientific researches.

1. Introduction

For centuries, useful plants were discovered and categorized into food plants, healing plants, and poisonous plants mostly by intuition or experimentation [1]. This knowledge, most of the time, transmitted orally from generation to generation through learning and practicing, was then written down due to the advent of the development of civilizations. The transcription of writings will allow them to preserve and expand this therapeutic knowledge allowing them a progressive adaptation and improvement according to practitioners, regions, and cultural influences. Nowadays, medicine consisting in healing directly with various preparations of plants: powdered, tinctures, macerates, decoctions or infusions is called traditional medicine most often practiced by traditional healers [2]. This kind of therapeutic exist worldwide but is overriding in poor countries because of constraints such as the high cost of conventional drugs or lack of access to health structures. Valorization of medicinal plants used in traditional practices to treat illnesses will offer new perspectives and new medical pathways to improved health care of various endemic diseases. The therapeutic approach combining traditional and conventional knowledge and practices appear to be a reliable solution for an amelioration of the global health system [3]. From this observation, since the last decade, researches on traditional plants has considerably increased. Every year, scientific papers showed new biological activities, mechanisms of action, and molecules isolated from well-known plant parts of worldwide pharmacopeia. Among them, the *Garcinia* genus takes an important place, particularly *Garcinia mangostana* a small evergreen tree with a pyramidal crown. It is highly considered for its fruit. Although it is mainly used for food because of its juicy fruit, almost all the parts of this tree, including the fruits, are used in traditional medicine for many different health affections, including skin infections,

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wounds, and diarrhea [4]. *Garcinia mangostana* contains many active phytochemicals who has been widely screened in several laboratory studies showing antioxidant [5] antibacterial [6] anticancer [7] antimalarial [8], *in vivo* and *in vitro* in anti-inflammatory [9, 10], antidiabetic and many other effects [11]. These biological activities could be explained by an abundance of active molecules already isolated and identified. The main compounds of *G. mangostana* fruit are prenylated xanthenes, dibenzo-g-pyrone derivatives [12]. Indeed, alpha, beta, and gamma mangostins, gartanin, 8-deoxygartanin, and garcinones C and D are the most abundant and wide screened for their activities. Till now, around 68 xanthenes have been isolated. There are natural antioxidants mostly concentrated in the pericarp. However, there is no reliable scientific evidence to confirm the effects of these molecules as there is a lack of preclinical and clinical trials [13].

In our review, we focus on providing an update and comparative report on the biological activities of the stem, bark, leaves, hull, pericarp, roots, and the whole fruit of *G. mangostana* from traditional knowledge and practices and scientific researches on the plant pharmacology and/or pharmacognosy. This kind of approach leads to a general overview of the potentialities of different parts of the plant tree for interesting and direct applicability of the plant preparation in treatments of some recurrent diseases. This article also comprises brief information on the monography of *Garcinia mangostana* and a qualitative and quantitative determination of the amount of scientific research papers on this traditional plant.

2. Botanical description

The *Garcinia mangostana* fruit tree has a very slow growth, erected, with a pyramidal crown, it can reach a height of varying between 6 to 25 m.

The bark is brownish or almost black, scaly, with a yellow latex, bitter and gummy. Its bark is most often corky and very thick.

Leaves are persistent, opposite, short, usually oval/oblong or elliptical, leathery and thick, dark green in color, slightly glossy, above and yellowish-green, and dull below. They are about 9 to 25 cm long and about 4.5 to 10 cm wide, with a visible and pale central vein. The new leaves are pink.

Flowers are about 4-5 cm wide, they are fleshy and can be male or hermaphrodite on the same tree. The first is in clusters of 3-9 flowers at the ends of the branches. They have 4 oval sepals, thick, fleshy, green with red spots on the outside and yellowish red on the inside with many stamens, although the aborted ants do not carry pollen. The hermaphroditic flower is worn alone or in pairs at the end of the young twigs. The petals can be yellowish-green with red edges.

The fruits are very characteristic, they are in a spherical berry, slightly flattened at the poles, with a diameter ranging from 5 to 7 cm for a weight of 50 to 150 g. It is crowned by a calice of four leaves at the base of the peduncle. It is a round fruit, dark purple, and smooth on the outside. The shell of the fruit is a thick diameter of about 6-10 mm. Inside, we find the flesh, divided into five to eight quarters - the arils - a little like a clementine containing one or more seeds. It is slightly acidic and sweet, juicy, and finely perfumed, but oxidizes quickly [14, 15].

3. Origins and distribution

Garcinia mangostana, mostly known as a cultivated species in most countries where we can find it, has its origins in South Asia [16]. Indeed, there is a resemblance between this species and two others, the *Garcinia hombroniana* and *Garcinia malaccensis*, which are indigenous in Malaysia. This fruit tree may be an allotetraploid hybrid of these two species [17]. Therefore, they are wild specimens in the Peninsular of Malaysia, particularly in Indonesia, Borneo and Thailand. This tree had increased popularity in its native range because of its fruit collected for the markets, so it has been planted as a garden tree or in specific habitations over all the region extended to Vietnam, Cambodia, New Guinea, Philippines [18]. Its cultivation has been limited to South-East Asia for centuries, however, during the last two centuries, because of the advent of colonial movements it has been progressively spread to other tropical areas, firstly in Sri Lanka, South India, West Africa, Central America, Brazil and Australia [19]. In fact, the gradual interest and pervasion purposes of *G. mangostana* outside of its native range was a long and slow process. Some explorers who traversed the region attempted to transport back this tree to Europe and later to the Americas but were mostly unsuccessful. The fruit was too perishable and fragile, and seeds dry out or die in a week. Transportation needed much-elaborated measures. Many efforts were made to introduce the fruit tree successfully into the Western Hemisphere. The first introduction of the *G. mangostana* in England was recorded during the 18th and 19th centuries [20].

A French naturalist named Laurent Garcin, who traveled through the South Asia region collecting and describing native plants, particularly the *Garcinia mangostana*, was honored by Linnaeus. Indeed, in the 18th century, he gave Garcin's name to the genus as reward for his incredible botanist work [21]. The folklore said that Queen Victoria of England would have made it her favorite fruit, even offering the title of a knight to anyone who could provide her, but there is no written proves of that [22].

For centuries, this fruit plant has aroused the interest of all who get to know it, especially for its fruit which interior is known for its amazing sweet-sour flavors, but also for its uses in Ayurvedic medicine practices in its native range has many applications in traditional medicine. Only in the late 20th century, the α -mangostin, an antioxidant substance of the xanthone family, was isolated in the laboratory followed by about sixty other xanthenes discovered in the *G. mangostana* preparations, especially in the skin of the fruit [23]. Nowadays, studies on this plant are attempted worldwide as the increase in traditional medicine awareness and the spread of diseases requiring other medicinal pathways to be dammed.

The *Garcinia mangostana* tree can now be found in many regions, and countries generally summarize: West Africa, Andamans, Asia, Australia, Brazil, Burma, Cambodia, Cameroon, Central Africa, Central America, China, Cook Islands, Costa Rica, Dominican Republic, East Africa, East Timor, Fiji, Ghana, Haiti, Hawaii, India, Indochina, Indonesia, Laos, Malaysia, Myanmar, Nicaragua, North America, Pacific, Papua New Guinea, Philippines, Puerto Rico, South East Asia, Singapore, Solomon Islands, South America, Sri Lanka, Thailand, Timor-Leste, United State of America, Vietnam, West Africa, West Indies, Zambia [24].

4. Main compounds: The Xanthenes

Garcinia mangostana is one of the major fruit trees because of its nutritional and pharmacological properties. His fruit is plenty of active and interesting compounds such as tannins, bi-flavonoids, vitamins, various minerals like calcium, phosphorus, thiamine, riboflavin, acid ascorbic, and mostly Xanthenes. They are an especial class of molecules whose basic structure is showed in **Figure 1**.

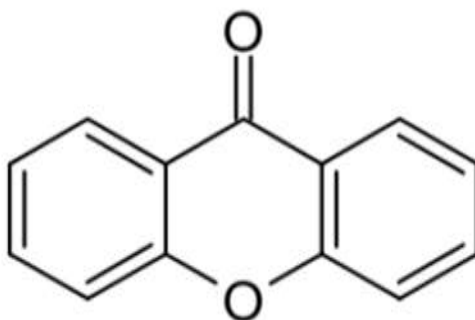


Figure 1 Basic chemical structure of a Xanthone

Basically, they are constituted by three conjugated platter rings of six carbon molecules. Various chemical groups are attached to this central system consisting of two benzene rings structured with carbonyl group and oxygen. Each ring is connected in a fusional way to prevent a free rotation around the double carbon link. This unique structure, along with the type and position of the attached chemical groups, define specific functionalities of the xanthenes [25]. They are colorless, and crystalline compounds derivate from salicylate, found in nature in few plants. *Garcinia mangostana* is the one from which different derivatives where isolated and extracted. Four basic xanthenes molecules are represented, Mangostins, Garcinones, Epicatechin, and Gartanin.

The mangosteen contains many of their derivates. Before the 21st century, almost 40 xanthenes were isolated from the different parts of *Garcinia mangostana*, and more than ten new found since 2001 until now. When considering each part of the plant, in gross 50 xanthenes have been isolated from the mangosteen pericarp, 18 xanthenes from the whole fruit, 18 xanthenes from bark, and 3 from the leaves [26]. Xanthenes can be described as a group of plant polyphenols biosynthetically related to flavonoids. Indeed, polyphenol represents a group of substances characterized by the presence of more than one phenolic group and responsible for the color of some plants, flavonoids have a general structure of a 15-carbon skeleton consisting of two phenyl rings and a heterocyclic ring, they fulfill many functions, but the most important is plant being a plant pigment.

Garcinia mangostana is the natural reservoir of several different xanthenes possessing numerous bioactive abilities.

5. Extensive research on *G. mangostana*

The *Garcinia* genus is a wide group, including more than 260 species [27]. Many bioactive molecules have been isolated from these plants such as terpenes, flavonoids, polysaccharides, hydroxycitric acid, procyanidines, and polyisoprenylated benzophenone derivatives like, xanthochymol, guttiferone isoforms and garcinol [28]. These findings have retained the interest of pharmaceutical industries due to the high medicinal capacity. Each of these molecules has been tested and was associated with various biological activities like antibacterial, hypolipidemic property, antioxidant, apoptotic, anticancer, anti-inflammation, anti-viral, anti-fungal, antiulcer, anti-protozoal, or HAT inhibiting properties [29]. Beyond this genus, *Garcinia mangostana* is best known and widely studied, like the one having the largest potentialities with multiple applications in culinary, pharmaceutical, ornamental, and industrial fields. The popularity of this fruit tree was also made by its use in traditional Indian medicine preparations to threaten many pathophysiological disorders. As the increase in interest, the investigation carried out on the mangosteen also increases year after year, like shown in **figure 2**.

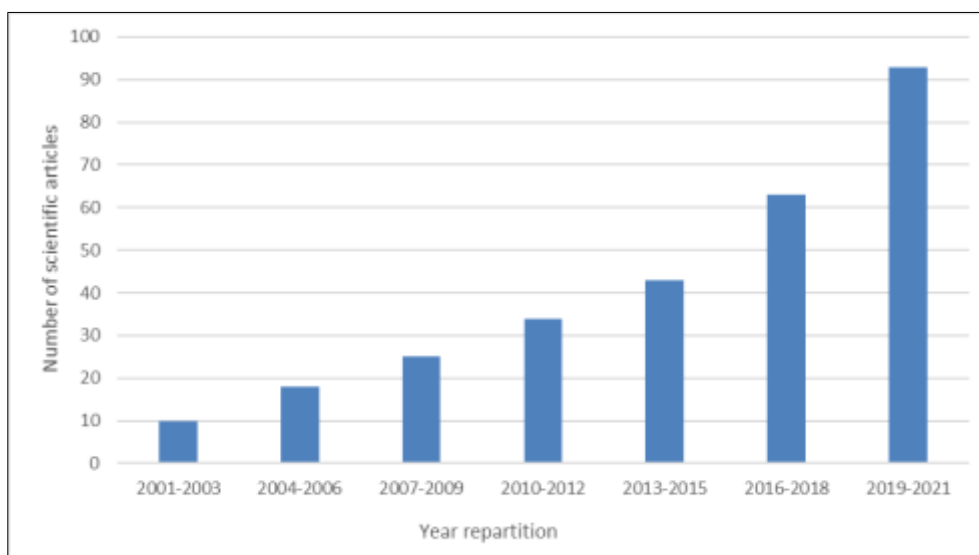


Figure 2 Amount of research papers on *Garcinia mangostana* released from 2001 to 2021 based on PubMed, Google scholar, sciences direct databases

A brief qualitative and quantitative review of articles on this traditional plant was made to have an insight into the infatuation and the knowledge around it. The study was conducted considering only research papers affording pharmacological aspect and present the major scientific journal motors on Pubmed, Google scholar, and Sciences Direct from 2001 to the present distributed by publication every 3 years. Between 2001 and 2021, 286 articles were indexed, which represent a considerable database on the mangosteen biological properties and phytochemical compounds and their activity. The figure clearly showed a significant increase in the number of publications concerning this plant through years. While in 2001-2003, only ten articles were identified, ninety-three have been identified since only 2019. They cover a wide range of information. Though almost all the molecules were discovered before the 20th century, ten new bioactive compounds were identified. Moreover, articles show more precision on biological pathways action of molecules to induce their effect against some pathologies. New pathophysiological disorders are targeted. In fact, each study is a step towards an improved exploitation that will be a benefit to both traditional and conventional medicine.

6. Ethnomedicine of each plant's part

Traditional medicines, also known as popular medicines, have a long history proper to every country and varying each from another according to culture, millenarian beliefs, local practices, and legacy experiences [30]. This folk medicine appears to work as complete health care intervention at all levels of disease management in healing seasonal health issues as well as in prevention, diagnosis, and treatments. Traditional medicine has its own preparation and administration methods depending on the kind of plant used, and also in the case of aerial or underground parts, hard parts such as bark or seed, there will be differences in the concoction protocol. Some traditional medicine practices were improved through the years, but generally, they do not undergo major changes. Furthermore, every regions or

country has their own pharmacopeia depending on the flora of their territory. Indeed, *Garcinia mangostana*, native to the South-East of Asia, takes an important place in Ayurveda medicine [31]. This antique medicine attributed to Indian ancestral civilization was also influenced by Greek and Egyptian knowledge about how to heal with plants. Although the use of this fruit plant slightly differs from one region to another, generally, they share the same medicinal applications. As showed in **Table 1**, all parts of *Garcinia mangostana* are used in folk medicine, either by oral administration after decoction, aqueous maceration or infusion, or by external application in the form of an ointment.

Almost all parts are used to treat the same illnesses. Indeed, while in Thai and Malaysian traditional medicine, the fruits of the mangosteen are the most used as a remedy, in Indian medicine, they use more bark and leaves [32]. However, diseases treated by *G. mangostana* in ethnomedicine are predominately fever, respiratory disorders, dysentery, aphtha, wounds, urinary disorders, diarrhea, skin infection, and arthrosis [33]. When we considered the causes leading to each pathology, it appears that they are due to inflammatory disorders, parasitic or bacterial infections by organisms like *Escherichia coli*, *Pseudomonas aeruginosa*, etc., and various other allergens. The biological correlation between these illnesses and the curative pathway to treat them imply that the different parts of this fruit plant have various properties, especially anti-inflammatory, anti-parasitic, antipyretic, antibacterial, and even anticancer activities. Indeed, this plant would contain active molecules part of their secondary metabolism, also known as specializing metabolism, which is sufficient in quantity to cause significant biological activities for human therapeutics. Traditional knowledge on *Garcinia mangostana* as a curative fruit plant already gives a therapeutic overview of its medicinal potential. However, ethnopharmacology approaches of plants present some drawbacks [34]. In herbal medicine practices, there is a lack of precise and complete information about the molecular profile of the plant, also possible long-term toxicity. Scientific approaches would provide a concrete and deep assessment of their pharmacological qualities and safety.

Table 1 List of the ethnopharmacological properties of *Garcinia mangostana*

Used plant's part	Preparation type	Mode of administration	Treated illness	Biological activity involved in treatments	Authors
Bark	Decoction	Oral	Amoebic dysentery	Anti-bacterial Anti-parasitic	<u>[32]</u>
	Decoction	Oral	Affection of genito-urinary tracts	Anti-bacterial	
	Decoction	External	Aphtha or Thrush	Anti-parasitic	
Leaf	Decoction	External	Aphtha or Thrush	Anti-parasitic	
	Decoction	External	Fever	Antipyretic	
	Infusion	External	Wound infections and inflammation	Anti-bacterial Anti-inflammatory	
	Decoction	Oral	Urinary disorder	Anti-cancer Anti-bacterial Anti-parasitic Anti-inflammatory	
Peel/Rind	Rubbing	External	Skin infection	Anti-bacterial	
	Decoction	Oral	Dysentery	Anti-bacterial Anti-parasitic	
	Maceration	Oral	Diarrhoea	Anti-bacterial	
	Ointment	External	Eczema	Anti-inflammatory Anti-allergic	
	Decoction	External	Cystitis	Anti-bacterial	
	Decoction	External	Gonorrhoea	Anti-bacterial	

Pericarps	Decoction	Oral	Intestinal Catarrh	Anti-parasitic	[33]
	Decoction	Oral	Dysentery	Anti-bacterial Anti-parasitic	
	Infusion	Oral	Respiration disorders	Anti-allergic	
	Rubbing	External	Skin affection	Anti-bacterial	
	Maceration	Oral	Diarrhoea	Anti-bacterial	
	Fresh	External	Arthritis	Anti-inflammatory	
Root	Decoction	Oral	Dysmenorrhea	Anti-inflammatory	
Fruit hulls	Decoction	External	Skin infection	Anti-bacterial	
	Infusion	External	Wound infections	Anti-bacterial Anti-inflammatory	
	Maceration	Oral	Diarrhoea	Anti-bacterial	
	Maceration	Oral	Chronic ulcer	Anti-bacterial	
	Decoction	External	Abdominal pain	Anti-inflammatory	
	Decoction	Oral	Dysentery	Anti-bacterial Anti-parasitic	
	Decoction	External	Suppuration	Anti-inflammatory	
Whole fruit	Fresh	Oral	Allay thirst in fever	Nd	

7. Pharmacological activities findings

G. mangostana is widely studied for its fruit containing a large amount of xanthones and other active molecules, the fruit richness and flavor is the major cause of its migration and cultivation over the world. However, in its native region, this plant is mostly used in folk medicine as a treatment for various endemic diseases. Many in vivo toxicity studies were fulfilled, proving that this plant is not toxic for human consumption [35]. Moreover, several research papers demonstrated pharmacological properties of *G. mangostana* by both in vivo and in vitro study model, the main activities were resumed, sorted according to biological activities findings and reported in **Table 2**.

Table 1 Highlight on main pharmacological findings activities of *G. mangostana*

Activities	Authors	Part used	Extract type	Major Compounds	Experimental methods	Organisms / Cells Tested/	Key Results
Anticancer	Ee <i>et al.</i> 2008 [37]	Bark	Hexane	2,8-dihydroxy-6-methoxy-5-(3-methylbut-2-enyl)-xanthone	MTT	CEM-SS cancerous cell line	IC ₅₀ = 17µg/ml
		Root	Hexane	α-mangostin β-mangostin, γ-mangostin, garcinone D, mangostano, gartanin	MTT	CEM-SS cancerous cell line	IC ₅₀ = 0.3µg/ml
			Chloroform				IC ₅₀ = 14µg/ml
	A-R. Han <i>et al</i> 2009 [38]		Chloroform	3-isomangostin α-mangostin	MTT	HT-29 human colon	IC ₅₀ = 1.7µg/ml

						cancer cell line	
				β -mangostingarcinone D			
				9-hydroxycalabaxanthone			
	G. Li <i>et al.</i> 2014 [39]	Whole fruit	Nd	α -mangostin	BrdU assay	22Rv1 prostate cancer cell lines	inhibited tumor volume by 88%
	S. R. M. Ibrahim <i>et al.</i> 2018 [40]	Fruit hull	Chloroform	Mangostanaxanthone VII	SRB assay	A549	IC ₅₀ =26.1 μ g/ml
						MCF-7	IC ₅₀ =34.8 μ g/ml
	Cunha <i>et al.</i> 2014 [41]	Leaf	Ethanol	Nd	MTT assay	B16-F10 cancerous cell line	IC ₅₀ =29,75 μ g/ml
	J. Manasathien <i>et al.</i> 2015 [42]	Pericarp			MTT	MCF-7 human breast adenocarcinoma cell line	IC ₅₀ =430.91 \pm 2.21 μ g/ml
	L. Yu <i>et al.</i> 2009 [43]	Pericarp	Méthanol	1,3,6,7-tetrahydroxy-2,8-(3-methyl-2-butenyl)xanthone Epicatechin	MTT assay	human breast cancer cells MCF-7	Cytotoxicity = 73.06% 48.29%
	J. J. Wang <i>et al.</i> 2012 [44]	Pericarp	Ethanol	Nd	Crystal violet assay	A-431	IC ₅₀ =5.29 μ g/ml
						SK-MEL-28	IC ₅₀ =5.82 μ g/ml
						Human skin carcinoma cell lines	
Anti-bacterial	K.M.E.P. Fernando <i>et al.</i> 2007 [46]	Pericarp	Méthanol	Nd	Filter-paper disc-agar diffusion technique	Bacillus subtilis	MIC=0.0005 g/ml
						Staphylococcus aureus, Streptococcus faecalis	MIC=0.0005 g/ml

							MIC= 0.005g/ml
	B. L. A. Cunha <i>et al.</i> 2014 [41]	Leaf		Nd	Agar diffusion technique	Staphylococcus aureus	MIC= 1 mg/mL
		Whole fruit	Ethanol	Nd	agar diffusion test	Staphylococcus aureus Escherichia Coli	MIC= 0.1 mg/mL
	J. S. Soetikno <i>et al.</i> 2016 [47]	Peel/ Rind	Ethanol	Nd	total plate count method	E. Coli	MIC= 0.62 mg/ml
					2-fold serial microdilution assay	P. acnes S. epidermidis	MIC= 3.91 µg/ml
	Khartiga <i>et al.</i> 2018 [48]	Bark	Methanol	Nd	Agar well diffusion method	Escherichia coli Bacillus subtilis	Inhibition zone ≥ 20mm
Anti-oxidant	Chew <i>et al.</i> 2018 [50]	Leaf	Methanol	Polyphenols	FRS DPPH	-	IC ₅₀ = 4240 ± 493(mg AA/100 g)
	M. A. Hamid <i>et al.</i> 2011 [51]		Infusion	Nd	DPPH	-	IC ₅₀ = 34.30±1.25 µg/ml
	W. Pothitirat <i>et al.</i> 2009 [52]	Peel/ Rind	Dichloromethane	α-Mangostin	DPPH	-	IC ₅₀ = 5.56± 0.12µg/ml
	M. T. Chomnawang <i>et al.</i> 2007 [53]	Pericarp	Ethanol	Nd	DPPH	-	IC ₅₀ = 6.13 µg/ml
	J. Manasathien <i>et al.</i> 2015 [52]	Pericarp	Ethanol	Nd	DPPH	-	IC ₅₀ = 1 199.85 ± 47.16 µg/ml

	S. A Husen <i>et al.</i> 2017 [54]	Pericarp	Ethanol	Nd	DPPH	male mice (of the BALB/C strain)	IC ₅₀ =4.0835 µg/ml
	L. Yu <i>et al.</i> 2007 [55]	Fruit hull	Methanol	1,3,6,7-tetrahydroxy-2,8-(3-methyl-2-butenyl)	DPPH	-	DPPH (%) =
				1,3,6-trihydroxy-7-methoxy-2,8-(3-methyl-2-butenyl) xanthone			84.1 ± 1.3 %
				Epicatechin			
							53.5 ± 1.7 %
							70.4 ± 0.5 %
	N. Kosem <i>et al.</i> 2007 [56]	Fruit hull	Methanol	Nd	DPPH	-	IC ₅₀ =20.50 µg/ml
	W. Weecharansan <i>et al.</i> 2006 [57]	Fruit hull			DPPH	-	IC ₅₀ = 34.98 ± 2.24 µg/ml
							IC ₅₀ = 30.76 ± 1.66 µg/ml
	R. Jayakumar <i>et al.</i> 2011 [58]	Whole fruit	Juice	Nd	Nitric oxide scavenging by Griess reagent	MCF-7 cells	20% of inhibition at 640 µg/ml
Anti-inflammatory	W. Widowati <i>et al.</i> 2016 [60]	Peel/Rind	Ethanol	α-Mangostin	ELISA-based assay	COX-2	%Inhibition=
				γ-Mangostin		IL-1β	54.59±6.09
						IL-6	24.41±6.53
							54.95±8.27

						induce RAW 264.7 cells	
	H-S Chae <i>et al.</i> 2012	Pericarp	-	α -mangostin	Elisa assay	bone marrow derived	IL-6 suppression
	[61]			γ -mangostin		mast cell (BMMC) induced BALB/b mice	IC ₅₀ = 5.11 μ g/ml
							IC ₅₀ = 7.06 μ g/ml
	M. T. Chomnawang <i>et al.</i> 2007 [53]	Pericarp			Cytokine production assay (TNF- α) ELISA	P. acnes	Inhibition % = 94.59
Anti-parasitic	S. Tjahjani 2017	Leaf	Ethanol	Nd	Giemsa stained thin blood smear	Plasmodium falciparum	IC ₅₀ = 0.12
(Anti-malarial)	[62]						μ g/ml
Anti-fungal	F. E. B. R. I. N. A Rahmayanti <i>et al.</i> 2016	Pericarp	Ethylacetate	Nd	Test MTT	<i>C. albicans</i>	IC ₅₀ = 3.2 μ g/ml
	[63]						
Therapy of Alzheimer's Disease	S. Wang <i>et al.</i> 2016	Pericarp	Nd	α -Mangostin,	Thioflavin T Fluorescence Assay	β -Amyloid	Inhibition % 83.7
	[64]			8-Deoxygartanin, Gartanin,			
				Garciniafura			
				Garcinone C			
				Garcinone D			
Anti-diabetic	S. A Husen <i>et al.</i> 2017	Pericarp			Induction of streptozotocin (STZ)		- increased diameter of Langerhans cell by 50%
	[54]						- increased insulin level from 13 to 17 ng/ml

Cytoprotective activity	N. Kosem <i>et al.</i> 2007	Fruit hull			MTT	ECV304 endothelial cells,	Cell viability=
	[56]						80.9%
Neuroprotective activity	W. Weecharan <i>gsan et al.</i> 2006 [57]	Pericarp	Water	Nd	Protection against H ₂ O ₂ -induced oxidative stress	NG108-15 cells	Cell viability=
			Ethanol				74.89±7.56%
							98.27±5.79%

All the parts of the plant were found to have effective biological abilities; however, the degree of efficiency depends on various factors like part of the plant considered, type and conditions of extraction, and organisms or cells tested in the different studies. These scientific researches are focused on diseases representing current worldwide health issues and which management requires improvement in current treatments as well as new therapeutic pathways.

7.1. Anticancer activity

Cancer is one of the main health problems, nowadays, although there are many different types of treatments such as surgery, radiation therapy, chemotherapy, hormonal therapy, and immune therapy, they lead to various side effects that can occur during or month and even year later the treatment. Indeed, patients could suffer from bowel, dysfunction, heart damages, and accelerate immune suppression caused by molecules used in chemotherapy [36]. Natural molecules could be a reliable alternative to avoid those negative effects, and *Garcinia mangostana* efficacy was proved to have a toxic effect only on tumor cells.

Several works have demonstrated the anticancer effects of *G. mangostana* on numerous human cancer cell lines. Ee *et al.* 2008 [37] have tested the hexane extract (rich in 2,8-dihydroxy-6-methoxy-5-(3-methylbut-2-enyl)-xanthone) on CEM-SS cancerous cell line and showed important an important cytotoxic effect (IC₅₀= 17 µg/mL). In the same work, hexane and chloroform extracts of root have also showed interesting in vitro anticancer activity against CEM-SS cancerous cell line IC₅₀= 0.3µg/mL and IC₅₀= 14µg/ml. Moreover, the chloroform extract of the same part was tested by Han *et al.* (2009) [38] on HT-29 human colon cancer cell line and revealed a very remarkable cytotoxic effect (IC₅₀= 1.7µg/mL). 88% of inhibition of 22Rv1 prostate cell cancer was observed by Li *et al.* 2014 [39]. Recently, Ibrahim *et al.* 2018 [40], showed that the chloroform extract of fruit hull (rich in Mangostanaxanthone VII) possessed an important inhibition of A549 and MCF-7 cancerous human cell lines by an inhibition values of IC₅₀=26.1 and IC₅₀=34.8 µg/mL, respectively. Moreover, the leaf extract also showed important inhibition of B16-F10 cancerous cell line at IC₅₀=29.75 µg/mL (Cunha *et al.* 2014 [41]). The pericarp extracts were tested by several authors (Manasathien *et al.* 2015 [42], Yu *et al.* 2009 [43], Wang *et al.*, 2012 [44]). Methanol extracts showed the important cytotoxic effect on A-431 (IC₅₀= 5.29 µg/mL) and SK-MEL-28 (IC₅₀= 5.82 µg/mL).

7.2. Antibacterial activity

Antibiotics have always been effective to treat bacterial infections. However, the spread of their use brought a new phenomenon of bacterial resistance leading to a decline in their bactericidal capacity especially against *Enterococcus faecium*, *S. aureus*, *Klebsiella pneumoniae*, *Acinetobacter baumannii*, *Pseudomonas aeruginosa*, and *Enterobacter species* which have caused significant mortality. The mangosteen showed high bacterial inhibition abilities against some of them [45].

G. mangostana extracts have been tested against several bacterial strains and showed remarkable antibacterial properties. The methanolic extract of pericarp was tested against several strains gram- and gram+ by Fernando *et al.* (2007) [46]. The results showed important bacterial inhibition at low concentrations in particularly against *Bacillus subtilis* at a MIC= 0.0005 g/mL. Moreover, the leaves showed an important of *Staphylococcus aureus* at MIC= 1 mg/mL (Cunha *et al.* 2014 [41]). On the other hand, ethanol extract of peel/rind has inhibited the growth of *E. coli* at MIC= 0.62 mg/mL (Soetikno *et al.* 2016 [47]). Recently, Khartiga *et al.* (2018) [48] tested the methanolic extract of bark and showed the inhibition of *Escherichia coli* and *Bacillus subtilis* growth in solid medium.

7.3. Antioxidant activity

Oxidative stress plays a dual role concerning human condition. In a normal balance range, the oxygen reactive species (ROS) generated have several physiological roles in cell mostly in the signalisation pathways. However, an imbalance in production/elimination of this species may cause many cellular damages inducing health problem like cardiovascular, respiratory and kidney diseases [49]. The mangosteen with its large amount of xanthones known for their antioxidant capacities can play a major role in oxidative stress regulation. Indeed, Chew *et al.*, 2018 [50] investigated the reducing ability of the methanol extract of leaf having high inhibitory effect on free radical $IC_{50} = 4240$ mg AA/100g comparing with the other medicinal plant. Infusion extract of the mangosteen leaf showed a remarkable effect $IC_{50} = 34.30$ µg/ml (Hamid *et al.*, 2011) [51]. However, Pothitirat *et al.* 2009 [52] and Chomnawang *et al.* 2007 [53] obtained better inhibition results with respectively Dichloromethane extract of the peel $IC_{50} = 5.56$ µg/ml and Ethanol extract of the pericarp $IC_{50} = 6.13$ µg/ml. Ethanol extract of pericarp were investigated for its inhibitory effect by *in vitro* and *in vivo* method, the *in vitro* studied conducted by Manasathien *et al.* 2015 [42] presented moderate efficacy $IC_{50} = 1199.85$ µg/ml while *in vivo* study of Husen *et al.* 2017 [54] showed better results $IC_{50} = 4.0835$ µg/ml. Besides, many studies reported remarkable free radical scavenging of the Methanol extract of the fruit hull (Yu *et al.* 2007 [55], Kosem *et al.* 2007 [56], W. Weecharangsan *et al.* 2006 [57]). The researches of Jayakumar *et al.* 2011 [58] on the fruit juice lead a 20% inhibition at the concentration of 640 µg/ml.

7.4. Anti-inflammatory activity.

Generally, inflammation is a natural of the body's defense mechanism against external or internal pains. Indeed, the immune system recognizes and removes harmful stimuli and begins the healing process. However, when this normal also call acute inflammation is perpetual or chronic and persist over month and year after the primary injury, it become a problem requiring medical treatments. Chronic inflammation is associated with DNA damage which could lead to cancer [59]. However, treatment consisting in non-steroidal anti-inflammatory present many side effects. Thereby, new natural molecules are recommended to treat these illnesses some were found in *Garcinia mangostana*. Widowati *et al.* 2016 [60] showed that the Ethanol extract of peel had inhibitory effect on three inflammation mediators COX-2, IL-1β, IL-6 respectively by 54.59 %, 24.41% and 54.95%. According to Chae *et al.* 2012 [61] and Chomnawang *et al.* 2007 [53] the pericarp extract present also an anti-inflammatory activity in both *in vivo* and *in vitro* studies.

7.5. Other activities

Tjahjani, 2017 [62] have tested the ethanolic extract of leaf against *Plasmodium falciparum* (parasite responsible for malaria disease) and showed an important inhibition $IC_{50} = 0.12$ µg/mL. On the other hand, the ethyl acetate of pericarp has showed antifungal effect against *C. albicans* at $IC_{50} = 3.2$ µg/mL (Rahmayanti *et al.* 2016 [63]). Wang *et al.* 2016 [64] working on Therapy of Alzheimer's disease proved that the pericarp extract rich in α- Mangostin, 8-Deoxygartanin, Gartanin, Garciniafura, *Garcinone C* and *Garcinone D* had a inhibition action 83.7 % on β-Amyloid cells. The pericarp has also showed the potency to inhibit the *in vivo* diabetes development in rats (Husen *et al.* 2017 [54]). The fruit hull *G. mangostana* the cytoprotection activity by the protection of ECV304 endothelial cells (Kosem *et al.* 2007 [56]). On the other hand, *G. mangostana* extracts have demonstrated efficacy to protect brain against neuronal diseases. Indeed, Weecharangsan *et al.* 2006 [57] showed that pericarp possessed neuroprotective effects, especially via the protection of NG108-15 cells with cell viability ranging from 74.89% and 98.27%.

8. Integrative discussion and perspectives

Studies analyzed in this review clearly underline the promising therapeutic capacities of *Garcinia mangostana* as a novel candidate for new medicines designs based on traditional plants. This tree belongs to the Ayurveda ancestral traditional medicine, which is extensively known for its accuracy in healing practices spread over the world. This lends to the mangosteen a kind of notoriety as a traditional medicinal plant. All parts of the plant are used in its native region to treat pains, chronic and endemic illnesses like fevers, dysentery, respiratory diseases, eczema, arthritis, ulcers, gonorrhoea, wounds, and infections. Each part is used in different forms to target different diseases or painful conditions. Although preparation type and administration mode are known and formally listed, we should take into consideration the overall traditional healing process like religious beliefs, environmental characteristics and conditions like climate, storage, type of ground, humidity, and magical context [65]. Therefore, traditional based therapeutical abilities of plants should be taken with some reserve.

However, do to the actual popularity of folk medicine and the worldwide health context requiring new herbal-derived molecules [66], pharmacological studies on plants used in various traditional healing in different countries and regions have multiplied exponentially. Researches on mangosteen, following the same trend, have resulted in the increase of knowledge on the chemical composition of each plant's part extracted with various technics, toxicity range,

pharmacological qualities, mechanisms of action on signaling pathways and pharmacokinetic interactions. Scientific knowledge confirmed the traditional use of the different part of the mangosteen, mostly the pericarp, which is well studied as antioxidant, anti-inflammatory, antimicrobial, antipyretic and anti-parasitic remedy but also provided new therapeutic possibilities of using *G. mangostana* preparations as a drug to heal other kinds of diseases encounters nowadays. Studies showed that it could act as a potent anticancer agent against breast, colon, prostate, skin, lung and pancreatic cancers, or antidiabetic, neuroprotective, antibacterial against many gram-negative and gram-positive strains, anti-parasitic, therapy for Alzheimer conditions and anti-fungal.

As a result, we are confronted with two different types of medical knowledge. On the one hand, traditional medicine practices, which could be designated as a pragmatic system [67], provide confirmed healthcare results under routine therapeutical circumstances directly on patients. Here appears the notion of effectiveness referring to trials working in real-life conditions [68]. Traditional medicine could provide information about how effective a mangosteen-based treatment is in everyday practice since it is used for centuries. However, this kind of medicinal approach presents a lack in definite information about the composition of extracts and about the specificity and reproducibility of the treatment effect because herbal derived medicine is very dependent on his environment and its changes. On the other hand, pharmaceutical in vivo and in vitro trials designated as efficacy studies or explanatory researches provides reliable information on efficiency and safety of a plant extract under controlled conditions with standardized protocols including precise timing and dosage [63]. This theoretical medical knowledge presents a wide range of advantages showing conclusive biological validity of *G. mangostana* extracts. Its purpose is to maximize the effects of molecules present in various types of extracts since most of the time, the actives principles are present in low quantities in plants. However, these conditions are limited to a precise range and do not reflect the real curative potential on some heterogeneous population and also did not acquaint on effective healing in the case of multimodal illnesses. Moreover, many scientific researches on the mangosteen described its biological action on multiple signalization pathways only considering one particular isolated xanthone, however, in herbal medicine the concept of synergy between the various plant's constituents is fundamental [69]. It is described as the totum of the plant, meaning that the molecules "mixture" present in the different parts or in the whole plant has a collective energy that gives amplified activities compared to molecules took on after the other [70]. Nevertheless, traditional based healing knowledge and pharmacological findings by scientific studies are complementary in the acquisition of reliable data for better healthcare using *Garcinia mangostana*.

9. Conclusion

This review was interested in the pharmacological data concerning the different parts of the medicinal plant *G. mangostana* and their biological abilities to treat various diseases or painful conditions from both mainstream medicine and current scientific researches. Our purpose was to increase the value of this plant which could be a valuable candidate to improve current medicines. Standardized extracts of the mangosteen are interesting therapeutic drugs.

Compliance with ethical standards

Disclosure of conflict of interest

The author declares no conflict of interest.

Reference

- [1] Petrovska BB. Historical review of medicinal plants' usage. *Pharmacognosy reviews*. 2012; 6: 1.
- [2] Alamgir ANM, Alamgir ANM. Herbal drugs: their collection, preservation, and preparation; evaluation, quality control, and standardization of herbal drugs. *Therapeutic Use of Medicinal Plants and Their Extracts: Volume 1: Pharmacognosy*. 2017; 453–495.
- [3] Mpinga EK, Kandolo T, Verloo H, Zacharie Bukonda NK, Kandala N B, Chastonay P. Traditional/alternative medicines and the right to health: key elements for a convention on global health. *Health & Hum Rts*. 2013; 15: 44.
- [4] Karim N, Tangpong J. Biological properties in relation to health promotion effects of *Garcinia mangostana* (queen of fruit) A short report. *Journal of Health Research*. 2018; 32: 364–370.
- [5] Chatatikun M, Chiabchalard A. Thai plants with high antioxidant levels, free radical scavenging activity, anti-tyrosinase and anti-collagenase activity. *BMC complementary and alternative medicine*. 2017; 17: 1–9.

- [6] Asfour HZ. Antimicrobial and quorum sensing inhibitory activities of the pericarp of *Garcinia mangostana*. *Pakistan Journal of Pharmaceutical Sciences*. 2016; 29: 1353–1357.
- [7] Phan TKT, Shahbazzadeh F, Pham TTH, Kihara T. Alpha-mangostin inhibits the migration and invasion of A549 lung cancer cells. *PeerJ*. 2018; 6: e5027.
- [8] Tjahjani S, Biantoro Y, Tjokropranoto R. Ethyl acetate Fraction of *Garcinia Mangostana* L Rind Study as Antimalaria and Antioxidant in *Plasmodium berghei* Inoculated Mice. *Open Access Macedonian Journal of Medical Sciences*. 2019; 7: 1935.
- [9] Lim YK, Yoo SY, Jang YY, Lee BC, Lee DS, Kook JK. Anti-inflammatory and in vitro bone formation effects of *Garcinia mangostana* L. and propolis extracts. *Food Science and Biotechnology*. 2020; 29: 539–548.
- [10] Tatiya-Aphiradee N, Chatuphonprasert W, Jarukamjorn K. Anti-inflammatory effect of *Garcinia mangostana* Linn. pericarp extract in methicillin-resistant *Staphylococcus aureus*-induced superficial skin infection in mice. *Biomedicine & Pharmacotherapy*. 2019; 111: 705–713.
- [11] Ansori ANM, Fadholly A, Hayaza S, Susilo RJK, Inayatillah B, Winarni D, Husen SAA. Review on medicinal properties of mangosteen (*Garcinia mangostana* L.). *Research Journal of Pharmacy and Technology*. 2020; 13: 974–982.
- [12] Mamat SF, Azizan KA, Baharum SN, Noor NM, Aizat WM. GC-MS and LC-MS analyses reveal the distribution of primary and secondary metabolites in mangosteen (*Garcinia mangostana* Linn.) fruit during ripening. *Scientia Horticulturae*. 2020 ; 262 : 109004.
- [13] Mahendra J, Mahendra L, Svedha P, Cherukuri S, Romanos GE. Clinical and microbiological efficacy of 4% *Garcinia mangostana* L. pericarp gel as local drug delivery in the treatment of chronic periodontitis: A randomized, controlled clinical trial. *Journal of investigative and clinical dentistry*. 2017; 8: e12262.
- [14] Te-chato S. Floral and fruit morphology of some species in *Garcinia* spp. *Songklanakarin J Sci*. 2007.
- [15] Yuniastuti E. Morphological description of Jogorogo Mangosteen (*Garcinia mangostana* L.). *Journal of Biotechnology and Biodiversity*. 2010; 1: 20–25.
- [16] Eukun Sage E, Jailani N, Md. Taib AZ, Mohd Noor N, Mohd Said MI, Abu Bakar M, Mackeen MM. From the Front or Back Door? Quantitative analysis of direct and indirect extractions of α -mangostin from mangosteen (*Garcinia mangostana*). *Plos one*. 2018; 13: e0205753.
- [17] Litz RE, Pliego-Alfaro F, Hormaza JI. *Biotechnology of fruit and nut crops*. CABI, 2020.
- [18] Mukhtar E. The diversity of wild edible fruit plants and traditional knowledge in West Aceh region, Indonesia. *Environment*. 2016; 21: 28.
- [19] Osman MB. *Fruits for the future 9: Mangosteen *Garcinia mangostana**. *Crops for the Future*. 2006.
- [20] Morton JF. *Fruits of warm climates*. JF Morton, 1987.
- [21] Cook GA. Laurent Garcin (c. 1681-1751) et la circulation des connaissances naturelles entre l'Asie et l'Europe au XVIIIe siècle. *Histoire des savoirs à l'époque moderne (Europe, monde) : Méthodologie et historiographie Séminaire, Université Paris Diderot* ; 2019.
- [22] Piper JM. *Fruits of South-east Asia: Facts and folklore*;1989.
- [23] Kinghorn AD, Chai H, Sung CK, Keller WJ. The classical drug discovery approach to defining bioactive constituents of botanicals. *Fitoterapia*. 2011; 82: 71–79.
- [24] Zhang S, Li Z, Wang X, An L, Bao J, Zhang J, Guo Y. Isolation, structural elucidation, and immunoregulation properties of an arabinofuranan from the rinds of *Garcinia mangostana*. *Carbohydrate polymers*. 2020; 246: 116567.
- [25] Zhou L-Y, Peng J-L, Wang J-M, Geng YY, Zuo ZL, Hua Y. Structure–activity relationship of xanthenes as inhibitors of xanthine oxidase. *Molecules*. 2018; 23: 365.
- [26] Gutierrez-Orozco F, Failla ML. Biological activities and bioavailability of mangosteen xanthenes: A critical review of the current evidence. *Nutrients*. 2013; 5: 3163–3183.
- [27] Priya C, Hari N. A study on leaf and petiole anatomy of endemic and vulnerable species of *Garcinia*. *Journal of Emerging Technology and Innovative Research*. 2018; 5: 509–512.

- [28] Parthasarathy U, Nandakishore OP. A Study on Nutrient and Medicinal Compositions of Selected Indian Garcinia Species. *Current Bioactive Compounds*. 2014; 10: 55–61.
- [29] Schobert R, Biersack B. Chemical and Biological Aspects of Garcinol and Isogarcinol: Recent Developments. *Chemistry & Biodiversity*. 2019; 16: e1900366.
- [30] Kennedy DA, Lupattelli A, Koren G, Nordeng H. Herbal medicine use in pregnancy: results of a multinational study. *BMC Complement Altern Med*. 2013; 13: 355.
- [31] Tsabang N, Kadjob S, Mballa RN, Yedjou, CG, Nnanga N, Donfagsiteli NT, Tchounwou PB. New Approach for the Development of Improved Traditional Medicine: Case of a Preparation of an Oral Hypoglycemic Medicine from *Laportea ovalifolia* (Schumach. & Thonn.) Chew. (Urticaceae). *J Mol Pharm Org Process Res*. 2015; 3: 125.
- [32] Lim TK. *Edible Medicinal and Non-Medicinal Plants: Volume 12 Modified Stems, Roots, Bulbs*. Cham: Springer International Publishing. Epub ahead of print. 2016. DOI: 10.1007/978-3-319-26065-5.
- [33] Pedraza-Chaverri J, Cárdenas-Rodríguez N, Orozco-Ibarra M, Pérez-Rojas JM. Medicinal properties of mangosteen (*Garcinia mangostana*). *Food and Chemical Toxicology*. 2008; 46: 3227–3239.
- [34] Firenzuoli F, Gori L. *Herbal Medicine Today: Clinical and Research Issues. Evidence-Based Complementary and Alternative Medicine*. 2007; 4: 37–40.
- [35] Ovalle-Magallanes B, Eugenio-Pérez D, Pedraza-Chaverri J. Medicinal properties of mangosteen (*Garcinia mangostana* L.): A comprehensive update. *Food and Chemical Toxicology*. 2017; 109: 102–122.
- [36] Siegel RL, Miller KD, Goding Sauer A, Fedewa SA, Butterly LF, Anderson JC, Jemal A. Colorectal cancer statistics, 2020. *CA: A Cancer Journal for Clinicians*. 2020; 70: 145–164.
- [37] Ee GCL, Daud S, Izzaddin SA, Rahmani M. *Garcinia mangostana*: a source of potential anti-cancer lead compounds against CEM-SS cell line. *Journal of Asian Natural Products Research*. 2008; 10: 475–479.
- [38] Han A-R, Kim J-A, Lantvit DD, Kardono LB, Riswan S, Chai H, Carcache de Blanco EJ, Farnsworth NR, Swanson SM, Kinghorn AD. Cytotoxic Xanthone Constituents of the Stem Bark of *Garcinia mangostana* (Mangosteen). *J Nat Prod*. 2009 ; 72 : 2028–2031.
- [39] Li G, Petiwala SM, Nonn L, Johnson JJ. Inhibition of CHOP accentuates the apoptotic effect of α -mangostin from the mangosteen fruit (*Garcinia mangostana*) in 22Rv1 prostate cancer cells. *Biochemical and Biophysical Research Communications*. 2014; 453: 75–80.
- [40] Ibrahim SRM, Mohamed GA, Elfaky MA, Zayed MF, El-Kholy AA, Abdelmageed OH, Ross SA. Mangostanaxanthone VII, a new cytotoxic xanthone from *Garcinia mangostana*. *Zeitschrift für Naturforschung C*. 2018; 73: 185–189.
- [41] Cunha BLA, França JP de, Moraes AA de FS, Chaves ALF, Gaiba S, Fontana R, França LPD. Evaluation of antimicrobial and antitumoral activity of *Garcinia mangostana* L. (mangosteen) grown in Southeast Brazil. *Acta Cir Bras*. 2014; 29: 21–28.
- [42] Manasathien J, Khanema P. Antioxidant and Cytotoxic Activities of Mangosteen *Garcinia mangostana* Pericarp Extracts. *Asia-Pacific Journal of Science and Technology*. 2015; 20(4), 381-392.
- [43] Yu L, Zhao M, Yang B, Bai W. Immunomodulatory and anticancer activities of phenolics from *Garcinia mangostana* fruit pericarp. *Food Chemistry*. 2009; 116: 969–973.
- [44] Wang JJ, Shi QH, Zhang W, Sanderson BJ. Anti-skin cancer properties of phenolic-rich extract from the pericarp of mangosteen (*Garcinia mangostana* Linn.). *Food and Chemical Toxicology*. 2012; 50: 3004–3013.
- [45] Zaman SB, Hussain MA, Nye R, et al. A Review on Antibiotic Resistance: Alarm Bells are Ringing. A review on antibiotic resistance: alarm bells are ringing. *Cureus*. 2017; 9(6).
- [46] Fernando KMEP, Dasanayaka PN. Antibacterial Activity of Extracts of Pericarp of *Garcinia mangostana*. 2006.
- [47] Sulisty J. Assay for antimicrobial activity of mangosteen rind extracts. *Journal of Innovations in Pharmaceuticals and Biological Sciences*. 2016; 3: 54–60.
- [48] Karthiga P. Preparation of silver nanoparticles by *Garcinia mangostana* stem extract and investigation of the antimicrobial properties. *Biotechnology Research and Innovation*. 2018; 2: 30–36.
- [49] Latini A, Pereira PJS, Couture R, Campos MM, Talbot S. Oxidative Stress: Neuropathy, Excitability, and Neurodegeneration. *Oxidative Medicine and Cellular Longevity*. 2019; 2019: e2715326.

- [50] Chew Y-L, Lim Y-Y. Evaluation and Comparison of Antioxidant Activity of Leaves, Pericarps and Pulps of Three *Garcinia* Species in Malaysia. *Free Radicals and Antioxidants*. 2018; 8: 130–134.
- [51] Hamid MA, Sarmidi MR, Park CS. Mangosteen leaf extract increases melanogenesis in B16F1 melanoma cells by stimulating tyrosinase activity in vitro and by up-regulating tyrosinase gene expression. *International Journal of Molecular Medicine*. 2012; 29: 209–217.
- [52] Pothitirat W, Chomnawang MT, Supabphol R, Gritsanapan W. Comparison of bioactive compounds content, free radical scavenging and anti-acne inducing bacteria activities of extracts from the mangosteen fruit rind at two stages of maturity. *Fitoterapia*. 2009; 80: 442–447.
- [53] Chomnawang MT, Surassmo S, Nukoolkarn VS, Gritsanapan W. Effect of *Garcinia mangostana* on inflammation caused by *Propionibacterium acnes*. *Fitoterapia*. 2007; 78: 401–408.
- [54] Husen SA, Kalqutny SH, Ansori ANM, Susilo RJK, Alymahdy AD, Winarni D. Antioxidant and antidiabetic activity of *Garcinia mangostana* L. pericarp extract in streptozotocin - Induced diabetic mice. *Bioscience Research*. 2017; 14: 1238–1245.
- [55] Yu L, Zhao M, Yang B, Zhao Q, Jiang Y. Phenolics from hull of *Garcinia mangostana* fruit and their antioxidant activities. *Food Chemistry*. 2007; 104: 176–181.
- [56] Kosem N, Han Y-H, Moongkarndi P. Antioxidant and Cytoprotective Activities of Methanolic Extract from *Garcinia mangostana* Hulls. *Science Asia*. 2007; 33: 283.
- [57] Weecharangsan W, Opanasopit P, Sukma M, Ngawhirunpat T, Sotanaphun U, Siripong P. Antioxidative and Neuroprotective Activities of Extracts from the Fruit Hull of Mangosteen (*Garcinia mangostana* Linn.). *Medical Principles and Practice*. 2006; 15: 281–287.
- [58] Pandiselvam R, Tak Y, Olum E, Sujayasree OJ, Tekgöl Y, Çalışkan Koç G, Kumar M. Advanced osmotic dehydration techniques combined with emerging drying methods for sustainable food production: Impact on bioactive components, texture, color, and sensory properties of food. *Journal of Texture Studies*. 2022; 53: 737–762.
- [59] Greten FR, Grivennikov SI. Inflammation and Cancer: Triggers, Mechanisms, and Consequences. *Immunity*. 2019; 51: 27–41.
- [60] Widowati W, Darsono L, Suherman J, Fauziah N, Maesaroh M, Erawijantari PP. Anti-inflammatory Effect of Mangosteen (*Garcinia mangostana* L.) Peel Extract and its Compounds in LPS-induced RAW264.7 Cells. *Nat Prod Sci*. 2016; 22: 147–153.
- [61] Chae H-S, Oh S-R, Lee H-K, Joo SH, Chin YW. Mangosteen xanthones, α - and γ -mangostins, inhibit allergic mediators in bone marrow-derived mast cell. *Food Chemistry*. 2012; 134: 397–400.
- [62] Tjahjani S. Antimalarial activity of *Garcinia mangostana* L rind and its synergistic effect with artemisinin in vitro. *BMC Complement Altern Med*. 2017; 17: 131.
- [63] Rahmayanti F, Suniarti DF, Masúd ZA, Bachtiar BM, Wimardhani YS, Subita GP. Ethyl acetate fraction of *Garcinia mangostana*-linn pericarp extract: Anti - *Candida albicans* and epithelial cytotoxicity. 2016; 9: 335–338.
- [64] Wang S, Li Q, Jing M, Alba E, Yang XH, Sabaté R, Chen JK. Natural Xanthones from *Garcinia mangostana* with Multifunctional Activities for the Therapy of Alzheimer’s Disease. *Neurochem Res*. 2016; 41: 1806–1817.
- [65] Hughes, S. Maya remedies and their influence on modern medicine. *Logos: A Journal of Undergraduate Research* 2019, 12.
- [66] Ozioma E-OJ, Chinwe OAN. Herbal medicines in African traditional medicine. *Herbal medicine*. 2019; 10: 191–214.
- [67] Mukherjee PK. Quality control and evaluation of herbal drugs: Evaluating natural products and traditional medicine. Elsevier, 2019.
- [68] Edwards S, Da-Costa-Rocha I, Lawrence MJ, Cable C, Heinrich M. Use and efficacy of herbal medicines: part 2—clinical effectiveness. *Pharmaceutical Journal*. 2012; 289: 270.
- [69] Moreira D de L, Teixeira SS, Monteiro MHD, De-Oliveira ACA, Paumgartten FJ. Traditional use and safety of herbal medicines1. *Revista Brasileira de Farmacognosia*. 2014; 24: 248–257.
- [70] Lloyd I. *The Energetics of Health: A Naturopathic Assessment*. Elsevier Health Sciences, 2009.