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An update review on *Hibiscus rosa sinensis* phytochemistry and medicinal uses

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ABSTRACT

Hibiscus rosa sinensis is known as China rose belonging to the *Malvaceae* family. This plant has various important medicinal uses for treating wounds, inflamation, fever and coughs, diabetes, infections caused by bacteria and fungi, hair loss, and gastric ulcers in several tropical countries. Phytochemical analysis documented that the main bioactive compounds responsible for its medicinal effects are namely flavonoids, tannins, terpenoids, saponins, and alkaloids. Experiment from recent studies showed that various types of extracts from all *H. rosa sinensis* parts exhibited a wide range of beneficial effects such as hypotensive, anti-pyritic, anti-inflammatory, anti-cancer, antioxidant, anti-bacterial, anti-diabetic, wound healing, and abortifacient activities. The few studies on toxicity exhibited that most extracts from all parts of this plant did not show any signs of toxicity at higher doses according to histological analysis. However, some of the extracts did alter biochemical and hematological parameters. Therefore, further research must be conducted to isolate the phytochemicals and explore their specific mechanism of action. This review summarizes the phytochemistry, pharmocology, and medicinal uses of this flower with the purpose of finding gaps demanding for future research and investigating its therapeutic potential through clinical trials.

Keywords: *Hibiscus rosa sinensis* , Medicinal uses, Phytochemicals, Cancer, Therapeutic potential.

INTRODUCTION

China rose or "Queen of tropics" is often a popular name for the gorgeous flowering plant *Hibiscus rosa-sinensis* , as it is mainly found in south-east China and some islands in the Pacific and Indian Ocean. *Hibiscus* is one of Hawaii's admired national plants, and it is often seen worn in hair for cultural occasions [1,2]. This plant belongs to the subkingdom *Magnoliophyta* and to the class *Magnoliopsida*, meaning that it is a vascular plant that produces seeds. It belongs to the family *Malvaceae*, and it is one of the 300 species of the genus *Hibiscus* [1]. In addition, the juice extracted from the leaves and flowers has been used since a long time ago as natural remedy for some diseases and painful symptoms, as well as in herbal cosmetics as wilted [3,4]. Dark flowers' extract is used to make eyeliners, and in shoe-blacking [4]. It was believed that the species was given the name "rosa *sinensis* which means "Rose of China" in Latin, by the famous Swedish biologist, Carolus Linnaeus in the early 1750s [5].

Traditionally, *Hibiscus* flowers has been reported to possess antitumor properties, as well as have been used as analgesic, antipyretic, anti-asthmatic, and anti-inflammatory agents. Several studies have proved the presence of anti-oxidant, anti-fungal, and antimicrobial properties in flowers of *Hibiscus rosa-sinensis* [6]. Research on extracts of stems, roots, leaves, and flowers from *Hibiscus* have revealed that its photochemical components contributed to beneficial findings to human's health such as antioxidant activity, which is the removal of free radicals that can lead to DNA damage [7]. Other examples of antioxidants sources from plants would include *Senna bicapsularis* L. flower extracts, which is simply known as *Cassia* [7,8]. The flowers were also used as a contraception agent for males and females, as well as an abortifacient in rural regions of India [9].

Current scientific literature suggests that more than 50% of today's clinical medications were of natural product origin. Many of them have played a significant role in pharmacological industry and in developing better therapies for various diseases [10]. This plant is economically very essential owing to the herbal products and medicinal uses [10]. Because of insuffiecient current pharmacological information, there is not much scientific research or clinical trials conducted on the chemical extracts of *Hibiscus rosa-sinensis* that could be crucial in exploring its fast potential medicinial applications.

Classification and Botany

Hibiscus rosa-sinensis belongs to phylum '*Magnoliophyta*', because it is a flowering plant that has true leaves, stems and roots, as well as carpels enclosing ovules, and to the 'class' *Magnoliopsida*, as it is a eudicot type of plant meaning that it flowers in groups of four/five, its leaves display netlike viens, and its seeds contain two cotyledons [11]. Moreover, it is classified in the the order '*Malvalves*' due to the fact that petals of the flower overlap, has multiple stamens, and the phloem consist of fibers that leads to a tougher bark [11]. It is also belongs to the family '*Malvaceae*' as it is found in nearly all geographical areas except in extremely cold regions, habitually as small trees or shrubs, containing bristly pollen. Last but not least, *H. rosa-sinensis* species is part of the genus '*Hibiscus*' which encloses more than 250 native species [12].

Hibiscus rosa-sinensis grows in small trees that are called 'shrubs' and are usually 4 meters tall, evergreen, and has ovate branches with stalks that are 10 cm wide and 15 cm long [13,14]. Flowers are primarily found on long stalks, measures about 20 cm wide, and consist of 5 whorled oval petals (egg shaped) that has smooth edges and are merged at the base to the central stamina column [13,14]. This central column includes a style that has 5 lobes at the tip, and is covered with numerous yellow anthers. Moreover, moving to external part, the flower has a 2.5 cm long calyx (cup shaped), and an epicalyx that consist of 5 or 7 bracteoles (1 cm long each). Flowers are habitually borne in single forms on upper leaves which are oval in shapes, glossy green, and have pointed tip and pinnate veins [13,14]. Some sources suggest that fruits can possibly form as 3 cm long capsules but very rarely. Although *H. rosa-sinensis* appear in variety of different corolla sizes, shapes and colors (Figure 1) such as yellow, orange, pink, and white [15,16,17], the wild type for this plant remains as bright red flowers that grow in single forms [18].

Figure 1: Phenotypes of *Hibiscus rosa sinensis* : red (most common), pink, white, orange, and yellow [15,16,17,18].

Phytochemistry

Each part of *H. rosa sinensis* contains a wide range of compounds (Figure 2). It was reported that phlobatannins, glycosides, saponins, flavonoids, terpenoids including other compounds such as thiamine, riboflavin and niacin are present in leaves, flowers, stem and roots [19]. According to Patel and Adhav, whose their study was conducted on four different morphotypes of *H. rosa sinensis* , glucosides, flavonoids, phytosterols, terpenoids, tannins, and phenolic compounds contributed to the pharmacological effects of the plant as they were present in all of them [20]. This suggested that although the flower color differed, the phytochemical constitions were very similar. These findings also correlates with those of another study carried out by thin layer chromatographic analysis [21].

Generally, the edible flowers contain moisture, nitrogen, fat, crude fibre calcium, phosphorus, and iron. The yellow flowers contain several flavones such as cyanidin-3,5-diglucoside, cyaniding-3-sophoroside3-5-glucoside quercetin-3,5-diglucoside, and quercetin-3,7diglucoside. Including the mentioned compounds, kaempferol-3-xylosylglucoside isolate can be found in white flowers [22]. In addition to fatty acids, fatty alcohols, hydrocarbons, the leaves also contain about 7.34 mg / 100 gm of carotene, as well as gentisic acid, mucilage, and catalase. On the other hand, cyclopropenoids can be found in root barks. Although flowers, stems, and leaves contain minor amounts of cyanin and cyanidin chorides, quercetin can be found in all parts of *Hibiscus rosa sinensis* . However, ß-sitosterol, teraxeryl acetate, and malvalic acids can be found only in stems and leaves [22].

Using mass spectrum GC-MS interpertations, it was found that methanol extracts of *Hibiscus* flowers contained components such as Ethanimidic acid, ethyl ester, Propanal, 2,3dihydroxy, Propanamide, N-ethyl-, Ethylenediamine, O-Methylisourea hydrogen sulfate, Ethene, ethoxy-, Hexadecanoic acid, methyl ester , 7-Formylbicyclo(4.1.0) heptanes, 2-Butanamine, (S)-, 1,3,5-Triazine-2,4,6-triamine, N-Formyl-β-alanine, (Z)6,(Z)9-Pentadecadien-1-ol, Butanedial, 1-Propanol, 2-methyl- , and Methanecarbothiolic acid [23]. These components were shown to have anti-cancer, antioxidant, pesticide, hypocholesterolemic, dermatitigenic, and anemiagenic properties. Moreover, Propanal, 2,3-dihydroxy, Ethylenediamine, o-Methylisourea hydrogen sulfate, 2-Butanamine, (S), (Z) 6,(Z) 9-Pentadecadien-1-ol and 1Propanol, 2-methyl- all have antioxidant and antimicrobial activities [23].

Recently, another study on antioxidant effects of *H. rosa sinensis* showed that there was a strong correlation between antioxidant activity and flavonoids, phenolics, as well as anthocyanins found in the extracts.This confirmed that these componesnt were responsible for the observed antioxidant activity [24]. Although most of these phytochemicals have future potentitial medicinal uses, which will be more discussed in the next section, anthocyanins have special natural dyeing properties [25]. It was demonstrated that using metal mordant such as Cu, Sn and Al in conjunction with *Hibiscus rosa sinensis* anthocyanin extract, the dye uptake process of cotton and silk fabrics was enhanced as compared with the controlled sample in terms of fastness [25]. This is could be mainly due to its antioxidant activity mentioned earlier.

Another molecule, known as cyanidin-3-sophoroside, was also extratced from *Hibiscus rosa-sinensis* flowers. In this study, it was successfully used as an indicator for a wide range of acid base titrations and even used lower volumes of acids and bases comparted to the conventional indicators, such as methyl orange and phenolphthalein [26]. Moreover, natural pigments, such as cyanidin-3-Sophoroside, are biodegradable, eco-friendly, and non-carcinogenic compared to synthetic pigments [26]. The different extracts from all plant's parts and their pharmacological effects are presented in Table 1.

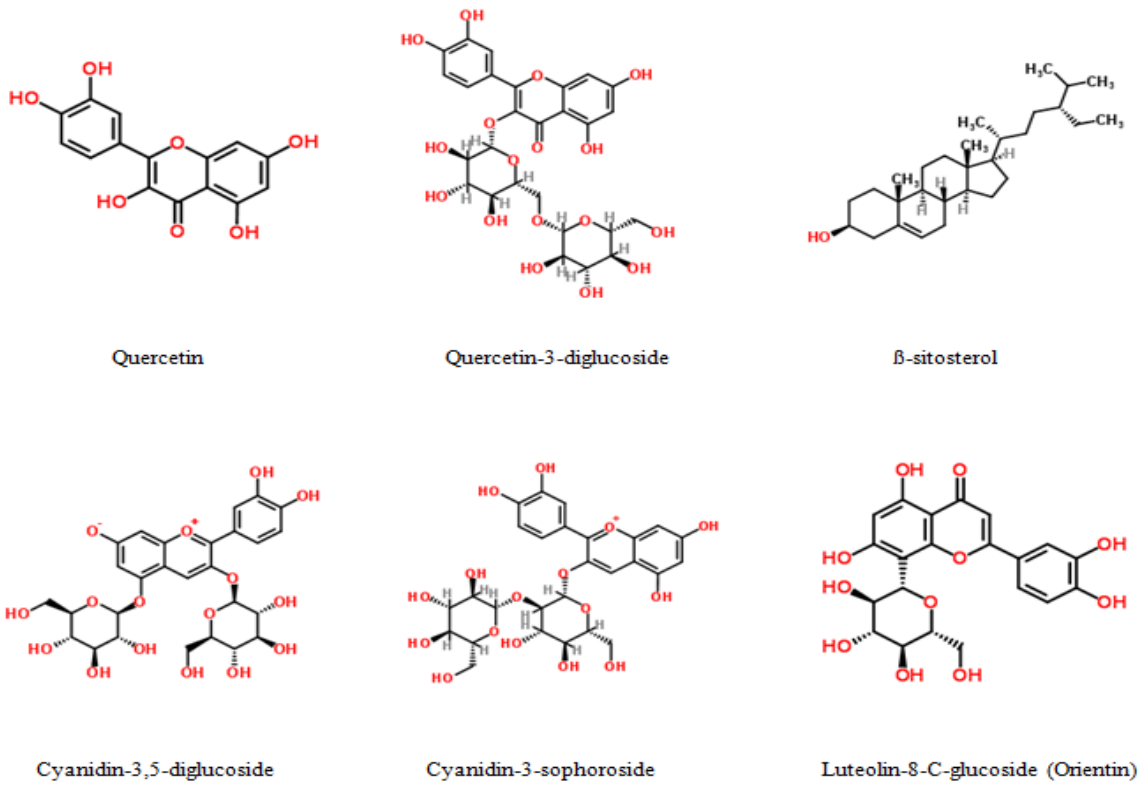

Figure 2: Structures of different bioactive compounds from H. rosa-*sinensis* : Quercetin, quercetin-3-diglucoside, ß-sitosterol, cyanidin-3,5-diglucoside [22], cyanidin-3-sophoroside [25,26], and luteolin-8-C-glucoside [52].

Table 1: List of pharmacological effects of *Hibiscus rosa sinensis*

Pharmacological activity	Part used	Extract/fraction	Dose tested/route of administration	Animals/cell line culture	Literature cited
Anti-bacterial	Leaves	Methanolic	80 µg/ml	*S. aureus, E. aerogenes*	[27]
		Aqueous	40 mg/ml	*B. subtilis, E. coli, S. aureus*	[28]
	Flowers	Hexane		*B. subtilis, E.coli*	[29]
		Methanolic	500 mg, 1 mg /ml	*E. col, S. aureus, S.pyogenes*	[30,33]
		Aqueous		*B. subtillis, E. coli*	[31]
		Ethanolic		*Salmonella sp., P. aeruginosa*	[31]
	Roots	Ethyl alcohol	7.5 µg/ml	*S. aureus, E.coli , B. subtilis*	[32]
Anti-fungal	Leaves	Methanolic	80 µg/ml	*Aspergillus niger, Candida albicans*	[27]
			100 mg/ml	*C. glabreta, A. flavus, C. albicans*	[34]
		Ethyl alcohol	10 µg/ml	*Candida parapsilosis*	[32]
	Flower	50% ethanol		*Aspergillus terreus, Aspergillus oryzae*	[35]
	Root	Ethyl alcohol	7.5 µg/ml	*Candida parapsilosis*	[32]
Anti-oxidant	Leaves	Aqueous		DPPH and hydrogen peroxide radicals	[40, 41]
		70% ethanol	500 µg/ml	superoxide hydrogen peroxide, nitric oxide radicals	[42]

	Flower	95% ethanol	50 µg/ml	hydrogen peroxide	[36]
		80% methanol, 80% ethanol		DPPH radicals	[37]
		Aqueous	1 mg/ml	DPPH radicals	[39]
	Stem	Aqueous, methanolic		DPPH, nitric oxide, superoxide anions, and hydrogen peroxide radicals	[38]
Anti-cancer		Oil extract	75 µg and 125 µg	Oral cancer cell lines KB (ATCC CCL-17)	[43]
	Leaves	90% methanol	250 µg	HT-29 colorectal AGS cell lines	[44]
		Methanolic	IC_{50} 87.6 ± 0.91 µg/ml	K-562 leukaemic cancer cells	[46]
		Ethyl acetate	IC_{50} of 57.6 ± 0.61 µg/ml		
		Aqueous	200 µg/ml	Breast MCF-7, liver HepG2, lung NCI-H23 and colon HT-29 cancer cells	[47]
	Flowers	Acetone	1000 µg/ml	HeLa cell lines	[45]
		Aqueous	2 mg/ml	B16F10 melanoma cells	[48]
Anti-diabetic	Leaves	Alcoholic		NOD mice	[49]
		Ethanolic	2 mg/kg bw	Alloxan induced diabetes in rats	[51]
		Methanolic	400 mg/kg	Streptozotocin induced diabetic rats	[52]
	Roots		500 mg/kg bw	Alloxan induced diabetic type II rats	[50]
	Flower	Ethanolic	500 mg/kg	Alloxan induced diabetes in hyperlipidemic Wister rats	[54] [55]
			50, 100, and 200 mg/kg	Albino rabbits	
		Powder		Clinical trial on type II diabetes mellitus patients aged 30- 60 years	[56]

Pharmacological activity	Part used	Extract/fraction	Dose tested/route of administration	Animals/cell line culture	Literature cited
Anti-fertility	Flower	Methanolic	100 mg/mL	alkaline phosphatase *(In vitro*)	[57]
		Aqueous		Spermatogenesis in male albino rats	[58]
	Powder	Propelyne glycol		Albino Wister rats (inhibition of implants)	[59]
				Pregnant female albino Wister rats	[60]
Hair growth promoting activity	Leaf	Petroleum ether		Wister albino rats (Sonic stress induced alopecia)	[61]
			1%	Male albino rats	[63]
		Ethanolic		Male albino rats	[64]
		5% hydrolcholic		Wister albino rats	[62]
	Flower	Aqueous	2%	Wister rats (*In vitro* and *In vivo*)	[65]
Neuroprotective	Root	Methanolic	200 mg/kg i.p	Swiss albino mice and Wistar rats	[66]
			300 mg/kg	Male Wistar strain rats	[67]
			300 mg/kg	Wistar albino rats with scopolamine-induced cognitive	[68]

				decline	
		Ethanolic	500 mg/kg	mice and rats (antidepressant)	[69]
Wound healing activity	Flower	Ethanolic	120 mg /kg	Sprague Dawley rats	[70]
	Leaves	Aqueous	0.01g/ml	Sprague Dawley rats	[71]
		Ethanolic	200 mg/kg, p.o.	Swiss albino mice	[72]
Anti-inflammatory	Leaves	Hydroalcoholic	200 mg/kg, p.o.	Acetic acid induced colitis in male Wister rats	[73]
	Flower, leaves	Ethanol	100 mg/kg	carrageenan induced paw edema Sprague-Dawley rats	[74]
Immune response	Flower	Aqueous	500 mg/ kg	Male Swiss albino mice	[75]
		ethyl acetate	100 mg/kg	Albino Wistar rats	[76]
Cardioprotective	Leaves	Aqueous	200 mg/kg	Hypertensive and non-hypertensive albino rats	[77]
	Flowers		360 µg/mL	Langendorff-perfused hearts of Wistar rats *(In Vitro)*	[78]
Gastroprotective	Aerial parts	Aqueous-ethanolic	500 mg/kg	Albino Wistar rats	[79]
	Flower	Aqueous	500 mg/kg	Albino Wistar rats	[80]
Anti-pyritic	Root	Aqueous	250 mg/kg	Yeast-induced pyrexia in albino Swiss rats	[81]
	Leaves	Aqueous	500 mg/kg b.w	mice	[82]
Antihyperlipidemic	Flower	Ethanolic	500 mg/kg b.w	Triton and atherogenic diet induced hyperlipidemia in albino Wistar rats	[83]
Hepatoprotective	Leaves	Ethanolic	30 mg/kg b.w.	Piroxicam induced liver toxicity in Swiss albino mice	[84]

Medicinal Applications

Anti-bacterial activity

The methanol extracts prepared from the leaves of the *H. rosa-sinensis* were shown to have antimicrobial activities against *Pseudomonas aeruginosa, Escherichia coli, Enterobacter aerogenes*, and *Streptococcus pyogenes*. Using well diffusion method and after an incubation period of 24 hours at 37° C, the maximum observed zone of inhibition was 13 ± 00 mm and it was against *E. coli* followed by 12 ± 00 mm against both *S. aureus* and *E. aerogenes* at 80 µg/ml concentration of leaves methanolic extract [27]. These microorganisms were obtained from infected skins, and the chemical coumpounds responsible for the antibacterial activity may be due to flavonoids, tannins, terpenoids, saponins, or alkaloids identified in the study [27].

In another study conducted using disc diffusion method, aqeuous leaves extracts of 40 mg/ml showed maximum zone of inhibition against *Bacillus subtilis* (14.00 ± 1.05 mm), *E. coli* (12.30 ± 0.95 mm) and *S. aureus* (11.00 ± 1.20 mm), while the methanol extract showed the following zones of inhibitions against *B. subtilis* (18.82 ± 0.18 mm), *E. coli* (17.30 ± 0.51 mm), *S. aureus* (15.20 ± 0.90 mm) after 48 hours of incubation at 34° C. The screened phytochemicals were cardiac glyxosides, anthraquinones, and phlobatanins, including those mentioned earlier [28]. Intresingly, another research reported similar results as the aqueous extracts showed a maximum zone of inhibition against *B. subtillis* as 15.00 ± 2.81 mm, and *E. coli* as 12.50 ± 1.81 mm, while hexane extracts gave the highest zone of inhibition against *B. subtillis* as 19.86 ± 0.15 mm, and *E. coli* as 18.00 ± 1.53 mm [29]. Although same methodology was applied, however, in this study flowers of *H. rosa sinensis* were used and the results were observed after an incubation period of only 24 hours [29].

Antibacterial activity has been also observed using disc diffusion method against *E.coli* and *S. aureus* at different concentrations of methanolic flower and leave extracts varying from 31.25 to 500 mg/ml. These were compared with positive control gentamicin (1 mg/ml) and methanol as negative control [30]. In both extracts' types, the antibacterial activity was increased with extract concentration. The highest zones of inhibitions observed were at concentration 500 mg for *E. coli* were 23 ± 1.01 mm and 13.75 ± 0.99 mm for leaf and flower methanolic extracts respectively. Conversely, for *S.aureus,* methanolic leaf and flower extracts gave 19.33 ± 0.29 mm and 9.75 ± 0.76 mm as highest zones of inhibitions respectively at concentration 500 mg [30]. In this study, carbohydrates, phytosterols, and proteins were identified from flower extracts and glycosides, tannin, phenols, and flavonoids from leave extracts. However, alkaloids and saponins were found in both extracts [30].

The cold aqueous extractions of flowers gave highest zones of inhibition against *B. subtillis* as 17.00 ± 2.94 mm, and against *E. coli* as 14.50 ± 1.71 mm. In contrast, the hot aqueous extraction inhibited *E. coli* growth for 11.60 ± 3.14 mm, and Salmonella sp. for 10.66 ± 3.09 mm as maximum zones of inhibition [31]. The methanol extracts showed highest zones of inhibition against *B. subtillis* as18.86 ± 0.18 mm, against *E. coli* as 18.00 ± 1.63 mm. The ethanol extracts gave zones of inhibition against *Salmonella sp.* as 20.40 ± 1.54 mm, and *P. aeruginosa* as 16.30 ± 0.94 mm. All these mentioned microorganisms are considered as human pathogens [31]. The antibacterial activities of both pure and crude protiens from flowers were also investigated such that crude protein inhibited the growth of *Salmonella sp.* for 16.55 ± 1.16 mm, and *E. coli* for 14.30 ± 2.86 mm as maximum inhibition zones, compared to pure protein which inhibited *Staphylococcus sp* for 11.4 ± 1.74 mm, *E. coli* for 12.25 ± 0.97 mm. Moreover, the pure and crude *H. rosa-sinensis* flower proteins were run in poly acrylmide gel electrophoresis (PAGE), which resulted in various bands for the crude protein sample [31]. This suggests that the crude extract may contain components such as flavonoids, triterpenoids, tannins, alkaloids. For example, flavonoids are considered antimicrobial agent as they are able to complex with components of the bacterial cell wall and eventually deteriorate it [31].

The antibacterial activity of root extratcs from *H. rosa sinensis* was also investigated. It was reported that using disc diffusion method, the ethyl alcohol root extracts inhibited the growth of *S. aureus* for 2 cm and *E.coli* and *B. subtilis* for 1.5 cm as highest zones of inhibition at the concentration 7.5 µg/ml [32]. Similarly, methanol flower extracts exhibited highest inhibition zones at the concentration of 1 mg /ml against *E.coli* (27 ± 0.12 mm), *S. aureus* (21 ± 0.41 mm), and *Streptococcus pyogenes* (18 ± 0.65 mm), compared to 10µg of Chroramphenicol which was used as a positive control and resulted in a zone of inhibition of approximately 24 mm [33]. Compared to other extracts such as ethyl acetate extract, ethanol extract, and water extract, all phtochemicals that were involved in the antimicrobial activity were detected from the methanol extract. This suggests that it is a useful extract for further research [33].

Therefore, the flowers, leaves, and roots extracts can be used as vital antibiotics components to treat diseases caused by the different strains of bacteria. Even these results are encouraging, precise assessment is absolutely necessary before undergoing further pharmacological evaluation. Because pathogenic microorganisms are getting resistant to current antimicrobial agents, scientific research has continued to search for other sources of antimicrobial compounds.

Antifungal activity

According to previous studies, the methanol extracts prepared from the leaves of the *Hibiscus rosa-sinensis* were shown to have antimicrobial activities against *Candida albicans, Aspergillus niger, Candida parapsilosis* and *Trichophyton rubrum*. Using well diffusion method and after an incubation period of 24 hours at 37° C, the maximum observed zone of inhibition was 9.3 ± 0.57 mm and it was against *Aspergillus niger* followed by 6.6 ± 0.57 mm against *Candida albicans* at 80 µg/ml concentration of of leaves methanolic extract [27]. These fungi were obtained from infected skins, and the chemical coumpounds responsible for the antifungal activity may be due to flavonoids, tannins, terpenoids, saponins, or alkaloids identified in the study [27].

The antifungal activity of root, leaves, and flowers ethyl alcohol extratcs from *H. rosa sinensis* was also investigated. It was reported that using disc diffusion method, the growth of both *Candida parapsilosis* and *Aspergillus niger* for 1.5 cm were inhibited by flower extracts as highest zones of inhibition at the concentration 10 µg/ml [32]. In addition, *Candida parapsilosis* was inhibited optimally for 2.2 cm by leaves extracts and for 1.5 cm by roots extracts at 10 µg/ml and 7.5 µg/ml concentrations respectively [32].

H. rosa sinensis methanol leaf extracts also inhibited the growth of *C. glabreta* for 19 ± 00 mm, *A. flavus* for 17 ± 00 mm, and *C. albicans* for 20 ± 00 mm as highest inhibition zones at a concentration of 100 mg/ml [34]. Moreover, using agar disc diffusion method, flower extract was found to be active against all tested fungi except *Aspergillus flavus*. The highest inhibition zones recorded for each fungi were: *Aspergillus niger* (9 mm), *Aspergillus terreus* (17 mm), *Aspergillus oryzae* (17 mm), *Fusarium solani* (10 mm), *Fusarium verticillioides* (13 mm), and *Penicillium sp.* (15 mm) at 50 % ethanol concentration [35].

Antioxidant activity

Ethanolic (95.0%) extract of flowers strongly scavenged hydrogen peroxide for 96 ± 2.35 % inhibition with a concentration of 50 µg/ml while the standard antioxidant, ascorbic acid produced 76.33 ± 1.25 % radical scavenging activity at 100 µg/ml concentration. It was reported that molecules identified by GC-MS analysis mainly belonged to classes of alkaloids, tannins, steroids, glycosides, and flavonoids, and may be also the reason behind the high radical scavenging activity [36]. Free radicals such as those generated from hydrogen peroxide play a crucial role in the progress of tissue damage. Any substances which have the ability to remove these, such as *H. rosa sinensis* phytochemicals, will protect the cell system and components from cytotoxic damage [36].

DPPH (1,1-diphenyl-2-picrylhydrazyl) radical scavenging activity was observed using 80% methanol flower extract as 75.46 ± 4.67 %, and 80% ethanol flower extract as 64.98 ± 2.11%, compared to 77.54 ± 4.77% for BHT as a positive control. The scavenging of DPPH free radicals was measured at 515 nm using a UV visible spectrophotometer [37]. Moreover, the total phenolic contents of the methanolic and ethanolic extracts were 61.45 ± 3.23 and 59.31 ± 4.31 mg/100g dry extract, and total flavonoid contents were 53.28 ± 1.93 and 32.25 ± 1.21 mg/100g dry extract respectively. Because it was observed that methanolic extract had higher amount of phenolics and flavonoids as well as contributed to higher scavanging activity than ethanolic extract, this strongly suggest that they are responsible for the anti-oxidant activity [37].

According to another study, aqueous stem extracts resulted in 15.1 ± 4.5 scavenging activity against DPPH radicals compared to methanolic extracts which exhibited only 9.75 ± 1.15 scavenging activity. However, both extract types gave similar results towards nitric oxide, superoxide anions, and hydrogen peroxide radicals [38]. In addition, water extracts of petals scavanged DPPH radicals optimally for 71.9% with a concentration of 1 mg/ml. It was reported that this activity was due to iron content in *H. rosa sinensis* petals, which was isolated using TLC and partially purified by silica gel column chromatography. According to ICP-OES analysis, there was 0.8 mg/g of iron in the lyophilized petal powder [39].

Similarly, aqueous extratcs of *H. rosa sinensis* leaves exhibited slightly higher antioxidant activity than those of ethanol extracts against DPPH and hydrogen peroxide radicals, and in case of nitric oxide and ferric reducing antioxidant power assays, the ethanolic extracts contributed to much higher scavanging activity [40].

The relationship between number and flower colors and its leaves' antioxidant activity using DPPH assay was also investigated. In this research, leaves of a single plant for all nine colours (pink, yellow, white, orange, yellow/pink, white/pink, orange/pink, and two types of red shades) were collected separately [41]. The highest observed antioxidant activities with least IC_{50} values were 0.20 from white/pink

with many petals methanol extracts, and 0.19 from and yellow with 5 petals ethanol extracts. On the other hand, the samples orange/pink with many petals methanol extracts and red with five petals ethanol extratcs exhibited least antioxidant activity as 1.17 and 4.49 respectively [41].

The radical scavenging activity of 70% ethanol extracts from leaves were examined using butylated hydroxyanisole (BHA) as a standard, and highest antioxidant activity found against superoxide radicals was 60.4 ± 2.19 %, compared to 48.52 ± 3.03 % scavanging activity against hydrogen peroxide, and 36.3 ± 2.47 % against nitric oxide, all using a concentration of 500 µg/ml. The 200 µg/ml of BHA gave the following scavanging activities: 61.6 ± 3.15 %, 65.8 ± 2.21 %, and 37.3 ± 3.6 % respectively [42]. However, the total antioxidant capacity of *H. rosa sinensis* extract was nearly two-fold higher than that of BHT (butylated hydroxytoluene) that used as a standard with the same concentration of 500 µg/ml. This was investigated by the reduction of Fe^{3+} to Fe^{2+} and measuring the absorbance of the formed prussian blue complex at 700 nm. The higher the absorbance value, the higher capabilities of both reducing power and the antioxidant activity of the extract [42]. This activity could be generally due to flavonoids, the natural phenolics are which contain hydroxyl functional groups. BHT and BHA, which are synthetic antioxidants added in food, have been suspected correlated to carcinogenesis and liver damage. Therefore, it is important to use extracts from *H. rosa sinensis* as a potential sources of natural antioxidants [42].

Anti-cancer activity

Oral cancer cell lines KB (ATCC CCL-17) were treated with 75 µg and 125 µg of *H. rosa sinensis* oil extract for 24 hours. After subjecting the treated cells to DNA fragmentation assay, and using agarose gel electrophoresis, it was observed that the cells' DNA from both concentrations has been fragmented compared to control sample. This means that Hibiscus extract hindered the growth and proliferation of oral cancer cells [43]. It was also shown that 250 µg of 90% methanolic leaves extratc inhibited HT-29 colorectal AGS cell lines by 100%. The cell viability percentage was measured using MTT assay and the calculated IC_{50} was found to be 90.79 µg/ml. The phytochemical analysis suggested that this significant anticancer activity was mostly due to flavonoids and terpenoids content in the leaves [44].

Acetone extracts of *H. rosa sinensis* flowers effect on HeLa cell lines viability was investigated. Using MTT assay, it was found that at a concentation of 1000 µg/ml resulted in only 12.96% cell viability. The presence of flavonoids, tannins, and saponins detected by FT-IR spectra and qualitative screening tests are suspected for this activity [45].

Methanolic leaf extracts exhibited a higher activity against K-562 leukaemic cancer cells giving an IC_{50} value of 30.9 ± 1.1 µg/ml than petroleum ether (IC_{50} of 87.6 ± 0.91 µg/ml) and ethyl acetate extracts (IC_{50} of 57.6 ± 0.61 µg/ml), after 72 hours of incubation using MTS and MTT assays [46]. However, methanolic stem extracts resulted in an IC_{50} of 79.80 µg/ml compared to IC_{50} > 100 µg/ml from both petroleum ether and ethyl acetate extracts. In this study, MDBK (Mardin-Darby kidney) cells were used as a positive control and gave an IC_{50} > 100 µg/ml for all the extracts. Morphological detection with Hoeschst staining confirmed further for the anticancer activity as it exposed that treated K562 cells with 30 µg/ml of methanol leaf extract, caused apoptosis with nuclear segmentation after 24 hours of incubation [46].

The effect of aqueous leaf extract was tested on four cancer cell lines: breast MCF-7, liver HepG2, lung NCI-H23 and colon HT-29 cancer cells [47]. Using a dosage of 200 µg/ml, the extract inhibited the growth of HepG2 by 54.7 %, HT-29 by 54.6 %, and MCF-7 cells by 51.5 %, compared to lower effect on NCI-H23 cells with 49.2 % inhibition. Tamoxifen, which was used as a positive control for MCF-7 cells, resulted in 85.4 % inhibition, whereas 5-Fluoro Uracil, which was used as a positive control for other cell lines, resulted in 88.6 % inhibition [47]. Similarly, aqueous extract of flowers reduced the growth of B16F10 melanoma cells by 2 folds at 1 mg/ml, and 4 folds at 2 mg/ml after 72 hours of incubation. Nevertheless, it did not affect Src kinase activity in LA25 melanoma cells, which a potential target in chemotherapy. This study suggests that the extract's biocompounds affect other pathways related to viability of tumor cells [48].

Anti-diabetic activity

In non-obese type I diabetic mice, the alcoholic leaves extracts of *Hibiscus rosa sinensis* was proven to be an oral hypoglycemic agent. It reduced blood glucose levels from 281.6 ± 3.7 mg/dl to 92.2 ± 2.63 and 83.8 ± 3.15 mg/dl using the concentrations 100 and 200 mg/kg of body weight respectively, compared to 103.37 ± 2.13 mg/dl in insulin injected NOD mice, which was used as positive control [49]. The tested extracts also reduced levels of triglycerides, blood urea, glycosylated hemoglobin, and cholesterol significantly after 5 weeks of oral administration [49]. In alloxan induced diabetic type II rats (150 mg/kg), root extracts of 500 mg/kg of bw concentration decreseaed blood glucose levels from 300.23 ± 32.20 to 220.41 ± 20.40 mg/dl, compared to 175.38 ± 11.67 mg/dl in glibenclamide (600 µg/kgbw) treated rats, after 15 days of oral administration [50].

The anti-diabetic effect of ethanolic leaves extracts of *H. rosa sinensis* on alloxan induced diabetes in rats was also investigated. It was observed that at 2 mg/kg bw concentration, the blood glucose levels were reduced from 17.5 ± 0.69 to 13.8 ± 0.36 mmol, compared to those of metformin treated rats, which were reduced from 16.94 ± 0.51 to 12.90 ± 0.38 mmol after 4 hours [51]. In streptozotocin induced diabetic rats, 400 mg/kg of leaves methanolic extract has managed to lower blood glucose levels from 326.67 ± 25.76 to 154.11 ± 17.91 mg/dl. Moreover, it reduced levels of uric acid, creatinine, AST (aspartate aminotransferase) (AST), and ALT (alanine aminotransferase), suggesting renal and hepatic protective effects as confirmed by H&E histological analysis [52]. Intrestingly, the coumpound verbascoside (phenylpropanoids glycoside) and orientin (Luteolin-8-C-glucoside) that were identified by NMR spectroscopy, are highly responsible for this anti-diabetic activity [52].

In another study, 500 mg/kg of ethanolic flower extract exhibited best antidiabetic activity as well as anti-hyperglycemic activity against alloxan induced diabetes in hyperlipidemic Wister rats [53]. This was also noticed when the effect of flower aqueous extract was evaluated on female pregnant rats. The diabetic condition of these Wister rats was induced by streptozotocin before the mating. The treatment somewhat benefited the diabetic pregnant rats and their offspring, but not the non-diabetic pregnant ones [54]. This study would have been better conducted by extending treatment period and using alloxan instead, as it could have increased blood glucose levels more moderately for fairer evaluation [54].

Using albino rabbits as study models, flower ethanol extracts managed to lower blood glucose levels in a progressive manner in 72 hour period using all graded doses 50, 100, and 200 mg/kg. Glibenclamide (200 mg/kg p.o), which was used as positive control, caused a sharp decrease in blood sugar levels in 24 hour period, which is not desirable in clinical situations [55]. The antidiabetic activity of *H. rosa sinensis* was also evaluated in clinical trials, as 2 g of flower's powder was subjected to type II diabetes mellitus patients aged from 30 to 60 years. After daily oral administration for 60 days, fasting blood glucose levels were reduced from 147.8 ± 43.54 to 111.6 ± 35.32 mg/dl [56]. Post prandial glucose levels were also reduced from 184.6 ± 81.86 to 126.5 ± 34.14 mg/dl, compared to no change in control groups for both cases. The flower's powder resulted as well in siginificant decreases in total cholesterol and triglyceride levels [56].

Anti-fertility activity

Hibiscus rosa sinensis flower methanolic extract was proven to be effective against alkaline phosphatase in vitro activity. Quercetin-7-O-galactoside, which was isolated from its water soluble fraction, inhibited the enzyme activity reaching 100% at a concentration of 100 mg/mL [57]. This enzyme complete inhibition was correlated with inhibition of implantation, a mechanism that is closely related to the process of contraception [57]. Oral administration of aqueous flower extract also affected the spermatogenesis in male albino rats. According to histological analysis using H&E stain, prolonging treatment time with incresaed dosage of extract has lead to changes, such as broken and discontinous base membrane, total disorganization of spermatogenic cells, fragmented Sertoli cells, and absence of Leydig cells and mature spermatozoa [58]. However, after discontinuing the treatment for 30 days, the effect was completely reversed suggesting that it can be useful for temporary contraception [58].

In another study, *H. rosa sinensis* powder mixed with propelyne glycol was orally subjected to albino Wister rats before mating. This treatment resulted in 100% inhibition of implants in pregnant rats, compared with Overal L that was used as positive control [59]. The group treated with propelyne glycol as negative control, gave 100% deliveries on full term compared to 0% from groups treated with Overal L and H. rosa *sinensis* extract [59]. The phytochemical analysis of the aqeuous extract showed that steroids and saponins could have contributed to this anti-fertility activity [59]. Similarly, flowers of *H. rosa sinensis* has also lowered progesterone and estrogen levels in pregnant female albino Wister rats. This has lead to endometrial changes that in turn disrupted the estrous cycle, and caused non receptive conditions preventing blastocyst implantation [60].

Hair growth promoting activity

The petroleum ether leaf extract of *Hibiscus rosa sinensis* was proven to be a good hair growth promoter in a study involving Wister albino rats. After 14 days, the 5% w/w extract ointment resulted in 4.91 ± 0.261 mm hair length compared to 6.06 ± 0.431 mm in 2% minoxidil treated group, and 2.21 ± 0.108 mm in negative control group [61]. The extract also contributed to 1937 ± 37.84 hairs per cm^2 area, while Minoxidil gave 2315 ± 05.78 hairs per cm^2 area. The alopecia was induced by exposure to sonic stress, and there were no side effects such as erythema or edema, compared to synthetic hair growth promoting ointment [61]. Similarly, 5% hydrolcholic leaves extract ointment exhibited 5.97 ± 0.13 mm hair length, and 2058 ± 19.23 hairs per cm^2 area [62].

The effect of leaf petroleum ether extract was also investigated in male albino rats. The 1% extract resulted in 65% anagen, 2% catagen and 33% telogen in hair follicle population, compared to anagen 64%, catagen 1%, and 35% telogen in minoxidil treated group [63]. Phytosterols and triterpenoids found in this extract are advantageous for hair growth while tannins, which are absent, supress hair growth [63]. Leaf ethanolic extract contributed to 17 ± 1.2 mm hair length, compared to 19.36 ± 0.4 mm with minoxidil after 30 days. Although flower extract showed poorer results, this difference was insignificant [64].

The hair growth potential of *H. rosa sinensis* aqueous flower extract was evalutaed In-vitro and In-vivo. After 30 days, 2 % of extract resulted in a mean of 18.68 ± 0.3 mm of hair length, compared to 19.24 ± 0.4 mm with 2% of minoxidil in Wister rats. Increase in hair follicle length was observed In-vitro as 1.73 ± 0.18 mm, in comparison to 1.95 ± 0.14 mm by positive control, after 72 hours of incubation [65].

Neuroprotective activity

The methanolic extract of *H. rosa-sinensis* roots has beneficial effects on the central nervous system in Swiss albino mice and Wistar rats. Using acetic acid to induce writhing, 200 mg/kg i.p of extract resulted in an analgesic activity as inhibited the pain sensation by 78.5 %, compared to 81.0 % in 30 mg/kg Diclofenac treated group [66]. The number of head twitches induced by lithium was lowered to 10.2 ± 1.06, compared to 9.0 ± 1.7 by ondansetron, a 5HT3 antagonist, as a positive control. Pentobarbital induced sleeping period was also extended, suggesting sedative effect by reducing dopaminergic transmission [66]. The anxiolytic effect of roots extract was also demonstrated, as in elevated plus maze, mice spent more time in open arms. In addition, the extract's phytochemicals were tannins, flavonoids, saponins, and glycosides [66].

According to another study, 300 mg/kg of methanol root extract improved best learning and memory deficits in male Wistar strain rats, as well as anxiety induced by cerebral ischemia. This was investigated using elevated plus maze and Open field tests [67]. After 6 days, the extract managed to lower lipid peroxidation and raise superoxide dismutase, catalase and glutathione reductase levels that were altered after bilateral common carotid artery (BCCA) occlusion [67]. Similarly, Petroleum ether flower extract of H. rosa-sinesis at 300 mg/kg dosage increased spatial working and spatial reference memories, in Wistar albino rats with scopolamine-induced cognitive decline [68]. This was evaluated using Morris water maze, rectangular maze, and pole climbing apparatus. Moreover, acetylcholinesterase and malondialdehyde levels were reduced whereas DPPH and CAT levels were raised compared to control group, indicating antioxidant and neuroprotective actvity [68].

Ethanolic extract of *H. rosa sinensis* roots also exhibited an important antidepressant activity on both mice and rats. In forced induced swimming test using rats, 14 days of extract (500 mg/kg) administration reduced immobility time to 93.33 ± 9.66 seconds, compared to 107.50 ± 9.4 seconds in fluoxetine (15 mg/kg) group as positive control [69]. In tail suspension test using mice, the extract and fluoxetine decreased the immobility time significantly by 43.62% and 47.04%, respectively [69].

Wound healing property

The treatment of *Hibiscus rosa-sinensis* flowers ethanolic extract, which contained polyphenols, tannins, carboxylic acids, triterpenoids, and alkaloids, demonstrated wound healing activity in Sprague Dawley rats. After 15 days, using a daily dosage of 120 mg kg^{-1} decreased period of epithelialization to 11.2 ± 0.13, and resulted in 49% reduction in the wound area compared to only 33% in control group, evaluated by excision model [70]. In dead space wounds and incision models, the extract also increased strength of skin breaking to 515.0 ± 39.56, as well as granulation tissue's dry weight and hydroxyproline content to 33.50 ± 2.89 and 47.66 ± 10.64, respectively [70].

On the other hand, 0.01g/ml of leaves aqueous and ethanolic extracts exhibited 56.322 ± 10.17 and 62.855 ±12.41 g/mm2 tensile strengths respectively, compared to 62.433 ± 7.33 g/mm2 in 10 % cetrimide treated group as positive control [71]. H&E stain histological analysis also showed that wounds were re-epithelialised with nearly healed hair follicles, arranged collagen fibres, and replaced granulation tissues by fibrosis [71]. In Swiss albino mice, 200 mg/kg, p.o. of leaves ethanolic extract increased wound closure percentage and wound breaking strength to 96.41 ± 2.07 and 338.82 ± 6.91, compared to 97.23 ± 1.62 and 385.03 ± 4.91 in povidone iodine treated group, respectively [72]. Moreover, the epithelisation periods for extract and silver sulfadiazine treated groups were found to be 18.09 ± 1.6 and 17.23 ± 0.81 in thermally-induced burn wounds, as well as 17.1 ± 1.03 and 18.1 ± 1.03 in chemically-induced burn wounds, correspondingly [72].

Anti-inflammatory activity

In male Wister rats, H. rosa *sinensis* hydroalcoholic leaves extract had an ameliorative effect on 4% acetic acid induced colitis via rectal administration. The 7 days treatment with 200 mg/kg, p.o. of extract reduced the ulcer area of colon to 20.67 ± 2.40 mm^2, as compared to 10.00 ± 1.23 mm^2 from prednisolone treatment group taken as positive control, and 41.67 ± 1.96 mm^2 from negative control group [73]. The phytochemicals that were present such as steroids, polyphenols, alkaloids, and flavonoids, might have contributed to this activity [73].

Ethanol extracts of flowers and leaves from two *H. rosa-sinensis* morphotypes were also tested on carrageenan induced paw edema in Sprague-Dawley rats. After 6 hours, the paw volume (ΔV, ml) was measured using phetlysmometer, and 100 mg/kg dosage was observed to have most remedial effects [74]. The red Hibiscus (*H. rosa-sinensis* L.) flower and leaf extracts reduced edema to 0.04 ± 0.02 and 0.02 ± 0.02, respectively. Whereas the white Hibiscus (*H. rosa-sinensis* var alba) flower and leaf extracts reduced it to 0.08 ± 0.02 and 0.04 ± 0.02, respectively. Diclofenac treated group as positive control resulted in 0.02 ± 0.02, compared to 0.20 ± 0.03 edema volume from negative control group [74].

Immune response activity

The effect of aqueous extracts of flowers on immunomodulation was studied by intraperitoneally injecting 500 mg kg^{-1} BW of extract in male Swiss albino mice. After 15 days of treatment, cytokine IL-1α serum levels increased by 14.27% and IL-2 levels decreased by 32.70% in comparison to control group. The antibody titre also increased to 2.39 ng ml^{-1} compared to 1.73 ng ml^{-1} in control group [75]. Moreover, the extract increased the macrophage yield and viability, as well as the phagocytic index to 76.76 ± 1.40, which is only 72.85 ± 1.07 in control group. HPTLC chromatogram proved that it contains alkaloid and flavonoids [75].

Using forced swim test and albino Wistar rats as study models, ethyl acetate extract of *H. rosa sinensis* petals was evaluated at 100 mg/kg dosage. The treatment increased mean swim time by two fold, indicating better tolerance to stress, and nearly restored back the normal levels of enzymes such as alanine aminotranferase (73.81 ±1.88 IU/L), and aspartate aminotransferase (101.6 ±1.93 IU/L), compared to control values 66.79 ±1.44 and 93.61 ±4.49 IU/L, respectively [76]. Other physical stress indicators, such as glucose, cholesterol, and triglycerides, were also restored to their normal values compared to control groups [76]

Cardioprotective activity

The administration of 200 mg/kg of aqueous extracts of *H. rosa-sinensis* Linn leaves in lowered blood presure in both hypertensive and non-hypertensive albino rats. After the four weeks, the mean systolic and diastolic pressures were 155.0 ± 4.39 and 141.0 ± 2.45 mmHg, respectively in hypertensive treated group, compared to 92.0 ± 7.54 and 67.0 ± 8.67 mmHg, respectively in non-hypertensive treated group [77]. The hypertensive control group gave mean systolic and diastolic pressures of 168.0 ± 1.71 and 144.0 ± 1.76 mmHg. However, the extract increased urea and sodium levels in both groups suggesting it may interfere with kidney's function leading to more salt retention [77].

The cardioprotective effects of ethanolic flower extracts were also investigated In vitro using Langendorff-perfused hearts of Wistar rats. After 15 minutes of perfusion with 360 µg/mL of extract, LVDP (left ventricular developed pressure) was 80.7 ± 2.8 mmHg, and the heart rate was 292.1 ± 13.8 BPM, similar to those of pre-drug values, meaning that it improved post-ischemic recovery [78]. The treatement also reduced the number of VPB (ventricular premature beats) and lowered the VT (ventricular tachycardia) period to 13.2 ± 5.1 s, when compared with nontreated control group, suggesting antiarrhythmic protection [78].

Gastroprotective activity

The aqueous-ethanolic extract of *Hibiscus rosa sinensis* aerial parts exhibited protection of mucosal layer in albino Wistar rats gastric tissues subjected to 600 µg/kg carbachol and pylorus ligation. Extract treatment at the dose of 500 mg/kg resulted in 82% had protection percentage comapred to control group, whereas treatment with 2.5 mg/ kg cimetidine and 10 mg/kg b.w verapamil resulted in 88% and 81% protection, respectively [79]. Decline in gastric secretion volume, free and total acidity, with an increase in gastric juice pH was aslo observed. The extract treatment lowered ulcer index to 3.00±0.22 from 16.90±1.30 (negative control), in comparison to 2.10±0.40 and 3.20±0.15 from cimetidine and verapamil control groups, respectively. Moreover, the phytochemical screening indicated that carbohydrates, sterols, flavonoid, glycosides, and tannins are present [79].

In another study, aqueous flower extract at 500 mg/kg dosage had the best gastroprotective activity against pylorus ligation, aspirin, and ethanol induced ulceritis models in albino Wister rats, resulting in protection percentages of 81.85%, 73.7%, and 76.8%, respectively, whereas 8 mg/kg lansoprazole treated group (positive control) resulted in 84.99%, 80.10%, and 78.12% protection percentages, correspondingly [80]. This is highly attributed to free radical scavenging activity of tannins and flavonoids present in flower extract [80].

Anti-pyritic activity

The antipyretic effects of 250 mg/kg *H. rosa sinensis* aqueous root extract was investigated using yeast-induced pyrexia in albino Swiss rats. After 3 hours and a half, the extract reduced the rectal temperature from 39.0 ± 0.145 to 37.5 ± 0.25 ºC, whereas treatment with 30 mg/kg b.w paracetamol as positive control maintained it as 37 ºC [81]. The extract analgesic potentials were also examined at the same dosage using tail flicking test. The treatment increased reaction time as compared to 45 mg/kg b.w. diclofenac sodium treated and control groups, meaning that it weakened pain response [81]. Similarly, 500 mg/kg b.w of aqueous leaf extract managed to lower mice rectal temperature by 1.55 ºC, 5 hours after extract consumption, compared to 2.00 ºC using 10 mg/kg b.w acetaminophen as positive control [82].

Antihyperlipidemic activity

Oral administrations of *H. rosa-sinensis* Linn flowers ethanolic extract at 500 mg/kg b.w dosage were evaluated using 400 mg/kg triton and atherogenic diet induced hyperlipidemia in albino Wistar rats. After 48 hours, the extract has managed to lower serum lipid levels to 79.5 ± 1.652 total cholesterol, 80 ± 2.287 triglycerides, 87.16 ± 2.543 phospholipids, 68.16 ± 2.1 LDL, 19.33 ± 1.4 mg/dl VLDL, and increased HDL level to 35 ± 2.3 mg/dl in triton model, compared to negative control and 10 mg/kg simvastatin positive control values significantly [83].

In atherogenic diet induced model, the ethanolic extract reduced serum lipid levels after 14 days to 70 ± 2.854 total cholesterol, 68.66 ± 1.240 triglycerides, 71 ± 3.287 phospholipids, 45 ± 2.606 LDL, 35 ± 1.141 mg/dl VLDL, and increased HDL level to 29.16 ± 2.365 mg/dl significantly in comparison to all control groups [83].

Hepatoprotective effects

According to a recent study, *Hibiscus rosa-sinensis* ethanolic leaf extracts ameliorated piroxicam (6.6 mg/kg b.w.) induced liver toxicity in Swiss albino mice. After oral treatment with 30 mg/kg b.w. of extract for 15 days, alanine transaminase, aspartate transaminase, and alkaline

phosphatase serum activities were reduced to 12.87 ± 0.77, 51.82 ± 2.32, and 73.44 ± 4.32 respectively when compared to piroxicam treated group [84]. The treatment also significantly lowered lipid peroxidation and elevated levels of superoxide dismutase, catalase, and glutathione peroxidase in comparition to piroxicam treated group. This suggests combating hepatic damage induced by oxidative stress [84].

Toxicity

The Sprague Dawley male rats were subjected to 14 days oral administration of ethanol flower and leaf extracts of *H. rosa sinensis* up to dosage of 500 mg/kg. The histological studies showed that regardless the extract type or the flower morphotype (red and white); there were no toxicological effects on the liver that could have lead to hepatic injury [74].

In Balb/c mice bone marrow blood cells, treatment with 400 mg/kg of methanolic flower extract showed similar micronuclei frequency to negative control group suggesting no genotoxicity [85]. In cyclophosphamid (20 mg/Kg) induced DNA damage, using the same dosage reduced the number of micronucleated polychromatic erythrocyte by 67.80%. However, 1600 mg/kg dose resulted in 20% mortality [85].

It was reported that 500 mg/ml of *H. rosa sinensis* powder given orally with water for one month, histologically did not produce any signs of toxicity in livers of Swiss albino mice compared to control groups [86]. Similarly, subjecting mice orally with 2000 mg/kg of leaves methanol extract did not cause mortality or show any signs of toxicity during 14 days of observation [87]. The experiment however showed that administration of 800 mg/kg dose increased levels of alanine aminotransferase, aspartate aminotransferase, total bilirubin, urea and creatinine significantly. The histopathogy of kidneys and liver was also altered showing tubules and glomeruli disorganization, dilated sinusoids and inflamed sinusoidal capillaries, and apoptotic nuclei [87].

CONCLUSION

Hibiscus rosa sinensis , which belongs to *Malvaceae* family, has been widely used as a traditional remedial plant in China and several tropical countries. All of its parts have been used in the treatment of fever, inflammation, bacterial infections, and even as contraceptive agent. Flavonoids, tannins, terpenoids, saponins, and alkaloids are the main phytochemicals as they are present in different extracts, and are more likely responsible for their biological activities. Lower toxicity of this plant can be an advantage to qualify it to be used as new therapeutic agent.

This review has presented a comprehensive summary of recent studies on the phytochemistry and the medicinal uses of *H. rosa sinensis* . In some areas, the research is very limited and therfore further studies must be carried out to explore the phytochemicals mechanism of action such as anti-cancer activity. However, these biological compounds must be first isolated and identified successfully. Moreover, clinical trials on the toxicity of this plant and its pharmocological effects must be carried out to assess its safe application and desirable side effects.

REFERENCES

1. Braglia L, Bruna S, Lanteri S, Mercuri A, Portis E. An AFLP-based assessment of the genetic diversity within *Hibiscus rosa-sinensis* and its place within the Hibiscus genus complex. Scientia Horticulturae. 2010;123(3):372–378.
2. Melzer MJ, Simbajon N, Carillo J, Borth WB, Freitas-Astúa J, Kitajima EW, et al. A cilevirus infects ornamental hibiscus in Hawaii. Archives of Virology. 2013;158(11):2421–2424.
3. Reddy UK, Rajesh S, Sindhu G, Aruna B. Herbs used in formulating poly herbal hair oil – a review. Indo American Journal of Pharmaceutical Research. 2017;4(6):1527–1539.
4. Kumari OS, Rao NB, Reddy VK. Phyto-chemical analysis and anti-microbial activity of *Hibiscus rosa-sinensis* . World Journal of Pharmacy and Pharmaceutical Sciences. 2015;4(5):766–771.
5. Gomare KS, Mishra DN. FTIR spectroscopic analysis of phytochemical extracts from *Hibiscus rosa–sinensis* L. used for hair disorder. International Journal of Recent Trends in Science and Technology. 2018;70–75.
6. Vastrad JV, Byadgi SA. Phytochemical screening and antibacterial activity of *Hibiscus rosa - sinensis* leaf extracts. International Journal of Current Microbiology and Applied Sciences. 2018;7(3):3329–3337.
7. Zubairi SI, Jaies NS. *Hibiscus rosa sinensis* leaves: Analysis of proximate, antioxidant activities and inorganic compound. Malaysian Journal of Analytical Sciences. 2014;18(2):260-270.
8. Mak YW, Chuah LO, Ahmad R, Bhat R. Antioxidant and antibacterial activities of Hibiscus (*Hibiscus rosa-sinensis* L.) and Cassia (Senna bicapsularis L.) flower extracts. Journal of King Saud University - Science. 2013;25(4):275–282.
9. Bhakta S, Das SK. A review on *Hibiscus rosa sinensis* : a rural traditional medicine for contraception. International Journal of Engineering and Information Systems. 2017;1(9):77–79.
10. Udo IJ, Ben MG, Etuk CU, Tiomthy AI. Phytochemical, proximate and antibacterial properties of *Hibiscus rosa-sinensis* L. Leaf. Journal of Medicinal Plants Studies . 2016;4(5):193–195.
11. Pekamwar SS, Kalyankar TM, Jadhav AC. *Hibiscus rosa-sinensis* : a review on ornamental plant. World Journal of Pharmacy and Pharmaceutical Sciences. 2013;2(6):4719–4727.
12. Noman A, Aqeel M, Javed MT, Zafar S, Ali Q, Islam W, et al. Histological changes in *Hibiscus rosa-sinensis* endorse acclimation and phytoremediation of industrially polluted sites. The Journal of Animal & Plant Sciences. 2017;27(5):1637–1648.
13. El Sayed ZI, Ateya A-MM, Fekry M. Macro- and micromorphological study of the leaf, stem, flower and root of *Hibiscus rosa-sinensis* l . Journal of Applied Sciences Research. 2012;8(1):34–56.
14. Begum Z, Younus I, Ali SM. Anti-inflammatory, analgesic and anti-pyretic activities of *Hibiscus rosa sinensis* linn and phytochemicals. World Journal of Pharmacy and Pharmaceutical Sciences. 2015;4(12):116–123.
15. Hammad I. Genetic Variation among *Hibiscus rosa-sinensis* (Malvaceae) of Different Flower Colors Using Issr and Isozymes. Australian Journal of Basic and Applied Sciences. 2009;3(1):113–125.
16. Kadve S, Yadav M, Tiwari A. Genetic Analysis on Hibiscus Species by using Rapd Markers. International Journal of Biomedical and Advance Research. 2012;3(6):473–485.
17. San Pascual AO, Magdalita PM, Medina NG, Apacionado BV. Characterization, pollen behavior and propagation of five selected Hibiscus hybrids (*Hibiscus rosa-sinensis* Linn.). Australian Journal of Crop Science. 2017;11(12):1508–1519.
18. Kumar A, Singh A. Review on *Hibiscus rosa sinensis* . International Journal of Research in Pharmaceutical and Biomedical Sciences. 2012;3(2):534–538.
19. Salem MZM, Olivares-Pérez J, Salem AZM. Studies on biological activities and phytochemicals composition of Hibiscus species- A review. Life Science Journal . 2014;11(5):1–8.
20. Patel S, Adhav M. Comparative phytochemical screening of ethanolic extracts (flower and leaf) of morphotypes of *Hibiscus rosa- sinensis* Linn. Journal of Pharmacognosy and Phytochemistry. 2016;5(3):93–95.
21. Patel S, Adhav M. Thin layer chromatographic analysis for various phytochemical constituents in the ethanolic flower extracts of morphotypes of *Hibiscus rosa-sinensis* Linn. European Journal of Biotechnology and Bioscience. 2016;4(7):13–17.
22. Jadhav VM, Thorat RM, Kadam VJ, Sathe NS. *Hibiscus rosa sinensis* Linn – ''Rudrapuspa'': A Review. Journal of Pharmacy Research . 2009;2(7):1168–1173.
23. Rassem HHA, Nour AH, Yunus RM. GC-MS analysis of bioactive constituents of Hibiscus flower. Australian Journal of Basic and Applied Sciences. 2017;5(3):91–97.
24. Anand A, Sarkar B. Phytochemical screening and antioxidant property of anthocyanins extracts from *Hibiscus rosa-sinensis* . Applications of Biotechnology for Sustainable Development. 2017;139–147.

25. Vankar PS, Shukla D. Natural dyeing with anthocyanins from *Hibiscus rosa sinensis* flowers. Journal of Applied Polymer Science. 2011;122(5):3361–3368.
26. Senathirajah T, Rasalingam S, Ganeshalingam S. Extraction of the Cyanidin-3-Sophoroside from *Hibiscus rosa-Sinensis* : An Efficient Natural Indicator over a Wide Range of Acid-Base Titrations. Journal of Natural Product and Plant Resources. 2017;7(3):1–7.
27. Hemarana K, Jeyashree KV, Babu M, Kannan M. Preliminary bioactive compounds screening and antibacterial activity of methanolic extract of *Hibiscus rosa sinensis* against selected skin pathogens. . Research Journal of Pharmaceutical, Biological and Chemical Sciences. 2014;5(2):1210–1218.
28. Udo IJ, Ben MG, Etuk CU, Tiomthy AI. Phytochemical, proximate and antibacterial properties of *Hibiscus rosa-Sinensis* L. Leaf. Journal of Medicinal Plants Studies. 2016;4(5):193–195.
29. Agarwal S, Prakash R. Evaluation of antibacterial activity of *Hibiscus rosa-sinensis* flower extract against E. coli and B. subtillis. Biological Forum – An International Journal. 2014;6(2):194–196.
30. Tiwari U, Yadav P, Nigam D. Study on phytochemical screening and antibacterial potential of methanolic flower and leaf extracts of *Hibiscus rosa sinensis* . International Journal of Innovative and Applied Research. 2015;3(6):9–14.
31. Ruban P, Gajalakshmi K. In vitro antibacterial activity of *Hibiscus rosa-sinensis* flower extract against human pathogens. Asian Pacific Journal of Tropical Biomedicine. 2012;2(5):399–403.
32. Kumari OS, Rao NB, Reddy VK. Phyto-chemical analysis and anti-microbial activity of *Hibiscus rosa-sinensis* . World Journal of Pharmacy and Pharmaceutical Sciences. 2015;4(5):766–771.
33. Sobhy EA, Abd Elaleem KG, Abd Elaleem HG. Potential antibacterial activity of *Hibiscus rosa sinensis* linn flowers extracts. International Journal of Current Microbiology and Applied Sciences . 2017;6(4): 1066–1072 .
34. Sanjesh R, Kanu P, Vaidhun B. Isolation of herbal plants: antifungal and antibacterial activities. Journal of Pharmaceutical Science and Bioscientific Research. 2012;2(1):25–29.
35. Nilima W, Deepavali S. Antifungal activity of selected plant extracts against important seed borne fungi of maize. International Journal of Pharma and Bio Sciences. 2013;4(3):163–170.
36. Ghosh A, Dutta A. GC-MS analysis and study of potential antioxidant activity of the crude ethanolic flower extract of *Hibiscus rosa sinensis* L (wild variety) by hydrogen peroxide scavenging assay. International Journal of Current Trends in Science and Technology. 2017;7(11):20405–20410.
37. Khan ZA, Naqvi SAR, Mukhta A, Hussain Z, Shahzad SA. Antioxidant and antibacterial activities of *Hibiscus rosa-sinensis* Linn flower extracts. Pakistan Journal of Pharmaceutical Sciences. 2014;27(3):469–474.
38. Garg D, Shaikh A, Muley A, Marar T. In-vitro antioxidant activity and phytochemical analysis in extracts of *Hibiscus rosa-sinensis* stem and leaves. Free Radicals and Antioxidants. 2012;2(3):41–46.
39. Johnson S, Abdul Razack S, Sellaperumal P, Ramakrishnan G, Jayakrishnan P. Antioxidant activity of iron isolated from petals of *Hibiscus rosa sinensis* . EC Microbiology. 2017;7(1):14–20.
40. Prasanna R. Evaluation of antioxidant activity of phenol, *Hibiscus rosa sinensis* , neem and leaves extract at different infusion times. International Journal of Advance Research, Ideas and Innovations in Technology. 2017;3(1):281–286.
41. Prasad MP. In vitro Phytochemical Analysis and Antioxidant Studies of Hibiscus Species. International Journal of Pure & Applied Bioscience. 2014;2(3): 83–88.
42. Abdel Ghaffar FR, El-Elaimy IA. In vitro, antioxidant and scavenging activities of *Hibiscus rosa sinensis* crude extract. Journal of Applied Pharmaceutical Science. 2012;2(1):51–58.
43. Hinaz N, Gayathri R, Priya VV. Genotoxicity of *Hibiscus rosa sinensis* on oral cancer cell line. International Journal of Pharmaceutical Sciences Review and Research. 2017;44(1):21–23.
44. Divya MJ, Sowmia C, Dhanya KP, Joona K. Screening of antioxidant, anticancer activity and phytochemicals in methanolic extract of *Hibiscus rosa-sinensis* leaf extract. Research Journal of Pharmaceutical, Biological and Chemical Sciences . 2013;4(2):1308–1316.
45. Durga R, Kumar PS, Hameed SAS, Dheeba B, Saravanan R. Evaluation of in-vitro anticancer activity of *Hibiscus rosa sinensis* against hela cell line. Journal of Global Pharma Technology. 2018;10(1):1–10.
46. Arullappan S, Muhamad S, Zakaria Z. Cytotoxic activity of the leaf and stem extracts of *Hibiscus rosa sinensis* (malvaceae) against leukaemic cell line (k-562). Tropical Journal of Pharmaceutical Research. 2013;12(5):743–746.
47. Basha DP, Ravishankar K, Kiranmayi GVN, Subbarao M. Antitumour activity of *Hibiscus rosa*-Senensis. World Journal of Pharmacy and Pharmaceutical Sciences. 2013;2(6):4987–4996.
48. Goldberg KH, Yin AC, Mupparapu A, Retzbach EP, Retzbach EP, Goldberg GS, et al. Components in aqueous *Hibiscus rosa-sinensis* flower extract inhibit in vitro melanoma cell growth. Journal of Traditional and Complementary Medicine. 2017;7(1):45–49.
49. Moqbel F, Naik PR, Najma HM, Selvaraj S. Antidiabetic properties of *Hibiscus rosa sinensis* L. leaf extract fractions on nonobese diabetic (NOD) mouse. Indian journal of experimental biology. 2011;49(1):24–29.
50. Kumar V, Mahdi F, Khanna AK, Singh R, Chander R, Saxena JK, et al. Antidyslipidemic and antioxidant activities of *Hibiscus rosa sinensis* root extract in alloxan induced diabetic rats. Indian Journal of Clinical Biochemistry. 2013;28(1):46–50.
51. Al Mamun, Islam S, Alam K, Abdur Rahman A, Rashid M. Effects of ethanolic extract of *Hibiscus rosa-sinensis* leaves on alloxan-induced diabetes with dyslipidemia in rats. Bangladesh Pharmaceutical Journal. 2013;16(1):27–31.
52. Zaki LH, Mohamed SM, Bashandy SAE, Morsy FA, Tawfik KM, Shahat AA. Hypoglycemic and antioxidant effects of *Hibiscus rosa sinensis* L. leaves extract on liver and kidney damage in streptozotocin induced diabetic rats. African Journal of Pharmacy and Pharmacology. 2017;11(13):161–169.
53. Ghosh A, Dutta A. Antidiabetic effects of ethanolic flower extract of *Hibiscus rosa sinensis* (L) on alloxan induced diabetes in hyperlipidaemic experimental Wister rats (WNIN). International Journal of Engineering Development and Research. 2017;5(4):674–679.
54. Afiune LAF, Leal-Silva T, Sinzato YK, Moraes-Souza RQ, Soares TS, Campos KE, et al. Beneficial effects of *Hibiscus rosa-sinensis* L. flower aqueous extract in pregnant rats with diabetes. PLoS One. 2017;12(6):1–13.
55. Pethe M, Yelwatkar S, Gujar V, Varma S, Manchalwar S. Antidiabetic, hypolipidimic and antioxidant activities of *Hibiscus rosa sinensis* flower extract in alloxan induced diabetes in rabbits. International Journal of Biomedical and Advance Research. 2017;8(4):138–143.
56. Sharma K, Pareek A, Chauhan ES. Evaluation of hyperglycemic and hyperlipidemic mitigating impact of *Hibiscus rosa sinensis* (gudhal) flower in type ii diabetes mellitus subjects. International Journal of Applied Biology and Pharmaceutical Technology. 2016;7(2):223–228.
57. Salib JY, Daniel EN, Hifnawy MS, Azzam SM, Shaheed IB, Abdel-Latif SM. Polyphenolic compounds from flowers of *Hibiscus rosa-sinensis* linn. And their inhibitory effect on alkaline phosphatase enzyme activity in vitro. Zeitschrift für Naturforschung Journal of Biosciences. 2014;66(9-10):453–459.
58. Jana TK, Ray DS, Mandal D, Giri JS, Bhattacharya J. Study of the effects of Hibiscus-rosa-*sinensis* flower extract on the spermatogenesis of male albino rats. Journal of Physiology and Pharmacology Advances. 2013;3 (6):168–171.
59. Hadimur K, Sarashetti RS, Lone ND, Kanthi VG, Patil N. Anti implantation and pregnancy interruption activity of japakusuma (*Hibiscus rosa sinensis*) in albino rats. International Journal of Research in Ayurveda and Pharmacy. 2013;4(3):387–389.
60. Kumari M S, Kadam S, Mundugaru R, Bhat S. Anti fertility activity of japakusumadi yoga in female wistar albino rats. International Ayurvedic Medical Journal. 2018;2(2):928–933.
61. Pathan A, Pathan M, Garud A. Effect of *Hibiscus rosa sinensis* , calotropis gigantea and polyherbal formulation on stress induced alopecia. International Journal Of Pharmaceutical Innovations. 2012;2(6):20–29.
62. Singh N, Tailang M, Pathak AK. Evaluation of hair growth activity of *Hibiscus rosa-sinensis* and calotropis gigantea leaves on stress induced alopecia. World Journal of Pharmaceutical Research. 2017;6(17):477–484.
63. Agrawal A, Pal VK, Sharma S, Gupta A, Irchhiaya R. Phytochemical investigation and hair growth promoting activity of *Hibiscus rosa-sinensis* leaf extract. Journal of Chronotherapy and Drug Delivery. 2016;7(1):31–39.

64. Pathak SS, Gala MYN. Evaluation of hair growth potentiation activity of *Hibiscus rosa sinensis* in disturbed circadian rhythm. International journal of current research. 2018;10(3):67151–67155.
65. Agrawal KK, Singh K. Hair growth activity of aqueous extract of *Hibiscus rosa-sinensis* l. flowers. Indian Journal of Drugs. 2017;5(4):142–149.
66. Nade VS, Kawale LA, Dwivedi S, Yadav AV. Neuropharmacological evaluation of *Hibiscus rosa sinensis* roots in experimental animals. Journal of Natural Remedies. 2009;9(2):142–51.
67. Nade VS, Kawale LA, Dwivedi S, Yadav AV. Neuroprotective effect of *Hibiscus rosa sinensis* in an oxidative stress model of cerebral postischemic reperfusion injury in rats. Pharmaceutical Biology. 2010;48(7):822–7.
68. Hanumakonda A, Maheshwaram V. Neuroprotective activity of *Hibiscus rosa*-sinesis flowers in scopolamine induced cognitive decline rats. International Journal of Pharmacy Review & Research. 2016;6(1):15–21.
69. Begum Z, Younus I, Khan H, Ali SM. Ethanolic crude extract of roots of *Hibiscus rosa sinensis* ameliorates depression like behaviour in animal models. Advances in Biological Research. 2016;10(3):132–137.
70. Nayak BS, Raju SS, Orette FA, Rao AVC. Effects of *Hibiscus rosa sinensis* l (malvaceae) on wound healing activity: a preclinical study in a sprague dawley rat. The International Journal of Lower Extremity Wounds. 2007;6(2): 76–81.
71. Ali AA, Jusoh NH, Saridin N, Wahab MSA, Zohdi RM. Evaluation of *Hibiscus rosa-sinensis* leaves extracts as wound healing promoter on rats. In IECBES 2014, Conference Proceedings - 2014 IEEE Conference on Biomedical Engineering and Sciences: "Miri, Where Engineering in Medicine and Biology and Humanity Meet". Institute of Electrical and Electronics Engineers Inc.2015. p. 352-355. 7047519. Available from, DOI: 10.1109/IECBES.2014.7047519
72. Mondal S, Ghosh D, Sagar N, Ganapaty S. Evaluation of antioxidant, toxicological and wound healing properties of *Hibiscus rosa-sinensis* l. (malvaceae) ethanolic leaves extract on different experimental animal models. Indian Journal of Pharmaceutical Education and Research. 2016;50(4):620–637.
73. Kandhare AD, Raygude KS, Ghosh P, Ghule AE, Gosavi TP, Badole SL, et al. Effect of hydroalcoholic extract of *Hibiscus rosa sinensis* Linn. leaves in experimental colitis in rats. Asian Pacific Journal of Tropical Biomedicine. 2012;2(5):337–344.
74. Raduan SZ, Abdul Aziz MWH, Roslida AH, Zakaria ZA, Zuraini A, Hakim MN. Anti-inflammatory effects of *Hibiscus rosa-sinensis* l. and *Hibiscus rosa-sinensis* var. Alba ethanol extracts. International Journal of Pharmacy and Pharmaceutical Sciences. 2013;5(4): 754–762.
75. Mishra N, Tandon VL, Gupta R. Immunomodulation by *Hibiscus rosa-sinensis* : effect on the humoral and cellular immune response of Mus musculus. Pakistan Journal of Biological Sciences. 2012;15(6):277–283.
76. Desai SK, Mulgaonkar SS, Pandey CH. Comparative study of immunomodulatory and adaptogenic activity of *Hibiscus rosa sinensis* extracts in rats. International Journal of Pharmacy and Pharmaceutical Sciences. 2013;5(2):101–103.
77. Imafidon KE, Okunrobo LO. The effects of aqueous extracts of the leaves of *Hibiscus rosa-sinensis* Linn. on renal function in hypertensive rats . African Journal of Biochemistry Research. 2010;4(2):43–46.
78. Khandelwa VKM, Balaraman R, Pancza D, Ravingerová T. Hemidesmus indicus and *Hibiscus rosa-sinensis* affect ischemia reperfusion injury in isolated rat hearts. Evidence-Based Complementary and Alternative Medicine. 2011;2011(1):1–8.
79. Mandade RJ, Sreenivas SA, Sakarkar DM, Choudhury A. Pharmacological effects of aqueous-ethanolic extract of *Hibiscus rosa sinensis* on volume and acidity of stimulated gastric secretion . Asian Pacific Journal of Tropical Medicine. 2011;4(11):883–888.
80. Kumar PK, Annapurna A, Ramya G, Sheba D, Krishna G, Sudeepthi L. Gastroprotective effect of flower extracts of *Hibiscus rosa sinensis* against acute gastric lesion models in rodents. Journal of Pharmacognosy and Phytochemistry. 2014;3(3): 137–145.
81. Soni D, Gupta A. An evaluation of antipyretic and analgesic potentials of aqueous root extract of *Hibiscus rosa sinesis* Linn. (malvacae). International Journal of Research in Phytochemistry & Pharmacology. 2011;1(3):184–186.
82. Daud D, Arsad NFM, Ismail A, Tawang A. Anti-pyretic action of Caulerpa lentillifera, *Hibiscus rosa-sinensis* , and Piper sarmentosum aqueous extract in mice. Asian Journal of Pharmaceutical and Clinical Research. 2016;9(1):145-147.
83. Sikarwar MS, Patil MB. Antihyperlipidemic activity of *Hibiscus rosa sinensis* Linn. ethanolic extract fractions. International Journal of Health & Allied Sciences. 2015;4(2):73–78.
84. Sahu CR. Mechanisms involved in toxicity of liver caused by piroxicam in mice and protective effects of leaf extract of *Hibiscus rosa-sinensis* l. Clinical Medicine Insights: Arthritis and Musculoskeletal Disorders. 2016;9(1):9–13.
85. Meena AK, Jain A, Pandey K, Singh RK. Acute toxicity and genotoxic activity of *Hibiscus rosa sinensis* flower extract. American Journal of Phytomedicine and Clinical Therapeutics. 2014;2(4):524–529.
86. Bhakta S, Das SK. Effect of *Hibiscus rosa sinensis* on the liver of Swiss albino mice: a histo-morphological investigation. Progressive Agriculture. 2016;27(3):296–300.
87. Nath P, Yadav AK. Acute and sub-acute oral toxicity assessment of the methanolic extract from leaves of *Hibiscus rosa-sinensis* L. in mice. Journal of Intercultural Ethnopharmacology. 2014;4(1):70–73.

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