

The Review on Medicinal Uses of Hibiscus Flower

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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, inflammation, fever and coughs, diabetes, infections caused by bacteria and fungi, hair loss, and gastric ulcers in several tropical countries. The phytochemical analysis documented that the main bioactive compounds responsible for its medicinal effects are namely flavonoids, tannins, terpenoids, saponins, and alkaloiExperiments from recent studies showed that various types of extracts from all H. rSinensis 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, pharmacology, 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 rosasinensis, 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-blackening [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 insufficient 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 medicinal applications.

Classification: *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 veins, and its seeds contain two cotyledons [11]. Moreover, it is classified in the the order 'Malvales' 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. rosasinensis* 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]

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 chlorides, quercetin can be found in all parts of *Hibiscus rosa sinensis*. However, β -sitosterol, teraxeryl acetate, and malvalic acids can be found only in stems and leaves [22].

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 components were responsible for the observed antioxidant activity [23]. Although most of these phytochemicals have future potential medicinal uses, which will be more discussed in the next section, anthocyanins have special natural dyeing properties [24]. 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 [24]. This is could be mainly due to its antioxidant activity mentioned earlier.

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 [25]. These microorganisms were obtained from infected skins, and the chemical compounds responsible for the antibacterial activity may be due to flavonoids, tannins, terpenoids, saponins, or alkaloids identified in the study [25]. In another study conducted using disc diffusion method, aqueous 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 glycosides, anthraquinones, and phlobatanins, including those mentioned earlier [26]. Interestingly, another research reported similar results as the aqueous extracts showed a maximum zone of inhibition against *B. subtilis* 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. subtilis* as 19.86 ± 0.15 mm, and *E. coli* as 18.00 ± 1.53 mm [27]. 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 [27]. Antibacterial activity has been also observed using disc diffusion method against *E. coli* and *S. aureus* at different concentrations of methanolic flower and leaf extracts varying from 31.25 to 500 mg/ml. These were compared with positive control gentamicin (1 mg/ml) and methanol as negative control [28]. 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 [29]. 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 [29].

The cold aqueous extractions of flowers gave highest zones of inhibition against *B. subtilis* 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 [30]. The methanol extracts showed highest zones of inhibition against *B. subtilis* as 18.86 ± 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 [30]. The antibacterial activities of both pure and crude proteins 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 acrylamide gel electrophoresis (PAGE), which resulted in various bands for the crude protein sample [30]. 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 [30].

The antibacterial activity of root extracts 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 $7.5 \mu\text{g/ml}$ [31]. 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 $10\mu\text{g}$ of Chloramphenicol which was used as a positive control and resulted in a zone of inhibition of approximately 24 mm [32].

Compared to other extracts such as ethyl acetate extract, ethanol extract, and water extract, all phytochemicals that were involved in the antimicrobial activity were detected from the methanol extract. This suggests that it is a useful extract for further research [32]. 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.

Antioxidant activity

Ethanollic (95.0%) extract of flowers strongly scavenged hydrogen peroxide for 96 ± 2.35 % inhibition with a concentration of $50 \mu\text{g/ml}$ while the standard antioxidant, ascorbic acid produced 76.33 ± 1.25 % radical scavenging activity at $100 \mu\text{g/ml}$ 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 [33]. 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 [33].

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 scavenging activity than ethanolic extract, this strongly suggest that they are responsible for the anti-oxidant activity [34].

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 [35].

In addition, water extracts of petals scavenged 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 [36].

Similarly, aqueous extracts 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 scavenging activity [37]. 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 [38]

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 % scavenging activity against hydrogen peroxide, and 36.3 ± 2.47 % against nitric oxide, all using a concentration of 500 μ g/ml. The 200 μ g/ml of BHA gave the following scavenging activities: 61.6 ± 3.15 %, 65.8 ± 2.21 %, and 37.3 ± 3.6 % respectively [39]. 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 μ g/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 [39]. 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 [39].

Anti-cancer activity

Oral cancer cell lines KB (ATCC CCL-17) were treated with 75 μ g and 125 μ g 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 [40]. It was also shown that 250 μ g of 90% methanolic leaves extract inhibited HT-29

colorectal AGS cell lines by 100%. The cell viability percentage was measured using MTT assay and the calculated IC₅₀ 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 [41]. Acetone extracts of *H. rosa sinensis* flowers effect on HeLa cell lines viability was investigated. Using MTT assay, it was found that at a concentration 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 [41].

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 [41]. The tested extracts also reduced levels of triglycerides, blood urea, glycosylated hemoglobin, and cholesterol significantly after 5 weeks of oral administration [41]. In alloxan induced diabetic type II rats (150 mg/kg), root extracts of 500 mg/kg of bw concentration decreased 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 [42].

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.

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