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SHORT REVIEW

Ruellia tuberosa L: A Botanical Treasure Trove of Therapeutic Potency

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Abstract

People have been using medicinal herbs for thousands of years because they work well, are easily available and are economical with few side effects. The cracker plant, *Ruellia tuberosa* Linn. (*Acanthaceae*), has been used for a long time to treat kidney disease, syphilis, bronchitis, gonorrhoea and other diseases. This plant exhibited qualities that could be used to treat a range of illnesses, including cancer, diabetes, hypertension, inflammation, antinociceptive ulcers, gastroprotective effects, cytotoxicity, and analgesia. Today's antibacterial, antifungal, and pesticides are not just pricey and dangerous but are also quickly losing their effectiveness against microbes, especially bacteria, fungi, and insects. The growing use of herbal herbicides, antibacterials and antifungals is therefore seen as a better, more effective and less expensive solution. Recent studies have revealed the plant's strong antioxidant and antimicrobial properties, making it a promising candidate for developing natural therapeutic agents. Its bioactive compounds have also shown significant potential in regulating blood glucose levels and combating oxidative stress, reinforcing its value as a multipotent medicinal herb for future pharmacological applications.

Major Findings: *Ruellia tuberosa* Linn. exhibits significant antioxidant, antimicrobial, and antidiabetic activities. Its bioactive compounds show potential for managing oxidative stress and blood glucose levels, supporting its use as a multipotent natural therapeutic agent.

Keywords: Antidiabetic, Antioxidant, Glycosides, *Ruellia tuberosa*, Traditional Use

1. Introduction

Ruellia tuberosa L. *(Acanthaceae)* is a perennial plant that originated in Central America and has successfully adapted and spread to other tropical countries, throughout regions encompassing the southern and southeastern parts of Asia.

Other names for the plant include Sheep Potato, Fever Root, Minnie Root, Daniel's Great Gun, Snapdragon Root, and Large bellflower. Duppy Gun. *Ruellia tuberosa* is also known as Chatakani Phallis in Hindi, and Bandukadi in Gujarati[1].

In Peru, Guiana, Central America, and the West Indies, it is used medicinally. The common name for *R. tuberosa* (L.) is "Cracker plant"[2]. It has gained the title "Cracker Plant" in Sabah, Malaysia[3]. It has also gained popularity with the term "Popping Pod" due to the distinctive feature of its seeds explosively reacting to water contact.

Taxonomy given below[4].

Kingdom- *Planata*
Division- *Magnoliophyta*
Class- *Magnoliopsida*
Order- *Scrophulariales*
Family- *Acanthaceae*
Genus- *Ruellia*
Species- *tuberosa*

As a member of the *Acanthoideae* subfamily, this species, commonly referred to as "patpatey", is one of approximately 50 perennial plants in the *Ruellia* genus[5].

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This genus' members are referred to as wild petunias in broad. With more than 250 species, this genus is found throughout the temperate and tropical regions of both hemispheres, including the Indian subcontinent. There are ten species of *Ruellia* in India, two of which have been identified in the state of Maharashtra[6].

2. Morphological Features

This tiny plant can be identified by its beautiful violet bracteate flowers that grow on twisted few-flowered cymes and are shaped like funnels, linear hispid calyx lobes that are 12–20mm long, a corolla tube that is 4-6cm long and abruptly expands above, purple suborbicular lobes that are 12–15mm wide and 2–2.5mm across, a subcylindrical, sticky shell (fruit) that stays in place that is 2cm (0.8in) long and contains roughly twenty seeds in each locule, as well as bulky, spindle-shaped tuberous roots grouped[7]. Broadly spreading, upright stem reaching a height of 50cm, primarily at the base, with coarsely hairy and have an oval to elongated shape with petioles. The petioles are 1.5 centimetres in length, and the leaf blades are 4-6 × 1.5-2.5cm, pubescent, and have a wedge-shaped triangular bottom, blunt vertex, and undulating edge. In damp, shaded areas, *R. tuberosa* can be found. Although it is originally from Central America, it is currently found in many tropical xerophile and ruderal environments, as well as grasslands and roadside areas in South and Southeast Asia; frequently found in the form of weed in fields of crops[8].

3. Chemical Constituent

Malvidin-3,5-diglucoside is present in the flowers of *R. tuberosa*, while apigenin and luteolin are present in the leaves. Leuteolin-7-O-glucoside, apigenin-7-O-glucoside, apigenin-7-O-ruinoside and apigenin-7-O-glucuronide comprise 3% of the flower buds of *R. tuberosa*[9]. Three types of acids—myristic, capric, and lauric make up the seed oil[10]. The aerial sections of the plant comprise malvidin 3,5-diglucoside, masterol, B-sitosterol, campesterol, cholesterol, 21-methyldammer-22-en-3B, apigenin 7-B-D-glucuronide, 18,27-triol, tyclorebrine[11-13]. Tubers consist of n-hentriacotane (26.52%) and n-nonacosane (C29: 44.83%) in addition to B-sitosterol, sterol-stigmasterol and campesterol[14]. During the study into the biologically active components of the extract of ethanol from tubers, a total of twenty-five compounds were discovered. The compounds that are included in this category include lupeol, which accounts for 68.14%, stigmasterol, which stands for 8.89%, α-sitosterol, which counts for 3.99%, sucrose, which considers cholest-5-ene, 3-bromo-, with a purity of 2.24% and a stereochemistry of (3α-), which contributes to 2.24%, octadecane, 2-methyl-, which pays for 2.10%, nonadecane, 2-methyl-, which is 1.93 % eicosane, 2-methyl-, which accounts for 1.79%, heptacosane, which makes up 1.43%, and heptacosane, which constitutes 1.29 %[15]. Gas Chromatography-Mass Spectrometry (GC-MS) analysis revealed 16 compounds in the tuber's ethanol extract. The chemicals with the highest concentrations were flavone, phytol, 3,12-nonadecatriene 5, 14-diol, E, E, Z-1, and methyl-6-octadecenoate, with peak areas of 40.2%, 41.8%, 41.4%, and 50% respectively[16]. The four compounds rutin, syringaresinol, catechin and pulmatin were isolated from the plant's ethyl acetate fraction using column chromatography[17].

Studies on *R. tuberosa* Linn. revealed that the main components of the methanolic extract of the plants under study were flavonoid glycosides in addition to, phenolic glycosides, benzoxazinoid glucosides, sterols, megastigmane glycosides and lignans for phytochemical analysis[18].

4. Traditional and Ethnobotanical Uses

Ayurveda and several traditional medical systems use certain species of *Ruellia* in their formulations which comprises India's Ayush systems. *R. tuberosa* has been widely employed for the therapeutic management of gastrointestinal disorders and hypertension; it is also an antioxidant, antipyretic, diuretic, analgesic, and antidiabetic.[6] Traditionally used to cure, gonorrhoea, fever, constipation, cystitis, bladder stones, leprosy, bronchitis, and additional infections that are transmitted sexually, this plant is widely known for its emetic, antiseptic, depurative, purgative properties and diaphoretic[19,20].

In the *Siddha* medical system, the treatment of gonorrhoea and ear disorders involves the use of leaves in conjunction with liquid copal[21]. *Ruellia tuberosa*

is employed for the treatment of gastric carcinoma[22]. The dried and pulverised roots, given in two-ounce dosages, can cause abortions and are also used to treat sore eyes. These herbs have emetic effects, acting as an alternative to ipecac and are used to treat bladder stones. A decoction made from the leaves is used to treat bronchitis[23]. The concoction derived from the leaves is applied to alleviate skin conditions, injuries, abscesses, and similar issues. Seeds are used to treat conditions such as sexual debility, spermatorrhoea, as well as leucorrhoea[24]. The roots are used to induce oestrus and act as an antihelmintic[25]. Bladder ailments and frequent micturition are treated using the plant as a whole. Petiveria alliacea decoction is used as an abortifacient or as a dilatation and curettage technique for "cleaning" the uterine tract. Root decoction or infusion is used as a treatment for diabetes, whooping cough, along with renal illnesses. Tea made from tubers is used to purify blood. It is advised to make tea from both the leaves and roots to treat weakness while decreasing urine retention. To treat stomach aches and postpartum abdominal pain, tuber powder is administered with milk[23].

In some cultural practices, especially in Thailand, *R. tuberosa* is utilised as a natural colour. According to a study, blue-purple *R. tuberosa* Linn flowers can be used as a natural textile dye when mixed with suitable mordants[26]. Taiwanese herbal drinks have included *R. tuberosa*, demonstrating the plant's adaptability beyond conventional medical use[27,28]. It has been historically utilised for curing urinary tract irritation and lowering toxicity[29].

5. Pharmacological Properties (Table 1 and Figure 1)

5.1 Antioxidant Activity

A stem extract from *R. tuberosa* L. was tested in vitro for its antioxidant capabilities. by the utilisation of a variety of techniques, including hydrogen peroxide luminol chemiluminescence furthermore DPPH free radical scavenging experiments were conducted to evaluate the activity of 2,2-diphenyl-1-picrylhydrazyl (DPPH) in scavenging free radicals. It was determined whether or not the extract of methanol along with its four fractions (n-hexane, hxF, ethyl acetate and water) possessed active antioxidant properties. Based on the findings, it was determined that *R. tuberosa* possessed powerful antioxidant qualities. Antioxidant activity of the examined fractions was found to be EaF before CfF, ME, WtF, and HxF, as shown in the experiment involving the chemiluminescence of luminols produced by hydrogen peroxide. The outcomes of the luminol chemiluminescence test were not consistent with the given hierarchical ranking of HxF and WtF, however, the DPPH free radical-scavenging assay showed a

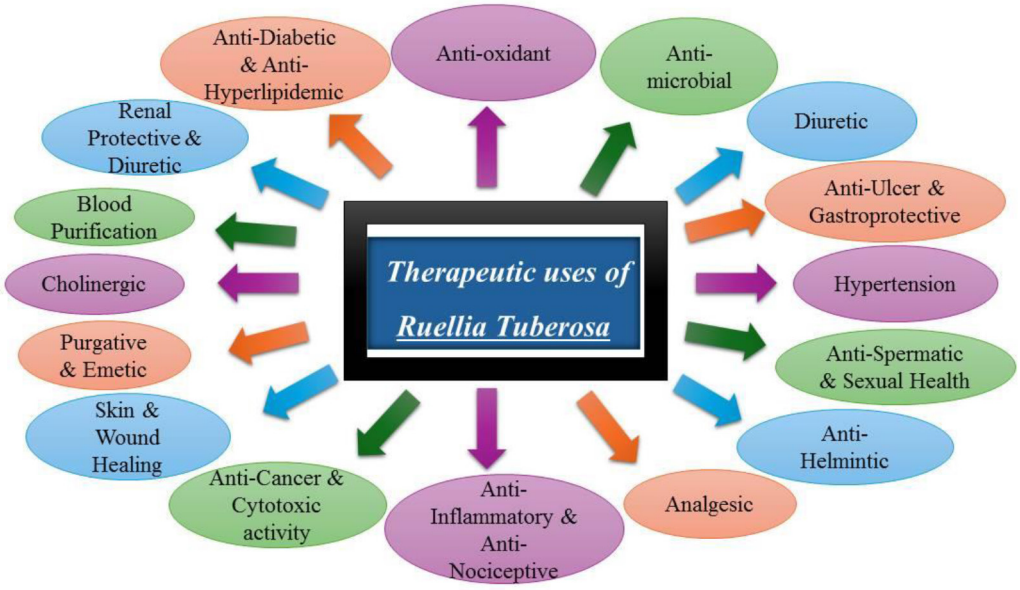


Figure 1. Therapeutic uses of *Ruellia tuberosa*.

similar tendency. The findings offer important insights into the pharmacological actions linked to free radicals in this conventional practice of customary medicine[30]. According to a study, 50% hydroethanolic extracts of the leaves of *Dipteracanthus patulus* and *Ruellia tuberosa* are beneficial for enhancing antioxidant capability in addition to regulating peroxide levels[31].

5.2 Antimicrobial Activity

Researchers looked at the antibacterial capabilities of *R. tuberosa* fractions derived from hexane, dichloromethane, ethyl acetate, and methanol against bacterial strains that were both Gram +ve and Gram -ve. The fractions comprising methanol and ethyl acetate exhibited the most potent antibacterial activity, particularly against *Pseudomonas aeruginosa* and *Staphylococcus aureus*[32]. Significant antibacterial activity was demonstrated using alcohol, chloroform, ethyl acetate and water-based extracts of the entire *R. tuberosa* plant. The water-based extract showed reduced efficacy against organisms that are fungal[33]. Kader *et al.,* demonstrated that the leaf extract of *R. tuberosa* had antibacterial activity, with the methanolic extract showing notable antimicrobial capability[34]. Significant antibacterial activity is antagonistic to *Escherichia coli*. The methanolic leaf extract exhibited antimicrobial action against *Bacillus subtilis, Klebsiella pneumonia,* Proteus mirablis*, and Pseudomonas aeruginosa,* as well as antifungal activity against *Penicillium* sp., *Mucor* sp., *Aspergillus* sp. and *Fusarium* sp. Senthilkumar *et al.,* reported identical findings.[35]

5.3 Antinociceptive, Anti-inflammatory and Gastroprotective Activity

The study examined the pain-relieving, anti-inflammatory, and gastroprotective effects of *R. tuberosa* extracts using experimental rodent models. The ethanol extract demonstrated significant antinociceptive activity, as observed in the hot plate test, where a 300 mg/kg dosage extended the response time to thermal stimuli, achieving a maximal analgesic effect comparable to diclofenac sodium. Additionally, the extract at 250 and 500 mg/kg significantly reduced acetic acid-induced writhing in mice, mimicking the action of diclofenac sodium. The anti-inflammatory properties were evident in rats, where doses of 300, 200, and 100 mg/kg effectively reduced hind paw oedema induced by serotonin and egg albumin. Furthermore, at a dosage of 5 mg/kg, the extract exhibited anti-inflammatory effects similar to indomethacin[36].

The aqueous extract obtained from soaking the roots of *R. tuberosa* in water demonstrated notable gastroprotective activity against alcohol-induced gastric lesions in rats. The extract also exhibited mild erythropoietic and moderate analgesic effects. Data analysis confirmed the gastroprotective properties of *R. tuberosa* root extract[37].

5.4 Anti-ulcer Activity

Ruellia tuberosa ethyl acetate extract has anti-ulcer properties, as demonstrated by researchers[38]. They have selected two dosages, namely 500 mg/kg (high dose) and 250 mg/kg (low dose) along with ranitidine being used as the reference medicine at a dosage of 20 mg/kg, by the guidelines set by the standards for economic cooperation and development. The stomach volume, total acidity, and free acidity all significantly decreased in the ethyl acetate extract. In comparison to the control group, the acidity level of the stomach elevated significantly ($p < 0.01$) only when high doses (500 mg/kg) were administered. They observed a dose-dependent decrease in the ulcer index value when comparing it to the control group[39].

5.5 Anti-cancer and Cytotoxic Activity

In vitro, cytotoxicity was demonstrated by active compounds extracted from *R. tuberosa* against both the KB and HepG2 cell lines[40]. In H460 and MDAMB231 cancer cells, methanol extract of *R. tuberosa's* aerial component was cytotoxic, respectively[23]. Only *R. tuberosa's* anticancer action has been documented thus far. Arun *et al.*, demonstrated the cytotoxicity of a methanol extract made from the aerial portion of the herb *R. tuberosa*[41]. It was discovered that the methanol extract's lowest inhibitory concentration 1.9 µg/mL in H460 and (IC_{50}) was 3.5 and MDAMB231 cells that are tumours, in that sequence. Using bioassay-driven column chromatography, they have also extracted Tylocrebrine from *R. tuberosa* and determined its potential anti-inflammatory and anti-cancer properties.

Similar research showing *R. tuberosa* extract's anticancer efficacy was also published by Nagarjuna *et al*[42]. Comparably, Samy *et al.,* observed that, against human lung cancer cell lines A459, *Ruellia patula* yields

methanolic extract, n-hexane, and EtOAc fractions, while *R. tuberosa* yields MeOH extract, n-hexane, and EtOAc fractions, shown considerable cytotoxic action at a dosage of 100 µg/ml[43].

5.6 Antidiabetic and Antihyperlipidemic Activity

Ruellia tuberosa leaf methanol extract was administered to diabetes-induced rats every day for a week at doses of 100 and 200 milligrams per kilogram of body weight, as per the research done by Rajan *et al*[44]. The findings showed that serum enzymes, lipid parameters (except HDL-C), and glucose levels in the blood had dropped dramatically ($p < 0.05$). Administration of glibenclamide at a dosage of 5g/kg resulted in a notable elevation of HDL-C levels, particularly when the dosage was increased to 200mg/kg. The researchers concluded that in diabetic rats treated with alloxan, the leaves of *R. tuberosa* were extracted using methanol, and the resulting extract demonstrated powerful hepatoprotective, antihyperlipidemic, and anti-diabetic properties.

Ullah *et al*., further investigated the hyperglycemic potential of various *R. tuberosa* organic extracts. They stated that the proportion of ethyl acetate (100 mg/kg) exhibited 34.31 ± 0.43%, a significant anti-diabetic activity[45]. A study was conducted to examine the effects of ethanolic (400 mg/kg) and aqueous (100 mg/kg) extracts of *R. tuberosa* L. on regulating glucose levels in rats with diabetes and high-fat diet. According to Ko CY *et al*. (2018)[46] Following a duration of therapy lasting four weeks, it was discovered that *R. tuberosa* L. might improve hyperinsulinemia, blood sugar and overload index of insulin resistance. Insulin-resistant C2C12 myoblasts were used to investigate the mechanism of glucose absorption by *R. tuberosa* L. at concentrations ranging from 25 to 800 g/ml. According to the cell model, the extract (25, 50, 200, 400, and 800 mg/ml) decreased resistance of insulin by 28-39 per cent at various doses and boosted the absorption of glucose in a dose-dependent manner. The optimal concentration of *R. tuberosa* L. for enhancing glucose absorption, out of the options described above, was 25 lg/mL[46,47]. By reducing insulin resistance by 28–39%, *R. tuberosa* L. elevated the absorption of glucose in a manner that was dependent on the dosage. Hyperinsulinemia, the index of insulin resistance and hyperglycemia were all improved[48].

Another study looked at how the lipid profiles of rats with alloxan-induced diabetes were affected by 50% hydroethanolic extracts of the leaves of *R. tuberosa* along with *D. patulus*. At 500 mg/kg bw, the total cholesterol level was considerably ($p<0.05$) decreased in the groups treated with plant extract. It was discovered that the therapy groups had higher HDL-c[49].

5.7 Antispermatic Activity

Administering the aqueous extract obtained from the tuberous roots of *R. tuberosa* orally to male albino rats at doses of 50, 100, and 150 mg/kg of body weight for 21 days resulted in a significant decrease in sperm count. The results suggest that the water-based extract of *R. tuberosa* has a contraceptive effect on male albino rats by inhibiting sperm production.[50] A different study examined the impact of *R. tuberosa* root powder on Swiss albino mouse male fertility. Sperm count, motility, and viability experienced a substantial reduction, according to the results ($p<0.001$). Sperm count was lower in the experimental group (15.97–19.24 million/ml) than in the control group (55.12 million/ml). In the recovery group, there was some reversal. The findings point to a possible use as an oral, reversible male contraception[51].

5.8 Antihelmintic Activity

The study investigated the anthelmintic properties of four common Philippine weeds: *R. tuberosa, Cyperous brevifolius, Chrysopogon aciculatus* and *Saccharum spontaneum*. The ethanol extract obtained from the dried aerial parts of these plants was divided into hexane-soluble and extracts soluble in chloroform by a series of steps. Subsequently, the extracts underwent testing against *Eudrillus eugenia*, earthworms that are African nightcrawlers. A dose-dependent toxicity relationship was found using anthelmintic bioassays. In hexane extracts, *R. tuberosa* worked better than the other materials. Also, among the chloroform-soluble extracts, *R. tuberosa* and *C. brevifolius* had the best antihelmintic activity across all studied concentrations[52].

5.9 Antihypertensive Activity

Ruellia tuberosa, a plant also known as Minnie root, is traditionally utilised in several places, such as Surinam, for its medicinal properties in treating diverse diseases including gastrointestinal disorders, gonorrhoea, diabetes mellitus, joint discomfort,

muscle strain, and hypertension[53,54]. The *R. tuberosa* preparations do not appear to have any direct pharmacological evidence of an antihypertensive effect. However, the decrease in the synthesis of hippuric acid from hippuryl-L-histidyl-L-leucine by Angiotensin Converting Enzyme (ACE) in the lungs of rabbits when exposed to an ethanolic extract of *R. tuberosa* leaves indicates that ACE inhibition may be involved in the blood pressure-lowering effects of *Ruellia* preparations. The attribution of this observation has been ascribed to the polyphenol, flavonoid, and/or steroid constituents present in the extract[55].

5.10 Antiurolithic Activity

The research investigated the antiurolithiatic properties of an ethanolic extract obtained from the roots of *R. tuberosa*. This evaluation included its effects against calcium oxalate urolithiasis induced by 2% w/v ammonium and 0.75% v/v ethylene glycol, as well as its antioxidant activity in countering oxidative stress induced by hyperoxaluria in male albino rats. The results demonstrated a notable decrease in calcium oxalate deposition, an elevated urinary calcium elimination, and a concurrent significantly low lipid peroxidation. Additionally, there was an enhancement in the urolithiasis-affected rats' kidneys that were examined to determine the levels of antioxidant enzymes[56].

5.11 Improvement of Renal Histopathology

This study aimed to investigate the effects of hydroethanolic root extracts of *R. tuberosa* on the kidneys of Wistar rats that had been treated with streptozotocin to develop diabetes. Severe histological changes were noted in the renal tissue of diabetic rats, accompanied by elevations in Tumour Necrosis Factor (TNF) alpha expression as well as Malondialdehyde (MDA) levels. TNF alpha expression in addition to MDA levels significantly dropped after treatment. Treatments that promoted the healing of renal tubular and glomerular damage[57].

Table 1. Pharmacological activities, plant parts used, chemical constituents, and mechanisms of action of *Ruellia tuberosa*

Pharmacological Activity	Parts of the Plant Used	Chemical Constituent	Mechanism of Action	References
Antioxidant activity	Leaves, stem	Flavonoids, Polyphenols	Scavenging of free radicals (DPPH, luminol chemiluminescence)	30,31
Antimicrobial Activity	Leaves, whole plant	Alkaloids, Flavonoids	Preventing the growth of bacteria and fungi	32-35
Anti-nociceptive, Anti-inflammatory and gastroprotective activity	Roots, whole plant	Flavonoids, Saponins	COX Inhibition, anti-inflammatory action and gastric protection	36,37
Anti-ulcer activity	Whole plant	Ethyl Acetate Fraction	Reduced ulcer index and stomach acidity	38,39
Anti-cancer and cytotoxic	Aerial parts	Tylocrebrine, Alkaloids	Cytotoxic effects on cancer cell lines	40- 43
Anti-diabetic and anti-hyperlipidemic activity	Leaves	Flavonoids, Polyphenols	Improvement of glucose absorption and decrease in insulin resistance	44- 49
Anti-spermatic activity	Tuberous roots	Steroids, Alkaloids	Spermatogenesis inhibition	50,51
Anti-helmintic activity	Aerial parts	Tannins, Alkaloids	Paralysis and death of helminths	52
Anti-hypertensive activity	Leaves	Steroids, Flavonoids, Polyphenols	Inhibition of angiotensin converting enzyme and vasodilation	53- 55
Anti-urolithic activity	Root	Antioxidants, Flavonoids	Decrease in the deposition of calcium oxalate	56
Renal histopathology improvement	Roots	Hydroethanolic extracts	Reduction of oxidative stress and TNF-α	57
In vitro purgative and cholinergic activity	Whole plant	Iridoid glycosides, Flavonoids, Sterols	Cholinergic and estrogenic effects	58

5.12 *In Vitro* Purgative and Cholinergic Activity

At 30 µg/mL, contractions were elicited in an electrically induced ileum tissue strip using extracts containing methanol, ethyl acetate, and water from *R. tuberosa*. After 350 mg/kg/day of *R. tuberosa* methanolic extract was used to study the effects on the uterus and gestation, more implantations were discovered. This research revealed that sterol and flavonoids may have an estrogenic effect, whereas iridoid glycosides may have a cholinergic effect[58].

Ruellia tuberosa has been shown to have anti-inflammatory and analgesic properties, which may make it useful for Rheumatoid Arthritis (RA) and other disorders. Research conducted on animal models has demonstrated that the roots' aqueous extract has strong anti-inflammatory and analgesic effects. Nevertheless, there are still few direct studies on how it affects osteoporosis or RA. Although its anti-inflammatory qualities suggest potential advantages for RA, further focused research is necessary to confirm its effectiveness and safety. It has been discovered that a variety of natural substances can increase bone density and stop bone loss. The rising desire for alternative therapies is highlighted by the increased interest in herbal medicine, especially plant-based therapies for RA and osteoporosis[59,60].

6. Conclusion

The earliest form of medical treatment that has ever been known to humans is herbal medicine. Throughout human history, every society has made use of herbs. During the creation of modern civilisation, it played a significant role. For centuries, the *R. tuberosa* plant has been used in the conventional therapy of several illnesses. Following a review of the relevant literature, it was discovered that various parts of the plant contained alkaloids, flavonoids and phenolic chemicals. According to the findings of the pharmacological review, the cracker plant, also known as *R. tuberosa* possesses antioxidant properties. Antibacterial activity, antifungal activity, anti-inflammatory effects, and other similar qualities. The development of a novel therapeutic drug might be possible if additional study is conducted on the active ingredients of *R. tuberosa*. There is a possibility that *R. tuberosa* is a viable botanical resource that has an extensive range of applications that might be used in the field of medicine.

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8. Author Contribution

All authors contributed to the conception and design of the review. Maitri Mahant performed the literature survey, critically analyzed the relevant studies, and drafted the manuscript. All authors have read and approved the final version of the manuscript.

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