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EXPLORING THE MEDICINAL PROPERTIES OF ROSELLE (HIBISCUS SABDARIFFA) PLANT

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Abstract:
The Roselle plant (Hibiscus sabdariffa L.), a member of the Malvaceae family, is an important medicinal herb widely cultivated in tropical and subtropical regions. It has been traditionally utilized in various indsigenous systems of medicine for its therapeutic potential and nutritional value. The plant, particularly its calyces, is a rich source of anthocyanins, flavonoids, phenolic acids, and organic acids, which contribute to its wide range of pharmacological properties. Numerous studies have demonstrated that extracts of H. sabdariffa exhibit strong antioxidant, antihypertensive, hypolipidemic, hepatoprotective, antidiabetic, antimicrobial, and anticancer activities. The potent antioxidant activity of Roselle is primarily attributed to its high anthocyanin and polyphenol content, which help in neutralizing reactive oxygen species and preventing oxidative stress–related cellular damage. Its antihypertensive and lipid-lowering effects have been linked to improved cardiovascular health, while hepatoprotective and nephroprotective activities suggest its potential in managing metabolic disorders. Moreover, the plant shows promising antimicrobial and anti-inflammatory effects, making it beneficial for treating infections and inflammatory diseases. Recent pharmacological and toxicological studies support the safety and efficacy of Roselle extracts, encouraging their inclusion in functional foods, herbal formulations, and nutraceuticals. However, variations in chemical composition due to geographic, climatic, and extraction factors underline the necessity for further standardization and clinical evaluation. This review explores the medicinal significance of H. sabdariffa, summarizing its phytochemical constituents, pharmacological mechanisms, and therapeutic potential. Overall, Roselle stands as a promising natural resource with multifaceted health benefits and considerable potential for pharmaceutical and nutraceutical applications.

Keywords: Hibiscus sabdariffa, Roselle, phytoconstituents, antioxidant, antihypertensive, hepatoprotective, pharmacological potential**.**

Introduction:

Roselle (Hibiscus sabdariffa L.) is a member of Malvaceae family, or "karkade", a significant annual crop widely cultivated under tropical and sub-tropical conditions [1]. The economically valuable component of the crop is fleshy calyx (sepals) that encloses the fruit (capsules). The entire plant is used as drink, or the dried calyces may be soaked in water to make a bright colored cold drink, or can be boiled in water and consumed as hot drink. It also possesses some medicinal value [2]. The seeds have 17.8–21% non-edible oil [3] and 20% protein, and are occasionally used as animal feed [4]. Roselle is an adaptable plant with various use It is planted intercropped with crop crops like sorghum and sesame, or seeded along field boundaries. It is low-maintenance. Leaves, seeds, capsules and stems of the plant are employed in traditional medicine [5]. The plant grows in nearly all the warm nations like India, Saudi Arabia, Malaysia, Indonesia, Thailand, Philippines, Vietnam, Sudan, Egypt and Mexico [6,7]. Roselle is largely grown to be eaten and the primary producers of Roselle flowers are Egypt, Sudan, Mexico, Thailand and China. Other hibiscus species are grown for their fibers they yield [8]. Hibiscus sabdariffa is often referred to as "red sorrel" or "roselle". Although the ideal soil is permeable, Roselle can survive on a range of soil in a warmer and more humid environment [9,10] Hibiscus comprises over three hundred species that are spread across the tropical and subtropical areas of the globe and find use as ornamental plants [11]. In some nations,

Roselle is also ranked among the most renowned folk medicinal herbs. Where, numerous chemical constituents found in Roselle possess possible health value and attest the ethno medicinal application of Roselle towards improving cardio-vascular fitness and prevention of hypertension, pyrexia and liver diseases, restriction of microorganism development, and as a diuretic, digestive and sedative. Antioxidant and cyclooxygenase inhibitory activities are present in red type of Roselle. Furthermore, Roselle inters find applications in pharmaceutical and cosmetic industries [12]. It is widely used to produce jelly, jam, juice, wine, syrup, gelatin, pudding, cake, ice cream and flavorings. The bright red color and distinctive flavor make it a premium food material [13]. Roselle seeds, which presently do not possess any commercial uses, contain a vegetable oil that is low cholesterol and having other phytosterols and tocopherols, more importantly β-sistosterol and γ-tocopherol. The world nature of roselle seed oil makes such oil very important in industrial use. Its characteristics provide an added value to this plant's culture [14]. The roselle flower's fleshy calyces (sepals) possess a nice acid flavor and extremely appealing red color, for which roselle is cultivated as a beverage crop in most nations. The drink beverage is referred to in Egypt as Karkadi and suggested as a mild laxative as acidulous drink. The red color is attributed to anthocyanins, while the acid flavor is a result of the presence of certain organic acids. Sepals acidity can also be the reason for their color variation. The darkest red color type contains the most content of anthocyanins, with the light red color type second, while the green color type contains no or only traces of anthocyanins [15]. Most chemical constituents in roselle possess possible health values and defend against ethnomedicinal use of roselle to enhance cardiovascular health and avoid hypertension [16]. The red types of roselle contained more total antioxidant and cyclooxygenase inhibitory activity than the white type, and thus they would also have greater health benefits. The white type can however also be utilized in antihypertensive uses, as its ethyl acetate extract possessed comparable cyclooxygenase inhibitory activity to aspirin and Ibuprofen [1]. However, more in vivo work needs to be done to validate the precise health benefits involved in the biological system, prior to enhanced intake of any of the three types of roselle being suggested [16]. The calyx is the most critical component of the plant. It holds the useful materials which decide the quality of the product namely: colour (anthocyanins), flavour (organic acid) and aroma. The acid calices of red succulent variety sabdariffa are used to make sorrel drink. They are also utilized to prepare jellies and preservetives. The young leaves and stalks are used as a salad and also as a pot - herb. Variety altissima is cultivated for fibre in India, Java and Phillipines. The root has been cited as an aperient owing to the presence of tartaric acid [17]. While as acidic as the calices, they are also counted as antiscorbutic components and is stated to relieve caugh [18]. Pharmacological properties of Roselle have been proven and exhibited with its antihypertensive, anti-hyperlipidaemic, anti-inflammatory, antimicrobial, diuretic, uricosuric, and anaemia-curing activities [19]. Roselle has been in traditional use in culinary applications (food, food coloring, and drinks) and as a medicinal remedy for many diseases. For example, in countries like China and Thailand, various components of the Roselle plant (flower, leaves, calyx, and corolla) are widely used as a refreshing drink. The use of chemistry-based drugs is related to intrinsic side effects and particular constraints. On the other hand, the use of herbal products could be an alternative option with a lower rate of side effects, under the condition that their use follows specific dosages and protocols [20]. The review here is to offer a medicinal properties and uses of roselle.

Fig .1. Morphology of Hibiscus Sabdariffa. 1)Leaves 2) Flower 3) Fruit 4) Seeds 5) Red fresh calyces

Table 1: Classification of Hibiscus Sabdariffa [92]

Kingdom	Plantae
Branch	Spermaphytes
Sub-phylums	Angiosperms
Clade	Dicotyledons
Sub-clade	Dialypetals
Series	Thalamiflora
Order	Malvales
Family	Malvaceae
Genus	Hibiscus
Species	Hibiscus sabdariffa L. (1753)

Medicinal use of Roselle:

Roselle is an aromatic, astringent, cooling herb that is widely employed in the Tropics. It is stated to have diuretic action, to reduce fever and is antiscorbutic. The leaves exhibited antiscorbutic, diuretic, emollient, sedative and refrigerant. The leaves has very mucilaginous taste and used as emollient and utilized for cough cure. The fruits exhibited antiscorbutic activity. Flowers contain gossypetin, glycoside hibiscin and anthocyanin. These could have choleretic and diuretic actions, lowering viscosity of the blood, inducing intestinal peristalsis and lowering blood pressure. The leaves and flowers of Roselle are used as a tonic to internal digestion and kidneys. The seeds are diuretic, laxative and tonic too. Those are employed in the treatment of debility. The plant is also antiseptic, astringent, aphrodisiac, cholagogue, digestive, demulcent, purgative and resolvent. Roselle plant is employed as folk remedy in the treatment of abscesses, bilious conditions, cancer, cough, debility, dyspepsia, dysuria, fever, heart disease, scurvy, hypertension, hangover, neurosis, and strangury [21]. The vegetative and fruit component viz. polyphenol and anthocyanin may be held responsible for the decreased risk of cancer [22]. Plants possess the ability

to synthesize secondary metabolites viz. proteins, steroids, alkaloids, etc that increased its nutritive value [23].

Medicinal Properties of Roselle:

Antimicrobial activities:

Roselle is commonly utilized for the management of disease. Olaleye [27] employed the aqueous methanolic extract of Roselle and indicated that the extract was rich in cardiac glycosides, flavonoids, saponins and alkaloids. It had antibacterial activities against Staphylococcus aureus, Bacillus stearothermophilus, Micrococcus luteus, Serratia mascences, Clostridium sporogenes, Escherichia coli, Klebsiella, pneumoniae, Bacillus cereus, Pseudomonas fluorescence. The findings corroborated the employment of Roselle plant in the management of abscesses, bilious disorders, cancer and coughs in traditional medicine, and also recommended for potential isolation of antibacterial and anticancer agents while the antimicrobial effect on Escherichia coli O157:H7.Salmonella enterica and Listeria monocytogenes isolates from food, veterinary, and clinical samples by Fullerton [28] showed that Roselle extract was effective and recommended for use of extracts as food antimicrobials. The antibacterial activities of Roselle calyx aqueous and ethanol extracts and protocatechuic acid against food pathogenic bacteria Salmonella Typhimurium DT104, E. coli O157:H7, Listeria monocytogenes, Staphylococcus aureus and Bacillus cereus were approximated by Chau et al. [29], and demonstrated that the inhibitory activity in dose-dependent pattern against test bacteria in ground beef and apple juice and proposed that it could be potent agents as food additives to avert contamination from such bacteria.

Antioxidant activities:

Roselle-Hibiscus anthocyanins (HAs) which are a series of natural pigments present in the dried calyx demonstrated antioxidant activity and liver protection mode. HA antioxidant bioactivity in rat primary hepatocytes and hepatotoxicity was investigated by [30]. The findings indicated that HA's, at the concentrations of 0.10 mg/ml and 0.20 mg/ml, effectively reduced leakage of lactate dehydrogenase and the production of malondialdehyde and serum concentrations of hepatic enzyme markers (alanine and aspartate aminotransferase) reduced substantially and decreased oxidative liver injury. An antioxidative effect was also described in cancer cell lines [35]. McKay et al. [36], in his animal models, described that extracts of Roselle calyces have exhibited hypok,holesterolemic and antihypertensive activity. Antioxidant activity of three fractions of the ethanol crude extract (HS-C: chloroform soluble fraction; HS-E: ethyl acetate soluble fraction; HS-R: residual fraction) isolated from dried flowers were assessed for their potential to quench free radical and inhibiting xanthine oxidase (XO) activity [37]. HS-E exhibited the highest potential of scavenging free radical, and HS-C exhibited the most effective inhibitory activity on XO activity. In addition, antioxidant bioactivities of crude extracts were tested on rat primary hepatocytes. All fractions were revealed to inhibit markedly the Unscheduled DNA Synthesis (UDS). These results indicated that the flower extracts dried (HS-C and HS-E) safeguard rat hepatocytes against cytotoxicity and genotoxicity by t-BHP. The research on hepatoprotective and antioxidant activities against the Carbon Tetrachloride (CCl_4)-induced hepatocyte damage in fish presented evidence of possible use as a medicine to treat liver diseases in aquaculture as Roselle extract raised substantially levels of Lactate Dehydrogenase (LDH), Glutamate Oxalate Transaminase (GOT), Glutamate Pyruvate transaminase (GPT), and Malondialdehyde (MDA) and low levels of Superoxide Dismutase (SOD) and Glutathione Peroxidase (GSH-Px) [38].

Anticancerous activity:

Akim et al. [35], analyzed the antiproliferative activities of Roselle juice using various cell lines such as ovarian (Caov-3), breast (MCF-7, MDA-MB-231) and cervical (HeLa) cancer cell lines and observed that it contained the highest anti-proliferative potentiality against the MCF-7 cancer cells. With the use of Roselle-anthocyanins (HA), the activities on human cancer cells (HL-60) investigated and demonstrated apoptosis of cells in a time and dose-dependent manner [39]. The anthocyanin induced apoptosis of

leukemia cells was by reactive oxygen species mediated mitochondrial pathways. Protocatechuic Acid (PCA), a phenolic acid isolated from the dried flower, inhibited the survival of human promyelocytic leukemia (HL-60) in a concentration and time dependent manner [37], and apoptosis was induced through inhibition of retinoblastoma phosphorylation and down regulation of Bcl-2 protein expression [40]. The research found that cells were subjected to intranucleosomal DNA fragmentation and morphological alterations typical of apoptosis while the mechanism of action against gastric carcinoma cells by triggering apoptosis was via JNK/MAPK signaling pathways [41]. Methanolic extract of Roselle on seven lines of cancer suggested the AGS cancer cells were most vulnerable in concentration-dependant manner acting upon both the intrinsic and extrinsic apoptotic pathways [42]. Mohamed et al. [43] presented that antioxidant capacity of Roselle (Hibiscus sabdariffa L.) extracts was investigated. Various plant organs, such as seeds, stems, leaves, and sepals, were examined in terms of their water-soluble antioxidant capacity, lipid-soluble antioxidant capacity, and tocopherol content. The Roselle seeds are a rich source of lipidsoluble antioxidants, especially γ-tocopherol. Its seed oil was isolated and characterized, and its physicochemical. The universal properties of Roselle seed oil indicate that it may have significant industrial uses, complementing the customary utilization of Roselle sepals in the preparation of karkade drink.

Pharmacological Activities of Hibiscus sabdariffa (Roselle):

Antihyperlipidemic Actions

There have been studies that have quantified the lipid-lowering activity of Roselle and established its potential to control hyperlipidemia. Aqueous extract of the calyces has been found to have the most potent antihyperlipidemic activity, followed by ethanolic extracts of the leaves [24]. Histopathological examinations show that animals fed on Roselle extracts have lower granular degeneration due to cholesterol feeding [25]. This indicates that polyphenol- and flavanol-rich fractions of the plant play an important role in its antioxidant and antihyperlipidemic activity.

The therapeutic benefits of Roselle were ascribed to its ability to inhibit lipid peroxidation and regulate cholesterol metabolism. Cholesterol-induced hyperlipidemic animal models demonstrated significant decreases in serum total cholesterol, LDL-C, VLDL-C, and triglycerides, and an increase in HDL-C levels after treatment with leaf and calyx extracts. Roselle administration also decreased atherogenic indices and hepatic enzyme levels (SGPT, SGOT, ALP), indicative of better lipid and liver profiles [26]. Overall, these results justify the utilization of Roselle as a potential natural agent in managing hyperlipidemia.

Antihypertensive Actions

The antihypertensive action of Roselle is one of its most widely known pharmacological attributes. Preclinical and clinical evidence has attested to its potency in lowering both systolic and diastolic blood pressure [31]. The intake of hibiscus tea, also referred to as "sour tea," has been described to decrease blood pressure even in the case of diabetic patients with mild or moderate hypertension.

Mechanistically, Roselle's antihypertensive effect is linked to its capacity to inhibit the action of angiotensin-converting enzyme (ACE), induce vasodilation, and increase diuretic action. In addition, anthocyanins in Roselle hinder the oxidation of low-density lipoprotein (LDL), thus enhancing lipid profiles and lowering the risk of atherosclerosis [32]. Other studies indicate that bioactive compounds in the plant induce the release of nitric oxide from the vascular endothelium, leading to enhanced renal function and decreased vascular resistance [33]. Initial studies validated these effects, demonstrating that withdrawal of Roselle tea caused a rebound surge in blood pressure, suggesting its direct and reversible hypotensive action [34].

Antiparasitic Activity

Roselle extracts have exhibited inhibitory activity against various parasitic organisms and hold promise as agents for treating tropical parasitic diseases. Leaf extracts had a significant impact on Brugia malayi

adult worms and microfilariae and this activity is mostly attributed to anthocyanin-glycosides in the butanol fraction [45].
Moreover, in Trypanosoma congolense-infected animal models, Roselle calyx extracts (9.94 mg/100 g/day) hastened hematological recuperation and protected against organ damage due to infection [47,46]. These observations emphasize the potential of Roselle as an exciting phytotherapeutic agent for parasitic infections in both human and veterinary medicine.

Antifungal Activity
The antifungal activity of Roselle has also been investigated against some Candida species. Methanolic fruit extracts with a concentration of 10 mg/mL exhibited inhibitory activity against Candida albicans [48]. In addition, aqueous calyces extract inhibited aflatoxin B_1 production by Aspergillus parasiticus and A. flavus with inhibition rates of 91.5–97.9% and 87.1–93.3%, respectively, without affecting the growth of fungi [49]. This selective antifungal activity makes Roselle a promising bio-control agent for food safety and fungal toxin control.

Anti-inflammatory Activity
The anti-inflammatory potential of Roselle is largely attributed to its high polyphenol content. Methanolic extracts of the petals significantly reduced carrageenan-induced paw edema in rats, producing effects comparable to the standard drug diclofenac [50]. The mechanism involves modulation of cyclooxygenase-2 (COX-2) expression and inhibition of pro-inflammatory transcription factors such as NF-κB, thereby reducing interleukin-1 (IL-1) production [51]. The dual antioxidant and anti-inflammatory properties position Roselle as a natural therapeutic option for inflammation-related diseases.

Antidiabetic activity
Roselle exhibits robust antidiabetic activity via various mechanisms such as glucose control, enhancing lipid metabolism, and inhibiting enzymes. Polyphenolic extracts given to diabetic rat models (200 mg/kg) were found to inhibit hyperglycemia, hyperinsulinemia, lipid peroxidation, and the production of advanced glycation end products [52].
Additionally, Roselle extracts contain inhibitory effects on major carbohydrate-digesting enzymes like pancreatic α-amylase and intestinal α-glucosidase, slowing down glucose absorption and maintaining postprandial blood sugar stability [53]. Ethnopharmacological use of Roselle in diabetes treatment has been confirmed by significant decreases in plasma glucose levels in alloxan-induced diabetic models by ethanolic Roselle extracts [54]. These observations justify the use of Roselle in ethnomedicinal diabetes treatment and justify its use in herbal formulations for glycemic regulation.

Anti-obesity Activity
Management of obesity is yet another promising pharmacological domain in which Roselle proves to be effective. Monosodium glutamate-induced obese mice studies proved that the aqueous extracts of Roselle (33.64 mg anthocyanins/120 mg extract) inhibited body weight gain for 60 days even with increased fluid consumption [55]. Analogously, ethanolic extracts proved beneficial in influencing fat absorption and excretion, which eventually led to lesser body mass [56]. The discovery highlights the potential of Roselle as a natural anti-obesity agent via lipid metabolism modulation and regulation of energy balance.

Antipyretic and Antinociceptive Effect
Roselle calyces have significant antipyretic and analgesic activities. Both ethanolic and aqueous extracts were shown to reduce yeast-induced pyrexia in rat models at doses of 200–800 mg/kg [57]. Acetic acid-induced writhing and xylene-induced edema tests also showed considerable pain relief and anti-inflammatory activities, validating the presence of bioactive phytoconstituents that are involved in the modulation of nociception [58]. This supports the plant's ethnomedical practice of fever and pain relief.

Anticholesterol Effect

Hibiscus sabdariffa has been found to have important lipid-lowering activity, validating its conventional use in the control of hyperlipidemia and cardiovascular wellness. The calyces are bioactive with flavonoids, phenolic acids, and organic acids that are said to regulate lipid metabolism and ensure healthy cholesterol levels [69,70]. Cholesterol-lowering activity of H. sabdariffa is presumed to have more than one mechanism. These can encompass the promotion of lipid metabolism, regulation of enzymatic pathways involved in cholesterol production, and inhibition of lipid deposition in vascular tissues. The plant also has anti-atherogenic activity by acting on factors involved in foam cell generation, smooth muscle cell migration, and vascular calcification, hence the role in protecting the cardiovascular system [69]. Generally, the anticholesterol activity of H4. sabdariffa seems to be an outcome of its dual actions on lipid control and vascular integrity. The pharmacological features serve as a scientific rationale for its traditional application as an over-the-counter natural remedy for hypercholesterolemia and associated cardiovascular conditions. More mechanistic research would be necessary in order to completely clarify the molecular mechanisms underlying these actions.

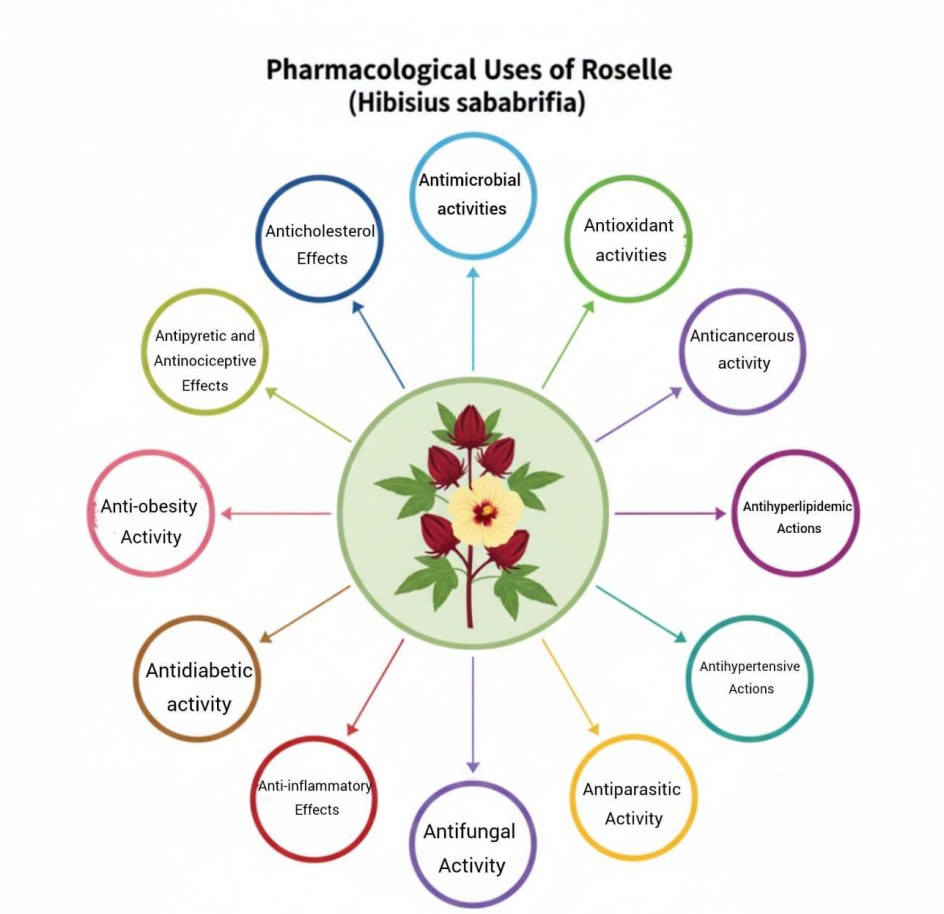

Fig 2. Various pharmacological activities of Hibiscus sabdariffa

Effect on Smooth Muscle

The pharmacological activities of Hibiscus sabdariffa on smooth muscle systems have been noted for their therapeutic significance in cardiovascular and gastrointestinal control. The extracts of the plant, especially aqueous solutions of the calyces, affect the tone and contractility of smooth muscle tissue, implying their role in vascular relaxation and uterine modulation [71,72]. The relaxant action of H. sabdariffa has been linked to endothelium-dependent and endothelium-independent mechanisms, suggesting the involvement of more than one signaling pathway. Modulation of calcAium influx through cell membranes has been postulated as one of the primary pharmacological targets. The flavonoids quercetin and essential oils

eugenol may be involved in this effect via regulation of calcium channels and nitric oxide-mediated pathways [72].

Furthermore, some reports indicate the ability of H. sabdariffa constituents to cause modest stimulatory activities on some smooth muscle preparations, e.g., uterine and intestinal tissues. This two-way action has been ascribed to the mixed composition of organic acids, minerals, and polyphenolic compounds in the extract [73]. Generally, the activities of H. sabdariffa on smooth muscle are multifactorial, representing both direct and indirect actions on contractile mechanisms. These actions can potentially offer pharmacological justification for its classical use in the treatment of hypertension, uterine ailments, and gastrointestinal disturbances. Systematic research and mechanistic reviews are needed to determine the involved biochemical pathways and establish a standard pharmacodynamic profile.

Effect on Blood Pressure

Hibiscus sabdariffa is well known for exerting antihypertensive activity, and this is mainly due to its multilevel action on the cardiovascular system. The hypotensive activity of the blood pressure is considered to be due to direct vasorelaxation of vascular smooth muscle, alteration of calcium channels, and inhibition of angiotensin-converting enzyme (ACE), through bioactive compounds like flavonoids, anthocyanins, and other polyphenolic components [73,74]. A variety of other mechanisms may include cholinergic and histaminergic mechanisms along with feeble diuretic action, which collectively produce the overall hypotension effect. The synergistic interaction of these pathways promotes enhanced vascular tone, lowered peripheral resistance, and fluid balance. Additionally, the antioxidant activity of the extract, and specifically through flavonoids and anthocyanins, can impart cardioprotection by mitigating oxidative stress and enhancing endothelial function. The clinical experience has suggested that daily use of H. Sabdariffa extracts can produce substantial lowering of both systolic and diastolic blood pressure, suggesting its utility as a natural adjuvant or alternative to traditional antihypertensive therapy. Encouraging as these results are, additional controlled trials are essential to best dose, determine long-term safety, and define accurate molecular mechanisms involved in its cardiovascular actions [74].

Renal Effects

Hibiscus sabdariffa has also been known to have its modulatory role on renal function, which is one reason it is traditionally used as a diuretic. The bioactive compounds of the plant are said to affect the balance of electrolytes and uric acid excretion, hence promoting kidney function and fluid homeostasis [75]. H. sabdariffa's diuretic and uricosuric effects are due to its phytochemical content, such as organic acids, polyphenols, and flavonoids. These compounds can be active in several pathways to control renal handling of electrolytes and metabolites, which proposes therapeutic interest in states like hypertension, fluid overload, and hyperuricemia [76,77]. Overall, the renal actions of H. sabdariffa seem to stem from a combination of modulating electrolytes and increased uric acid excretion. These actions lend pharmacological basis to its employment in ensuring renal well-being and treating mild renal or metabolic disturbances. There is a need for further research to identify the precise mechanisms and maximize its therapeutic use.

Phytochemical constituents present in roselle plant:

Phenolic Compounds in Roselle:

Roselle, one of the most widely used edible flowers, is widely acclaimed for its high phenolic compound content, and this is what makes it aesthetically pleasing and also gives it numerous health benefits. Some of these compounds include the total phenolic compounds (TPC), the total flavonoid compounds (TFC), and the total anthocyanin compounds (TAC). Phenolic content in roselle has been the focus of research in the past decade with changes noticed in the levels of the total phenolic compounds as TPC, TFC, and TAC. These variations may be caused by sample conditions including cultivars, growing conditions, and treatment during processing, as well as the extraction and analysis methods employed [59,60].

Phenolic Acids in Roselle:
Roselle consists of some phenolic acids, including hydroxybenzoic acids (gallic acid, protocatechuic acid, syringic acid, vanillic acid, genistic acid, and 4-hydroxybenzoic acid) and hydroxycinnamic acids (chlorogenic acid, caffeic acid, ferulic acid, p-coumaric acid, 3-p-coumaroylquinic acid, 5-p-coumaroylquinic acid, 3-O-caffeoylquinic acid, 4O-caffeoylquinic acid, and 5-O-caffeoylquinic acid). Some of the other phenolic acids found in roselle calyx are neochlorogenic acid, cryptochlorogenic acid, methyl digallate, methyl chlorogenate, dihydroferulic acid-4-Oglucuronide, methyl chlorogenate isomer II, 5-O caffeoyl shikimic acid, ethyl chlorogenate, and ethyl chlorogenate isomer II [61,62].

Flavonoids in Roselle:
Roselle has diverse flavonoids, such as flavan-3-ols (epicatechin, (+) catechin, (−)-epigallocatechin, and (−)-epigallocatechin gallate); flavonols (kaempferol and kaempferol 3-Orutinoside); myricetin (myricetin 3-sambubioside); quercetins (quercetin 3-O-glucoside, quercetin 3sambubioside, quercetin 3-rutinoside, and quercetin pentosylhexoside); rutin; quercitrin; and flavanones (hesperitin and hesperidin). Quercetins are the most commonly reported flavonoids in roselle calyx tissue [63,64].

Anthocyanins in Roselle:
Different studies have separated individual anthocyanin compounds from roselle calyx, showing glycosylated anthocyanins with three or more sugar moieties and octanol derivatives such as delphinidin-3-O-sambubioside and cyanidin-3-Osambubioside. The pigmentation of roselle calyx is controlled by the anthocyanin content, and genotype contributes 60–80% to calyx colour variation. Dark-red calyx colour roselle genotypes possess particular anthocyanin contents and higher antioxidant activity than light-red or white cultivars without red pigments [65,66].

Organic Acid and Volatile Compounds:
The maximum content of organic acids, primarily hibiscus acid and its compounds, was recorded in roselle extracts by the MAE (microwave-assisted extraction) technique with a combined content of 70 mg/g. Other organic acids reported in roselle calyx are citric acid, malic acid, tartaric acid, ascorbic acid, hydroxycitric acid, hibiscus acid, and oxalic acid. The content of volatile compounds has been studied in roselle tissue by various researchers for different cultivars of other countries and different methods of extraction [67,68].

Table 2: major phytochemical constituents of hibiscus sabdariffa:

Compound class	Example compound	Biological activity	references
anthocyanins	Delphinidin-3-sambubioside, Cyanidin-3-sambubioside	Antioxidant, anti-inflammatory, antihypertensive (ACE inhibition, vasodilation)	78,79
flavonoids	Quercetin, Hibiscetin, Gossypetin	Antioxidant, anti-inflammatory, enzyme inhibition, vasodilation	80,81
Phenolic acids	Protocatechuic acid, Chlorogenic acid, Caffeic acid	Antilipidemic, Hepatoprotective, antioxidant	82,78
Organic acids	Hibiscus acid, Citric acid, Malic acid	Diuretic, antihypertensive, Lipid metabolism regulation	83,78

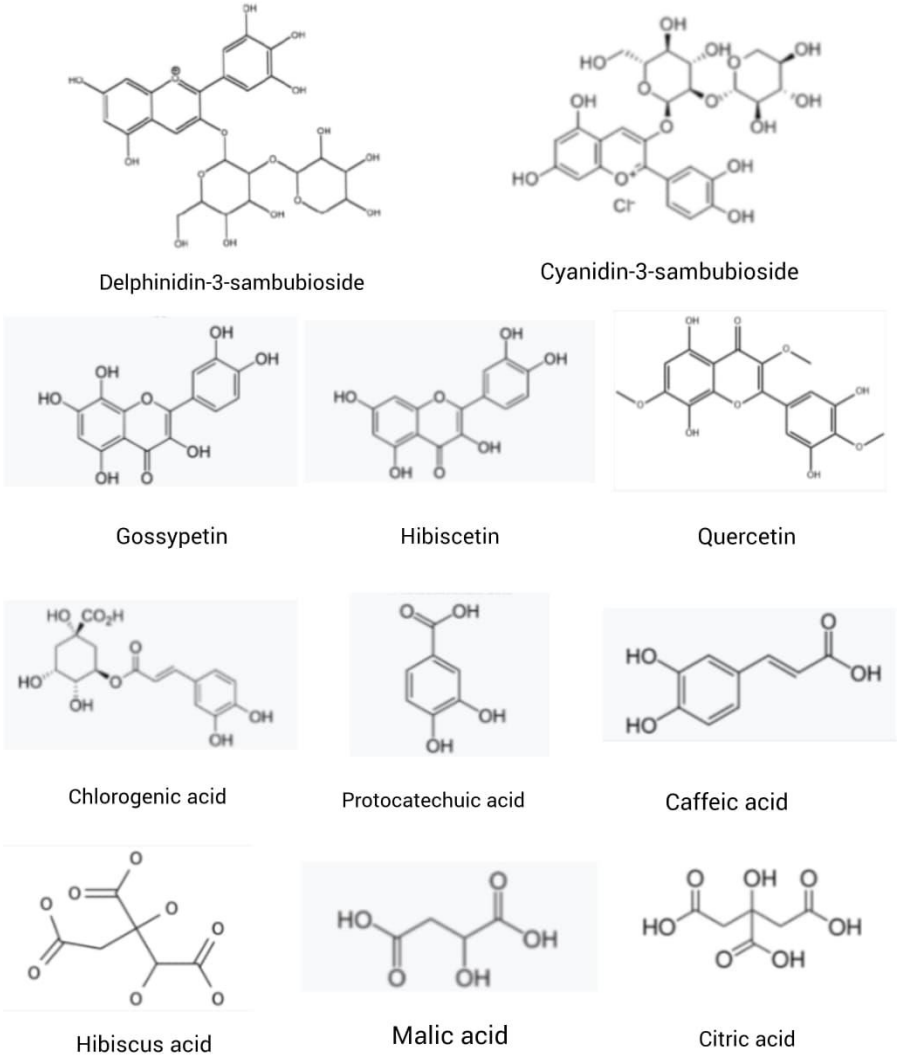

Fig. 3. phytochemical constituents of hibiscus sabdariffa

Traditional Medicinal Uses of Hibiscus sabdariffa (Roselle):

The plant has long been utilized in various traditional medicine systems for its broad spectrum of therapeutic properties. Traditionally, Roselle tea prepared from its dried calyces is consumed both as a hot and cold beverage and is believed to aid in the management of high blood pressure, liver diseases, fever, hypercholesterolemia, and gastrointestinal disorders.

The leaves of Roselle are valued for their mucilaginous content, which is used in pharmaceutical and cosmetic preparations as an emollient and soothing agent. Extracts of the plant have been used in folk medicine for the treatment of colds, toothaches, urinary tract infections, and hangovers. In Senegal, the leaf juice is traditionally applied to treat conjunctivitis, while poultices made from the leaves are used to alleviate sores and ulcers. The leaves also serve as an antiscorbutic remedy for scurvy, a refrigerant to reduce fevers, and as a sedative and diuretic. Similarly, a root decoction of Roselle has been reported to possess antiscorbutic properties and is used for general detoxification and fever relief [78].

Ethnobotanical documentation indicates that H. sabdariffa is traditionally employed as a diuretic, diaphoretic, uricosuric, antibacterial, antifungal, and mild laxative. It is also reputed to act as an antihypertensive, antitussive, and sedative agent, as well as a remedy for gastrointestinal disorders, kidney stones, liver damage, and hypercholesterolemia. Furthermore, Roselle preparations are used to reduce blood viscosity, promote renal function, and alleviate the aftereffects of alcohol consumption [94].

The ripe calyces of Roselle are particularly valued for their use in beverages and traditional medicine, where they are recognized for antispasmodic, hypotensive, and antimicrobial effects and for relaxing uterine muscles. Among Malaysians and other tropical communities, Roselle tea is a popular health drink consumed for its high vitamin C and anthocyanin content, which contribute to its antioxidant and immune-supporting functions. Anthocyanins and proanthocyanidins found in the calyces are believed to be the key bioactive compounds responsible for the blood pressure–lowering effect, while quercetin, another major constituent, has been shown to enhance nitric oxide activity, promoting renal vasodilation and improved kidney filtration [95].Overall, traditional medicinal practices across Africa, Asia, and the Caribbean highlight Hibiscus sabdariffa as a versatile therapeutic plant, serving both as a functional beverage and a natural remedy for various ailments, particularly those related to the cardiovascular, hepatic, and renal systems[78,94,95].

Table 3: Nutritional values of Roselle [44]:

Roselle (raw) per 100 g	
Energy	205 kJ (49 kcal)
Carbohydrates	11.31 g
Fat	0.64 g
Protein	0.96 g
Vitamin A equiv.	14 µg (2%)
Thiamine (B1)	0.011 mg (1%)
Riboflavin (B2)	0.028 mg (2%)
Niacin (B3)	0.31 mg (2%)
Vitamin C	12 mg (14%)
Calcium	215 mg (22%)
Iron	1.48 mg (11%)
Magnesium	51 mg (14%)
Phosphorus	37 mg (5%)
Potassium	208 mg (4%)
Sodium	6 mg (0%)

Table 4: Biochemical values of different parts of Roselle plant [93]:

Nutrients	**Calyxes**	**Seeds**	**Leaves**
Protein (g)	2	28.9	3.5
Carbohydrates (g)	10.2	25.5	8.7
Fat (g)	0.1	21.4	0.3
Vitamin A (L.E.)	-	-	1000
Thiamine (mg)	0.05	0.1	0.2
Riboflavin (mg)	0.07	0.15	0.4
Niacin (mg)	0.06	1.5	1.4
Vitamin C (mg)	17	9	2.3
Calcium (mg)	150	350	240
Iron (mg)	3	9	5

Drug Interaction:

1. Interaction with Diuretics

Methanolic extracts of H. sabdariffa enhanced urine output and decreased urinary pH and electrolytes when co-administered with hydrochlorothiazide in experimental animal models. This implies possible pharmacokinetic interaction, such that hibiscus can interfere with renal excretion and handling of

electrolytes, possibly increasing or interfering with diuretic activity [87]. Mechanistically, the hibiscus extract could modulate kidney tubular transport mechanisms to produce variations in sodium, bicarbonate, and chloride levels.

2. Interaction with Antimalarials

Hibiscus drinks consumption lowered the maximum plasma concentration (C max) and total exposure (AUC) of chloroquine among healthy volunteers, which could lower therapeutic activity [88]. The mechanism for this interaction could be through modulation of the intestinal absorption or liver metabolism of chloroquine, indicating a pharmacokinetic effect where drug bioavailability is influenced by hibiscus constituents.

3. Interaction with Analgesics

Hibiscus has been known to interact with acetaminophen, potentially modifying its biotransformation and clearance [89]. The action may be through inhibition or induction of liver cytochrome P450 enzymes involved in biotransformation of acetaminophen and hence influencing plasma concentration and risk of toxicity.

4. Interaction with Anticancer Drugs

A case report presented acute cutaneous toxicity in a patient on erlotinib (a tyrosine kinase inhibitor) following daily use of hibiscus tea. Withdrawal of hibiscus resulted in swift regression of skin lesions [90]. This indicates a pharmacodynamic interaction, wherein hibiscus compounds could modify drug effect or tissue sensitivity, perhaps through modulation of drug-metabolizing enzymes or interference in signaling pathways acted upon by erlotinib.

5. Cytochrome P450 Modulation

In vitro, hibiscus extracts have been demonstrated to inhibit several CYP450 isoforms, which are responsible for the metabolism of most drugs. Although there is some evidence from in vivo studies that in all cases may not result in significant clinical interactions [91], caution must be exercised because inhibition of CYP450 can lead to increased plasma concentrations of co-administered drugs, increasing the risk of adverse effects.

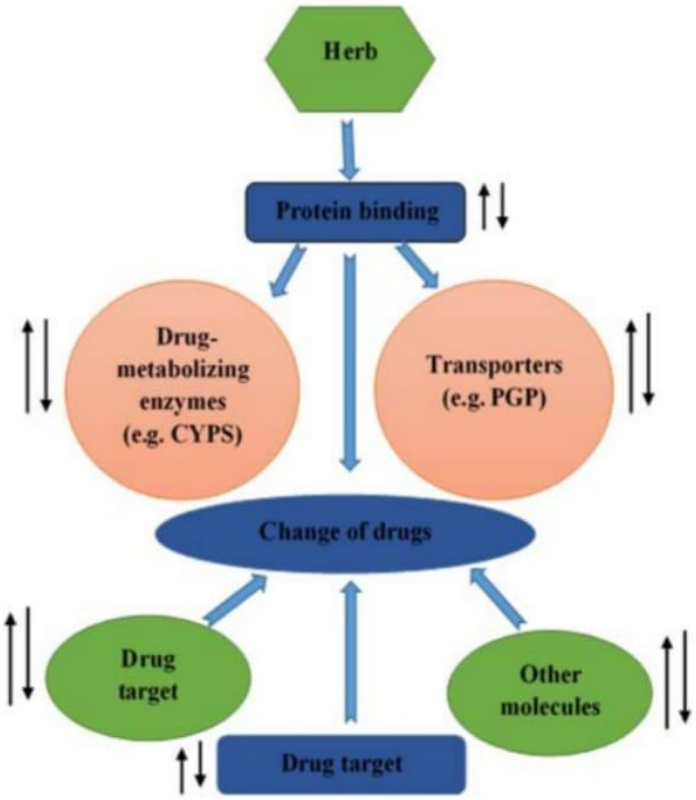

Fig. 4. Pharmacokinetic and Pharmacodynamic mechanism of drug-herb interaction [87]

Toxicology of Hibiscus sabdariffa

The growing popularity of Hibiscus sabdariffa (Roselle) as a complementary and alternative therapy for the treatment of different conditions has generated interest in its safety profile. While H. sabdariffa has been reputed to be safe at moderate or traditional dosing levels, toxicological data from animal and clinical investigations suggest that high doses or prolonged exposure could lead to dose-dependent toxicity, with particular effects involving the reproductive, hepatic, and renal organs [86,78].

Experimental results collated in recent reviews illustrate that chronic treatment with H. sabdariffa extracts at high doses (≥1000 mg/kg) could be damaging to testicular function, as measured by compromised sperm motility, number, and viability, and seminiferous tubule degeneration with reduced serum testosterone, LH, and FSH levels. These sexual dysfunctions are caused by the phytoestrogenic compounds of the plant, which could modulate gonadotropin release and interfere with steroidogenesis [86,85]. In addition, maternal exposure in gestation and lactation has been linked to developmental changes in offspring reproductive parameters, suggesting potential transgenerational endocrine effects. Notwithstanding these concerns, H. sabdariffa has a broad margin of safety. The LD_{50} values reported above 5000 mg/kg in rodents evidence low acute toxicity, and sub-chronic exposure to moderate doses (≤250 mg/kg) has evidenced little toxicological effect. Such levels of extracts usually have antioxidant, hepatoprotective, and cytoprotective actions against oxidative stress and enhancing tissue integrity [86,78].

Apart from reproductive outcomes, excessive or long-term consumption of H. sabdariffa products has been associated with mild hepatotoxic and nephrotoxic alterations as indicated by levels of changes in serum transaminases, urea, and creatinine [78,85]. These actions owe mostly to high contents of anthocyanins and organic acids that, on accumulating, can inhibit hepatic enzyme activity and renal electrolyte status. The intense diuretic action of H. sabdariffa may also cause electrolyte abnormalities, especially hypokalemia, if taken in excess or in conjunction with other diuretics [84]. However, all these biochemical changes are reversible upon drug withdrawal.

In general, H. sabdariffa has a wide margin of therapeutic safety and is found to be non-toxic when taken within established limits. Yet, chronic or high dose administration holds the risk of evoking reproductive, endocrine, and mild organ toxicities. Thus, it is necessary to use H. sabdariffa under controlled and rational conditions within safe dosages to guarantee its efficacy as well as safety in both traditional and contemporary therapeutic applications [78,84,85,86].

Future Directions

Although extensive review has highlighted about the therapeutic potential of Hibiscus sabdariffa (Roselle) through extensive studies, there are still some areas that need to be addressed in order to fully claim its pharmacological and clinical significance. Future research should aim to carry out well-designed clinical trials to replicate the preclinical data and to ascertain the effective dosage, safety, and long-term consequences of Roselle extracts in humans. Mechanistic studies in detail are also required to define the exact biochemical and molecular pathways responsible for its antihypertensive, antidiabetic, anticancer, and hepatoprotective activities. In addition, differences in the phytochemical composition based on variations in cultivation, geography, as well as extraction procedures highlight the need for standardization and quality control of Roselle-containing preparations. Careful toxicological evaluations, such as chronic and reproductive toxicity studies, must be conducted to establish safe and effective therapeutic ranges and to avoid potential side effects. Furthermore, new research should investigate innovative formulation technologies—such as nano formulations, encapsulation, and bioenhancer-based systems—to enhance the bioavailability and stability of the active constituents. Herb–drug interaction studies should also be conducted to provide a safe combination of Roselle with contemporary pharmacotherapy. Lastly, genetic enhancement and sustainable cropping techniques must be established to maximize yield, phytochemical uniformity, and environmental resilience. Through interdisciplinary collaboration involving pharmacology, clinical science, and biotechnology, Hibiscus sabdariffa can be promoted as a science-proven natural resource for pharmaceutical, nutraceutical, and functional food industries.

Conclusion

Hibiscus sabdariffa (Roselle) is a highly researched medicinal plant with immense therapeutic and nutritional value. Its dense phytochemical profile comprising anthocyanins, flavonoids, phenolic acids, and organic acids is responsible for its wide range of pharmacological actions like antioxidant, antihypertensive, hypolipidemic, hepatoprotective, antidiabetic, antimicrobial, and anticancer activities. These scientific data prove its age-old applications in controlling cardiovascular, metabolic, and inflammatory diseases. The multifunctional bioactivities of Roselle underscore its potential as a functional food additive and a source of new therapeutic drugs. While being generally regarded as safe at moderate levels, toxicological evidence suggests that overconsumption or prolonged intake can result in minor hepatic, renal, or reproductive toxicity. Hence, standardized extraction procedure, careful dosage determination, and long-term safety assessments are still critical. In total, Roselle is a dynamic natural resource with immense potential for integration into contemporary pharmaceutical, nutraceutical, and preventive healthcare uses.

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