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• Review

Health–promoting and disease–preventive potential of *Trianthema portulacastrum* Linn. (Gadabani) —An Indian medicinal and dietary plant

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ABSTRACT

It is estimated that 80% of the world population depends on traditional medicine for primary healthcare need. *Trianthema portulacastrum* Linn. (family: Aizoaceae) is a small perennial weed found in the Americas, Africa, India, and other regions of the world. This plant is used extensively in Indian traditional medicines and is also consumed as a vegetable throughout Asia for its perceived health benefits. Phytochemical analysis of *T. portulacastrum* reveals the presence of alkaloids, flavonoids, terpenoids, saponins, and phenolic compounds. Emerging studies demonstrate that crude extracts as well as bioactive phytoconstituents of *T. portulacastrum* exhibit potent antioxidant, anti-infective, analgesic, and anti-inflammatory activities. A growing number of *in vitro* and *in vivo* studies demonstrate various biological and pharmacological activities, including prevention and amelioration of hepatotoxicity, nephrotoxicity, hyperglycemia, hyperlipidemia, infectious diseases and cancer. This review aims to present and analyze available literature to understand the full potential of *T. portulacastrum* in health promotion and disease prevention. Current limitations and future directions of research on this medicinal and dietary plant are also critically discussed.

Keywords: *Trianthema portulacastrum*; phytochemistry; pharmacology; health benefits; review; herbal medicine

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1 Introduction

Compounds found in natural products have served as either templates or specific agents for the treatment of a number of different types of diseases. It has been reported that approximately 50% of approved drugs since 1994 were based on natural products[1]. Today, use of natural products is still prevalent in traditional and folkloric systems of medicine worldwide, particularly in developing countries where access to modern therapies may be challenging or expensive[1–3]. Specifically, India is considered to be one of the largest producers of medicinal herbs, where 2 500 species of plants known to have medicinal properties are found, and 150 of which are harvested for commercial use on a grand scale[4,5]. India is also one of the countries that produces large amounts of herbal raw materials.

Trianthema portulacastrum Linn. (also known as *Trianthema monogyna* Linn.; family: Aizoaceae), also known as horse purslane, carpetweed, giant pigweed, Punarnava, Gadabani and Labuni, has historically been valued by Indian and African cultures for its numerous medicinal effects[6–8]. It is widespread in Southeast Asia, tropical America, and Africa. The plant is capable of growing in sunny desert areas such as in Arizona, United States, and also grows abundantly as a "weed" in well irrigated and high-rainfall areas, particularly in India and neighboring countries. The biological classification and scientific taxonomy are presented in Table 1.

Table 1 Biological classification and scientific taxonomy of *Trianthema portulacastrum*

Biological classification	Scientific taxonomy
Kingdom	Plantae
Subkingdom	Tracheobionta
Superdivision	Spermatophyta
Division	Magnoliophyta
Class	Magnoliopsida
Subclass	Caryophyllidae
Order	Caryophyllales
Family	Aizoaceae
Genus	*Trianthema* L.
Species	*Trianthema portulacastrum* L.

The life cycle of *T. portulacastrum* is considered annual/perennial depending on the geographic location found, and the plant is propagated by seeds and fragments of the stem that can be spread by cuttings very easily. Two varieties of the plant can be found. One is red-flowered variety (also known as "Rakta Punarnava") and the other is white-flowered variety ("Shwet Punarnava"); the former is more abundant than the latter[6]. Both varieties are known to grow best under partial shade and thrive in neutral to alkaline soils.

Structurally, the plant is a glabrous, branched, and prostrate herb (Figure 1A) that produces colored flowers, and can grow up to 100 cm in height, but grows typically less as the plants are prostrate. The stems are fleshy, prostrate, and often reddish in color and usually are slightly angular, pubescent and branched (Figure 1B). The leaves are green, succulent, oval, and in opposite pairs of unequal size (Figure 1C). The flowers are small, 5-lobed, pink, purple or white in color, and open in the morning hours (Figure 1D). The fruits represent circumscissile capsules, partly exserted from the persistent perianth, and contain 2–8 seeds. The seeds are kidney-shaped, approximately 2 mm in diameter, hairless, and are brownish to black in color.

Figure 1 Several photographs of *Trianthema portulacastrum* showing a whole plant (A), stems (B), leaves (C) and flowers (D)

T. portulacastrum is known to exhibit allelopathic effects on other weeds and crops including cotton, maize, pumpkin, eggplant, and wheat through inhibition of seed germination. It has also been reported to have autotoxic effects, as its extracts can reduce its own seed germination and shoot length. Interestingly, a recent study found that *T. portulacastrum* extract can also exert stimulatory growth/germination effects on other weeds[9]. Thus, the components found in *T. portulacastrum* extracts are known to have a variety of biological activities on other plants, raising the plausibility that these components can also have biological activities in other living organisms.

T. portulacastrum has served as a source of organic matter in diets. In Africa (especially Cameroon, Ghana and Tanzania), the young leaves of the plant are eaten as cooked vegetables or in soups[7]. In India and other countries within South-East Asia, during the rainy

seasons when *T. portulacastrum* growth is plentiful, it is commonly consumed in vegetable dishes. Interestingly, as the plant ages adverse effects related to ingestion have been described, particularly with the consumption of old leaves, which have been reported to cause diarrhea and paralysis[7]. This has been reported to occur not only in humans but also in domestic animals. Furthermore, the seeds of *T. portulacastrum* are also avoided as they are known to be harmful[7].

In addition to being used in various food preparations, *T. portulacastrum* as a whole as well as specific plant components has ethnomedicinal uses. For example, the root is commonly used in Africa, India, and Asia for diseases of the liver, spleen, and malignancy. Its leaves have been used as diuretics for the treatment of ascites and edema[10] and old leaves have been used in Nigeria for the treatment of gonorrhea[11]. Each of these disease-modulating attributes is due to different pharmacological and biological activities. Although several prior publications provide fragmentary overview of various phytochemical, morphological, pharmacognostical, ethnomedicinal and allelopathic attributes of *T. portulacastrum*[6,10,12–14], a systematic, comprehensive, and critical evaluation of literature to examine the full potential of this dietary and medicinal plant in health and disease has not been performed. In order to fill this gap in our knowledge, this article aims to provide a complete and up-to-date review of the known pharmacological and biological effects of *T. portulacastrum* implicated in the prevention, mitigation, and management of various acute and chronic disease conditions. Current limitation and future directions of research on this plant are also critically discussed.

2 Methods for literature search

An extensive literature search was conducted for all available literature. Searches were carried out using PubMed, Ovid, NextBio, and Google Scholar to identify scientific studies conducted with *T. portulacastrum* and its uses and properties related to disease prevention and therapeutic effects. There were no date restraints on the published literature. Only English language publications or reports with abstracts in English were considered for this work. Key words used in various combinations for literature searches included *Trianthema portulacastrum*, Aizoaceae, ethnomedicine, biological and pharmacological effects, and health benefits. The bibliography of the primary literature was also studied to find additional relevant publications.

3 Nutritive value

Nutrition is a fundamental requirement of humans for development, productivity, and overall health. As the earth's population continues to increase, so does the demand for food. Over 80% of vegetation used for consumption is based solely on twelve main crops, however in arid and semi-arid regions of the world, small local communities rely heavily on wild vegetation as a source of food, nutrients, and as medicine[15–17]. Hence, in this section the current data available on the nutritional value of *T. portulacastrum* will be discussed. This information is particularly important as *T. portulacastrum* is consumed by individuals in various regions of the world as a food and nutritional source.

3.1 Sources of energy (carbohydrate, protein, and lipid content)

Carbohydrates, proteins, and lipids provide energy in the form of calories, with carbohydrates and proteins contributing approximately 4 kCal/g each, and lipids approximately 9 kCal/g. Khan *et al*[16] recently investigated the carbohydrate content of *T. portulacastrum* and found that the content was much smaller amount compared to other edible plants such as sweet potato or spinach leaves. Bharathidhasan *et al*[18] found the crude protein content of *T. portulacastrum* to be approximately 21%, a value that is similar to leguminous forage. A more recent study found the percentage of protein contained per 100 g of *T. portulacastrum* to be lower, at 9%, however the authors concluded that *T. portulacastrum* was a good source of daily proteins. Additionally, it was also found that *T. portulacastrum* contains a low percentage of lipids at 2%, and a fiber content of 43% indicating that it is a good source of dietary fiber.

3.2 Vitamin and mineral content

Vitamins and minerals play key roles in the health and nutrition of individuals. Many are used as building blocks of tissues and organs, *e.g*., calcium and phosphorus in bones, while others are required as cofactors for enzymes and reactions that take place within the body. Many of these vitamins and minerals play such critical roles that the World Health Organization and United States Department of Agriculture provide recommended daily intake values. To compliment the information of *T. portulacastrum* nutritional values in regards to carbohydrates, lipids, and proteins, investigators have also explored the vitamin and mineral contents of *T. portulacastrum*.

It was demonstrated that *T. portulacastrum* provides a sufficiently high level of minerals, such as calcium, magnesium, manganese, iron, zinc, copper, and cobalt. Sodium and potassium levels were also high and were found in higher concentrations compared to other green leafy vegetables[16,18]. All of the above minerals were found in quantities above the critical level of recommended daily intake. However, phosphorus was found at lower concentrations that would require additional sources for supplementation. Also, the plant is a good source for

vitamin B3 and vitamin C[19]. Additionally, the toxic heavy metals cadmium and lead were found to be present in only trace amounts, and would not be of health concern[16,17].

4 Phytochemical constituents

The phytochemical analysis of *T. portulacastrum* has been shown to contain various categories of secondary metabolites, such as saponins, steroids, alkaloids, flavonoids, terpenes, benzoic acid derivatives and cinnamic acid derivatives. Figure 2 shows the structural diversity of the compounds isolated from *T. portulacastrum*[20–22].

Nawaz *et al*[20] have isolated a novel tetraterpenoid from the chloroform extract, which was named as trianthenol. The authors established the structure as 15-hydroxymethyl-2,6,10,18,22,26,30-heptamethyl-14-methylene-17-hentriacontene by utilizing advanced structure identification analytical methods, such as two-dimensional nuclear magnetic resonance (NMR) and high-resolution mass spectrometry. Trianthenol is a 40-carbon atom molecule with 8 isoprene units and a *trans*-double bond, which is responsible for its *E*-configuration. Also, the authors reported the presence of a few previously identified compounds, such as 5-hydroxy-2-methoxy benzaldehyde, 4-methoxy benzoic acid, 4-propoxy benzoic acid and a pentacyclic triterpenoid 3-acetyl aleuritolic acid. Another tetraterpene, β-carotene, has also been isolated from the organic extracts[19].

Kokpol and coworkers[23], isolated plant sterols β-sitosterol, stigmasterol and their respective β-glucopyranosides from the organic extracts of the dried plant. They also isolated and confirmed the presence of a previously unknown flavonoid, 5,2′-dihydroxy-7-methoxy-6,8-dimethylflavone (*C*-methylflavone) and a previously identified flavone 5,7-dihydroxy-6,8-dimethylchromone (leptorumol) from the organic extracts through NMR and X-ray crystallography analysis. Plant steroid ecdysterone, also known as 20-hydroxyecdysone, has been isolated from the extracts of *T. portulacastrum*[24]. Quercetin and a number of benzoic and cinnamic acid derivatives, such as *p*-hydroxy benzoic acid, protocatechuic acid, vanillic acid, ferulic acid, caffeic acid, 3,4-dimethoxy cinnamic acid, *o*-coumaric acid and pyrogallol, have been reported from the extracts of *T. portulacastrum*[9]. The phytochemical investigation also revealed the presence of alkaloids, trianthemine and punarnavine[25]. β-Cyanin, the most

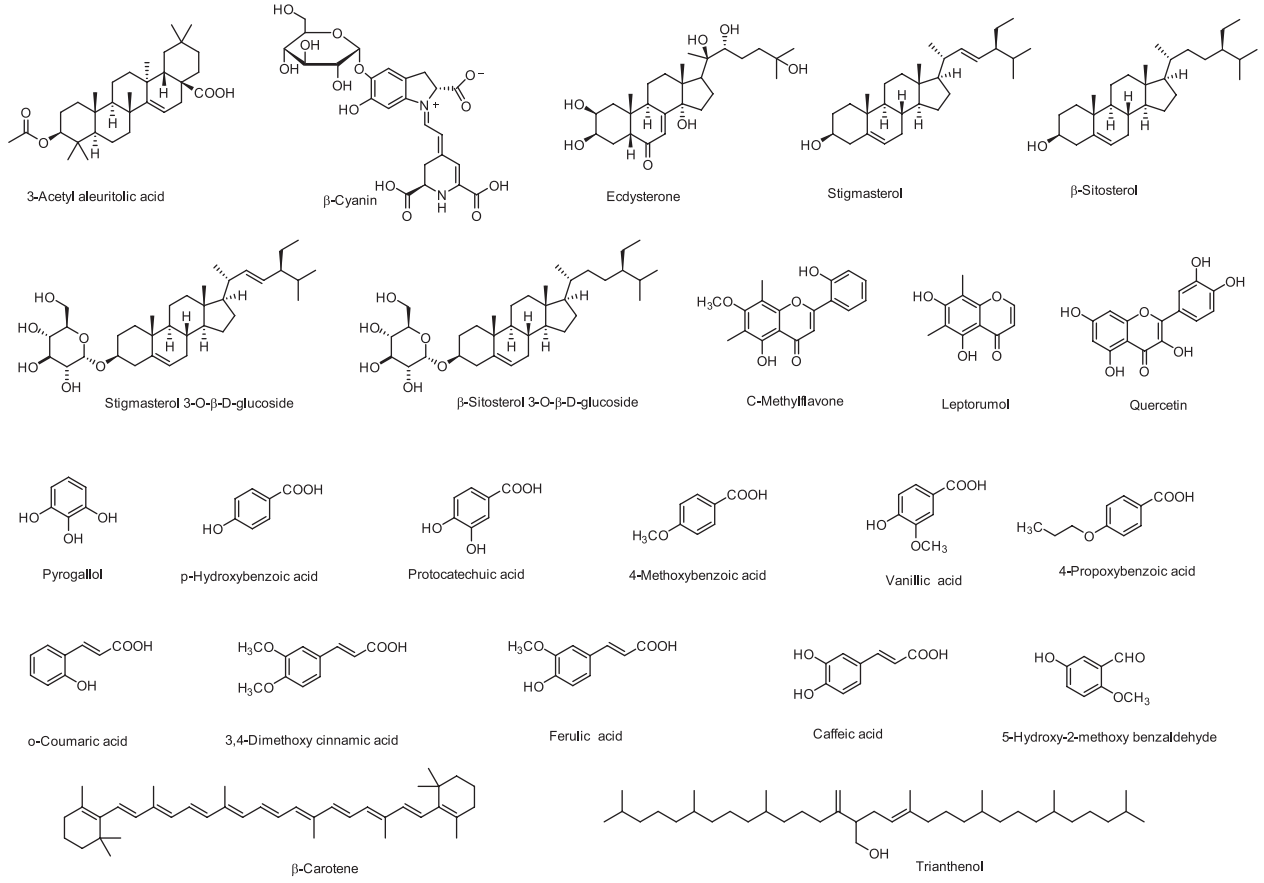

Figure 2 Structures of phytochemicals present in *Trianthema portulacastrum*

prevalent red pigment flavonoid present in several plant species, has also been reported in *T. portulacastrum*[26].

5 Pharmacological activities of *T. portulacastrum*

5.1 Antioxidant properties

It is known that oxidative stress can cause damage to tissues and cells within the body. Free radicals, such as nitric oxide, superoxide anions, and hydroxyl radicals, can result in oxidative stress and may inflict damage in almost every organ, including the eyes, brain, lungs, kidneys, and heart. Furthermore, certain cancers are thought to arise from excess reactive oxygen species (ROS) that can damage cellular DNA[27]. Hence, major focus has been traditionally placed on antioxidant properties of vitamins, fruits, and vegetables with the hope that products high in antioxidants may help to eradicate and offset deleterious effects of ROS.

The antioxidant potential of a methanolic whole plant extract of *T. portulacastrum* was investigated by 1,1-diphenyl-2-picryl hydrazyl (DPPH) and hydrogen peroxide assays. The results indicated that the methanolic extract possessed a concentration-dependent free radical-scavenging activity against DPPH and hydrogen peroxide radicals, which was comparable with standard ascorbic acid[28]. In another study, Yaqoob and colleagues[29] determined total phenolic constituents and antioxidant properties of hydrolysates of *T. portulacastrum* in acidified methanol utilizing *in vitro* DPPH radical-scavenging activity, inhibition of linoleic acid peroxidation, and ferric-reducing power. The root, shoot and leaf extracts of *T. portulacastrum* were found to contain 50.75–98.09 mg gallic acid equivalents per gram dry weight. These fractions also exhibited substantial reducing potential abilities to inhibit peroxidation and DPPH radical-scavenging capabilities.

5.2 Anti-inflammatory activities

Inflammation is the body's normal response and defense to infections, and in controlled fashion can prevent disease. However, if inflammation is not closely controlled, chronic diseases can arise and have detrimental effects to the host. States of chronic inflammation have been associated with disease states such as diabetes[30], coronary heart disease[31], and cancer[32,33]. The possible anti-inflammatory response of ethanolic extract of the whole plant of *T. portulacastrum* was evaluated against formaldehyde-induced arthritis in rats. The extract at 100 mg/kg (i.p.) elicited a significant inhibition of chemically-induced arthritis, indicating its anti-inflammatory potential[34]. In a recent study using the same dose of 100 mg/kg of ethanolic extract, Kendri *et al*[35] confirmed the above findings. In a rat model of acute inflammation of the paw induced by carrageenin and a formalin-induced peritonitis model, the *T. portulacastrum* extract significantly reduced the amount of edema present in the paws of treated rats, as well as significantly decreased exudate formation in the peritonitis model.

5.3 Antimicrobial properties

Within the past decade a number of multidrug resistant organisms have emerged and pose an immediate public health threat[36]. Compounding this problem further is the lack of interest and investment from pharmaceutical companies in developing new antibiotics due to the low return on investment when novel antibiotics become available[37]. Hence, with the lack of investment and elevated public health risk, exploration of natural compounds as antimicrobial medications or structural backbones for novel antimicrobial compounds should be explored.

Anti-infective effects of *T. portulacastrum* have been studied by a number of investigators. Extracts from this plant have demonstrated significant activity against Gram-positive and Gram-negative bacteria, fungi, and helminthes. *T. portulacastrum* extract has been demonstrated to have activity similar to standard therapies against all of the above organisms. In one of the earlier studies, Vohora and coresearchers[34] found that an ethanolic extract of the whole plant of *T. portulacastrum* exhibited moderate antibacterial activities predominantly against Gram-positive organisms.

Nawaz *et al*[20] identified a tetraterpenoid compound by chloroform extraction of *T. portulacastrum*, now referred to as trianthenol-1. The investigators performed *in vitro* antifungal susceptibility bioassays to test for activity against common fungal pathogens, comparing crude extract, purified trianthenol-1, and the standard drugs, namely miconazole and ketoconazole. Overall, trianthenol-1 inhibited growth of all fungal organisms tested, ranging from 40% to 70% growth inhibition depending on the organism. Trianthenol-1 also displayed superior antifungal activity when compared to crude extract. While both the crude extract and purified trianthenol-1 demonstrated antifungal activity, it should be considered to have only a moderate effect, as miconazole and ketoconazole demonstrated 90%–100% growth inhibition of organisms tested[20].

More recently, it was found that both the methanolic and chloroform extracts of *T. portulacastrum* had antifungal activity against a number of human fungal pathogens, including *Aspergillus spp, Candida albicans* and *Rhizopus oryzae*. However, no activity was observed against *Mucor spp*. Further investigation identified that the main antimicrobial effects were found in the flavonoid fraction of extracts[22]. The same group also investigated the antibacterial effects of the methanolic, aqueous, and chloroform extracts of *T. portulacastrum* against some important human bacterial pathogens, namely *Pseudomonas aeruginosa*, *Staphylococcus aureus,*

Klebsiella pneumoniae, *Salmonella typhi, Shigella flexneri* and *Escherichia coli*. Importantly, the bacterial isolates tested were clinical isolates giving a more "real world" representation. Initial antibacterial activity screening was performed with agar well diffusion of the three extracts, followed by minimum inhibitory concentration (MIC) and minimum bactericidal concentration (MBC) testing of the most potent extract—the methanolic extract. The MICs and MBCs of the methanolic extract ranged from 1.25 to 2.5 mg/mL of the tested bacteria; however no extract was found to have activity against *Klebsiella pneumoniae*[22]. Phytochemical analysis of the methanolic extract of leaves revealed the presence of alkaloids, flavonoids, phenols, steroids and terpenoids. The antimicrobial activity of isolated alkaloid, flavonoid, and phenol fractions was further explored for their antibacterial and antifungal activity, where it was found that the flavonoid extract exhibited the strongest antibacterial and antifungal activities followed by the alkaloid extract and then the phenolic extract[22].

The antimicrobial effects of the methanolic extract of *T. portulacastrum* described above confirmed observations originally made by Hussain *et al*[38], where the investigators tested the *in vitro* and *in vivo* effects of methanolic extract on gastrointestinal nematodes that affect sheep. The extract was not only lethal to *Haemonchus contortus* and *Musa paradisiaca in vitro* but also inhibited egg hatching. *In vivo*, both powder and methanolic extract forms of *T. portulacastrum* caused a reduction in eggs per gram of feces in sheep, as well as a decrease in larvae present in sheep feces compared with nontreated controls.

While the above studies have demonstrated moderate antimicrobial effects against a number of human and animal pathogens, the concentration at which the activity was observed is quite high. For example, most antimicrobial therapies used in allopathic medicine exhibit inhibitory activity at μg/mL concentrations, while in the study of Kavitha and colleagues[22] concentrations of mg/mL were required. Thus, extracts of *T. portulacastrum* would not likely be sufficient for antimicrobial therapy, as reaching such high serum concentration in patients would require very high doses. However, these data suggest that the phytochemical constituents of *T. portulacastrum* may provide a source of lead molecules for drug discovery that can be used in developing novel therapeutics for the treatment of infectious diseases.

5.4 Analgesic and antinociceptive activity

In Indian and other traditional medicines, *T. portulacastrum* has been prepared in teas for its perceived analgesic properties. Several investigators tested the efficacy of *T. portulacastrum* in preventing writhing and pain sensation using murine models. Ethanolic extract of *T. portulacastrum* at 100 mg/kg caused a significant increase in the voltage threshold of mice in a pododolorimeter. The extract also elicited a significant reduction in the acetic acid-induced writhing episodes in mice. However, the tail clip and caudal immersion techniques failed to demonstrate analgesic activities[34]. In a separate study, an ethanolic extraction of *T. portulacastrum* whole plant was found to exhibit analgesic activity in mice. It was found that acetic acid writhing of mice's paws was reduced in a dose-dependent manner, where 250 mg/kg of the extract exhibited similar effects to that of aspirin. The same investigators also determined antinociceptive activity by hot-plate reaction time method in mice. The ethanolic extract showed significant antinociceptive action and the effect was comparable to standard aspirin-treated controls, suggesting *T. portulacastrum* is a centrally acting analgesic[39].

5.5 Antipyretic activity

Pyrexia or fever, which is commonly defined as a temperature of ≥38.3 °C, is a natural innate immune response typically associated with infections and results from the synthesis of prostaglandins by cyclooxygenase[40,41]. While this response can be beneficial during acute infections, prolonged high fever can have detrimental effects such as dehydration, seizures, and increased risk of death in critically ill patients[40]. The antipyretic effects of *T. portulacastrum* has been investigated by Vohora *et al*[34]. In their experiments, yeast-induced stable pyrexia in rats was suppressed by ethanolic extract from *T. portulacastrum* (50 mg/kg, i.p.) and this effect was comparable to that of sodium salicylate.

5.6 Antihyperglycemic effects

Diabetes is a metabolic disorder that is characterized by hyperglycemia due to lack of insulin production and/or insulin resistance in peripheral tissues. If left uncontrolled and allowed to continue to progress, a number of serious complications can arise, including micro- and macro-vascular complications. As the incidence of diabetes continues to increase in the United States and around the world and the dangers associated with diabetes medications such as the thiazolidinediones, novel therapeutics for diabetes have been explored from plant sources, including *T. portulacastrum*[42,43].

Methanolic extracts of whole plant *T. portulacastrum* have been found to induce antihyperglycemic effects in diabetic rats. Shyam Sunder *et al*[26] explored the effects of methanolic extracts on streptozotocin-induced diabetic rats that demonstrated serum glucose levels above 200 mg/dL. The investigators found that the diabetic rats treated with 100 and 200 mg/kg of methanolic extract had statistically significant reductions in overnight plasma blood glucose levels at 1 h after oral administration compared to non-treated controls, with the 200 mg/kg dose having a stronger antiglycemic effect. The effects of the methanolic extract at both doses were more pronounced at 4 and 8 h

post-administration. Relative to the treatment a control group that received the drug glibenclamide, both the 100 and 200 mg/kg had less antiglycemic effects. At 4 h post-dose, the glibenclamide group had a 37.4% reduction in plasma glucose concentration, while the 100 and 200 mg/kg doses had reductions of 23.8% and 29.9%, respectively.

Anreddy *et al*[44] later confirmed the antihyperglycemic effects observed in the previous study. This group also used the methanolic extract of *T. portulacastrum* and investigated its antihyperglycemic potential in alloxan-induced hyperglycemia in rats. The methanolic extract was given orally at 100, 200 and 300 mg/kg and compared to the untreated (diabetic control) and glibenclamide (standard oral hypoglycemic agent)-treated control animals. All three extract-treated groups demonstrated significant reductions in plasma glucose levels after 1 day of treatment and further reduction occurred at days 3, 5, and 7. The most significant reduction in plasma glucose occurred in the 300 mg/kg treatment group, which had an even greater reduction in plasma glucose than the glibenclamide treatment control group.

The studies above, which are also summarized in Table 2, demonstrated that in a controlled test environment *T. portulacastrum* could cause a reduction in plasma glucose. This reduction in glucose was similar to that of the positive control glibenclamide, which is a therapeutic agent used in the treatment of diabetes. Thus, these data give rise to the potential identification of phytochemical constituents that may be further developed as novel therapeutics. Additional studies are necessary to determine what compounds present in *T. portulacastrum* are responsible for the antiglycemic effects. Furthermore, the mechanism of action by which glucose is lowered should be investigated, for example whether *T. portulacastrum* causes increases in insulin secretion or increases insulin sensitivity in tissues.

5.7 Antifertility activity

It has been claimed that *T. portulacastrum* possesses antifertility activity and has been used by Indian tribes and rural communities as an abortifacient and contraceptive. This effect is thought to be due to the steroid, ecdysterone, which is a major chemical constituent of *T. portulacastrum*[10]. Initial reports of the hormonal activity of *T. portulacastrum* were obtained through *in vivo* models using insects[45,46]. More recently, investigation into the steroid effects of *T. portulacastrum* was explored in a mammalian rodent model. Pare *et al*[11] explored the potential abortifacient effects of the aqueous, chloroform, and alcoholic extracts of *T. portulacastrum* stem, leaves, and roots in albino rats. All extracts were found to exhibit significant pregnancy interceptive activity. A dose of 400 mg/kg body weight of aqueous, chloroform, and alcoholic extracts showed 64%, 73% and 94% abortifacient activity, respectively. Lower doses of 100 and 200 mg/kg showed approximately 23% and 48% abortifacient activity, respectively. The percent fetal resorption index increased from zero in the control group to 94.02% in the 400 mg/kg body weight of alcoholic extract-treated rats[11]. Thus, this study, through controlled experimentation in a mammalian model, supports the claim of abortifacient activity of *T. portulacastrum*.

While the above study demonstrated that *T. portulacastrum* can exhibit antifertility effects likely due to the steroid component, ecdysterone, it should be noted that this was only found in an animal model and this observation may not necessarily occur in humans. As

Table 2 Biological and pharmacological effects of *Trianthema portulacastrum*

Test material	Animal model	Biological endpoints	Dose; duration	Route	Reference
Aqueous, chloroform and alcoholic extracts of whole plant	Female Wistar rats	↑Embryo resorption; ↑uterine weight; ↑diameter of the uterus; ↑thickness of endometrium; ↑abortifacient activity	100, 200 and 400 mg/(kg·d); for 5 d	p.o.	Pare *et al*, 2013[11]
Aqueous solution of whole plant	Albino rats and mice	↑Urine output; ↑diuretic index; ↑Lipschitz value (rats); no toxicity (mice)	10, 30 and 50 mg/kg	i.p.	Asif *et al*, 2013[21]
Methanolic extract of whole plant	Male and female Lohi sheep	↓*Haemonchus contortus* eggs per gram of feces	1, 4, and 8 g; biweekly for 15 d	p.o.	Hussain *et al*, 2011[38]
Methanolic extract of whole plant	Male Wistar albino diabetic rats (streptozocin-induced)	↓Plasma glucose	100 and 200 mg/kg over 8 h	p.o.	Shyam Sunder *et al*, 2009[26]
Methanolic extract of whole plant	Diabetic Wistar rats (alloxan-induced)	↓Plasma glucose; ↓total cholesterol; ↓triglycerides; ↑high-density lipoprotein	100, 200 and 300 mg/kg	i.p.	Anreddy *et al*, 2010[44]

mentioned above, the effects of ecdysterone in mammals have been evaluated, and the effects observed were not found in human subjects when studied[47].

5.8 Diuretic properties

Cardiovascular disease is a major cause of morbidity and mortality throughout the world and uncontrolled hypertension can lead to a number of other types of disease states such as stroke, congestive heart failure, and microvascular complications[48]. A number of different types of pharmacological agents are currently available for the treatment of hypertension, such as angiotensin-converting enzyme inhibitors, β-blockers, calcium channel blockers, and diuretics. Current recommendations by the American Academy of Family Physicians list diuretics as the first-line therapy for the treatment of hypertension, since they have been shown to significantly decrease morbidity and mortality outcomes in patients with hypertension[49]. Diuretics work by stimulating urine output, leading to a decrease in fluid retention resulting in a decrease in blood pressure.

A myriad of plants and herbs are known to cause diuresis and are used for ethnomedicinal purposes, such as decreasing blood pressure through their diuretic and natriuretic effects. Controlled studies now exist, demonstrating the effects of many of the plants used for the purpose of diuresis including a study with the use of *T. portulacastrum*.

The use of *T. portulacastrum* as a diuretic has been common practice in India and Pakistan. However, as with many traditional and ethnomedicinal practices, no literature was available supporting this activity. Recently a group of investigators explored the diuretic activity *in vivo* with the use of albino rats and crude aqueous extracts of *T. portulacastrum*[21]. The authors compared three different doses of the crude extract, such as 10, 30 and 50 mg/kg, with a nontreatment control group and a group of mice treated with the high-ceiling loop diuretic, furosemide at 10 mg/kg. Parenteral (i.p.) administration of crude extract of *T. portulacastrum* increased urinary flow in a dose-dependent manner. When compared with the non-treatment control group, the groups receiving 10, 30, and 50 mg/kg of *T. portulacastrum* extract had approximately a 2, 3 and 5 times increase in urine output, respectively. The diuretic index values (mean urine volume of experimental group/ mean urine volume of control group) of the 10, 30 and 50 mg/kg groups were 1.95, 3.06 and 5.09, respectively, indicating good diuretic activity. Furthermore, *T. portulacastrum* extract also induced natriuretic effects; in fact the 50 mg/kg group excreted more sodium than the furosemide reference group. Overall, the 50 mg/kg dose of extract had the most diuretic activity almost equivalent to the furosemide 10 mg/kg dose. Similar results of the diuretic properties of *T. portulacastrum* were found in a study conducted by Karim and colleagues[50].

In another study exploring the antilithiatic effects of *T. portulacastrum* conducted by Sree and colleagues[51], similar results were obtained. It was found that in male Wistar rats with experimentally induced urolithiasis, urine output, urine concentrations of calcium, phosphate, magnesium, and oxalate, and serum parameters related to proper kidney function, including creatinine, uric acid, and blood urea nitrogen (BUN) levels were restored to near normal values after treatment with 200 and 400 mg/kg of ethanolic extracts of *T. portulacastrum*. The authors speculate that the results observed may be due to the diuretic properties and phytochemical constituents of *T. portulacastrum*.

The mechanisms behind the diuretic activities of *T. portulacastrum* are not known. However, it is likely due to one or more of the phytochemical constituents of the plant. One study using a different plant known for its diuretic activities, *Orthosiphon stamineus*, found that its activity was due to flavonoid binding with adenosine A1 receptors[52]. While others have also shown that diuretic activity might be consequence of alkaloids, caffeine, terpenes, and phenolics[53]. Thus, the precise molecular and cellular mechanisms still remain to be elucidated and should be further explored for the development of novel diuretics.

5.9 Hepatoprotective effects

Several laboratories investigated potential protective or repairing effects of *T. portulacastrum* against various acute and chronic models of liver damage in rodents (Table 3). In one of the initial studies, Bishayee and colleagues[54] reported that oral administration of an ethanolic extract at a dose of 50, 100 or 150 mg/kg for 3 d in concomitant with alcohol-carbon tetrachloride (CCl_4) treatment lowered serum enzymatic activities of aspartate aminotransferase (AST), alanine aminotransferase (ALT), lactate dehydrogenase (LDH), alkaline phosphatase (ALP), sorbitol dehydrogenase (SOD) and glutamate dehydrogenase, decreased serum levels of bilirubin and urea, and improved hepatic histopathological indices. The extract also dose-dependently prevented the elevation of hepatic malondialdehyde formation (indicative of lipid peroxidation) and depletion of reduced glutathione (GSH) content in mice subjected to alcohol-CCl_4-mediated acute liver damage[54].

The same investigators confirmed the hepatoprotective activity of *T. portulacastrum* extract against CCl_4-evoked chronic liver damage in mice. In addition to restoring aforementioned serum enzymatic activities, the extract normalized γ-glutamyl transpeptidase, 5′-nucleotidase, acid phosphatase, acid ribonuclease, glucose-6-phosphatase, succinic dehydrogenase and adenosine 5′-triphosphatase (ATPase) activities. The observed antihepatotoxic effect of *T. portulacastrum* extract was comparable to that of silymarin, a standard hepatoprotective drug[55]. To understand the underlying

Table 3 Hepatoprotective effects of *Trianthema. portulacastrum* in preclinical animal models of liver damage

Test material	Animal model	Biological endpoints	Dose; duration	Route	Reference
Ethanolic extract of aerial parts	Alcohol-CCl_4-induced acute liver damage in male Swiss albino mice	↓AST; ↓ALT; ↓LDH; ↓ALP; ↓SOD; ↓GLDH; ↓bilirubin; ↓urea; ↓lipid peroxidation; ↑GSH;	50, 100 and 150 mg/kg; once daily for 3 d	p.o.	Bishayee *et al*, 1996[54]
Ethanolic extract of aerial parts	CCl_4-induced chronic liver damage in male Swiss albino mice	↓AST; ↓ALT; ↓LDH; ↓ALP; ↓SOD; ↓GLDH; ↓GGT; ↓5′-NT; ↓ACP; ↓ACR; ↓G-6-pase; ↓SDH; ↓ATPase; ↓bilirubin; ↓urea; ↓lipid peroxidation; ↑GSH; ↓GSSG; ↑GSH/GSSG; ↓CAT; ↓GPX; ↑GR; ↓GST; ↓ESR; ↑albumin; ↓globulin	100 and 150 mg/kg; once daily for 7 weeks	p.o.	Mandal *et al*, 1997 and 1998[55–57]
Ethanolic extract of aerial parts	CCl_4-induced acute and chronic hepatotoxicity in Swiss male albino mice	↓DNA chain breaks; ↓chromosomal aberrations	150 mg/kg; once daily for 2–13 weeks	p.o.	Sarkar *et al*, 1999[58]
Ethanolic extract of leaves	Paracetamol- or thioacetamide-induced liver disorders in male and female Wistar rats	↓AST; ↓ALT; ↓ALP; ↓bilirubin; ↓total protein; lipid peroxidation; ↑GSH; ↑Na^+-K^+-ATPase; ↑GR; ↑GPX; ↑GST, ↑SOD; ↑CAT	100 and 200 mg/kg; once daily for 10 d	p.o.	Kumar *et al*, 2004[59] and 2005[60]
Ethanolic extract of leaves	AFB1-induced hepatic damage in male Wistar rats	↓AST; ↓ALT; ↓ALP; ↓LDH; ↓lipid peroxidation; ↑CAT; ↑SOD; ↑GPX; ↑GR; ↑G6PD; ↑GST; ↑GSH; ↑Vit. C; ↑Vit. E	100 mg/kg; once daily for 7 d	p.o.	Sharmila Banu *et al*, 2009[61]
Ethanolic extract of leaves	AFB1-induced hepatic damage in male Wistar rats	↓AST; ↓ALT; ↓ALP; ↓bilirubin	50–800 mg/kg; 4 times in 12 h	p.o.	Sharmila Banu *et al*, 2009[62]
Methanolic extract of whole plants	Atherosclerotic diet-induced liver disorder in male Wistar rats	↓AST; ↓ALT; ↓ALP; ↓LDH; ↑albumin; ↓total cholesterol; ↓triglyceride	100 and 200 mg/kg; one week	p.o.	Shyam Sunder *et al*, 2010[63]

ACP: acid phosphatase; ACR: acid ribonulease; AFB1: aflatoxin B1; ALP: alkaline phosphatase; ALT: alanine aminotransferase; AST: aspartate aminotransferase; ATPase: adenosine 5′-triphosphatase; CAT: catalase; CCl_4: carbon tetrachloride; ESR: erythrocyte sedimentation rate; GGT: γ-glutamyl transpeptidase; GLDH: glutamate dehydrogenase; G-6-Pase: glucose-6-phosphatase; G6PD: glucose-6-phosphate dehydrogenase; GPX: glutathione peroxidase; GR: glutathione reductase; GSH: glutathione; GSSG: oxidized glutathione; GST: glutathione *S*-transferase; LDH: lactate dehydrogenase; 5′-NT: 5′-nucleotidase; SDH: succinic dehydrogenase; SOD: sorbitol dehydrogenase.

mechanisms of the hepatoprotective activity, Mandal and colleagues[56] investigated the effects of the extract on antioxidant and free radical defense system in mice following chronic CCl_4 intoxication. The extract therapy lowered hepatic lipid peroxidation, increased GSH, decreased oxidized glutathione, inhibited catalase (CAT), glutathione peroxidase (GPX) and glutathione S-transferase (GST) and induced glutathione reductase (GR) activity, indicating involvement of antioxidant defense mechanisms. The chronic administration of CCl_4 alone manifested hepatocellular necrosis, severe anemia, leucopenia, lymphocytopenia, neutrophilia, eosinophilia and hemoglobinemia along with an alteration of plasma albumin and globulin. All these effects were reversed following the extract treatment.

Oral feeding of the extract restored CCl_4-induced alterations of the hematological parameters to near normal levels[57]. These results suggest that the hepatoprotective effect of *T. portulacastrum* could be achieved by its critical involvement in modulating several key factors associated with erythropoiesis and the augmentation of general immunity of CCl_4-intoxicated animals. Sarkar and coinvestigators[58] explored antigenotoxic mechanism of action of *T. portulacastrum* during CCl_4-induced acute and chronic hepatic injury in mice. In the acute model, CCl_4 treatment produced a substantial increase in aberrant single-stranded DNA regions, showing the direct DNA damaging potential of this hepatotoxin. In contrast, a significant decrease in the total single-stranded DNA population was observed in the extract-treated mice. Chronic administration of CCl_4 increased the frequency of mouse liver structural chromosomal aberrations and *T. portulacastrum* extract offered unique protection against the induction of chromosomal anomalies. Ancillary *in vitro* experiments showed that the extract afforded protection against CCl_4-induced Fe-dependent DNA

sugar-base damage in purified mouse liver chromosomal DNA.

The hepatoprotective activity of *T. portulacastrum* has been confirmed in other chemically induced liver disorder models in rats. The ethanolic extract of dried leaves of *T. portulacastrum* demonstrated a dose-dependent protective effect against paracetamol (acetaminophen)- or thioacetamide-induced hepatocellular damage in rats as reflected in serum biochemical parameters, such as AST, ALT, ALP, bilirubin and total protein[59]. In a follow-up study, the same investigators found that *T. portulacastrum* extract increased GSH level in blood and liver and reversed the lipid peroxidation and activities of Na^+-K^+-ATPase, GR, GPX, GST, SOD and CAT in the liver in paracetamol- or thioacetamide-intoxicated animals[60].

Oral administration of aflatoxin B1 (AFB1), a potent hepatotoxin and hepatocarcinogenic agent, was found to inflict liver damage in rats as indicated by elevated AST, ALT, LDH and ALP activities in serum. AFB1 also increased lipid peroxidation, reduced CAT, SOD, GPX, GR, glucose-6-phosphate dehydrogenase and GST activities and depleted nonenzymatic antioxidants, namely GSH, vitamin C and vitamin E in the liver. Pretreatment of AFB1-exposed rats with *T. portulacastrum* ethanolic extract reversed the aforementioned conditions, indicating hepatoprotection. Interestingly, the results were comparable to that of silymarin[61]. In an extended study, the same authors reported that the extract (50–800 mg/kg) administered 4 times within 12 h exerted hepatoprotection against AFB1-initiated liver damage as reflected in serum biochemical markers and histopathological characteristics[62].

Shyam Sunder *et al*[63] investigated the protective effect of methanolic extract of *T. portulacastrum* in atherosclerotic diet-induced hepatic toxicity in rats. The experimental diet, consists of 4% cholesterol, 1% cholic acid and 0.5% thiouracil, induced atherosclerosis and hyperlipidemia in rats by elevating serum total cholesterol and trigyceride and also produced early fatty changes in the liver. Treatment of rats with *T. portulacastrum* extract elicited a marked reduction in serum lipid levels and protected against hepatic damage caused by the atherosclerotic diet. The beneficial role of the extract was confirmed by the reduced serum enzyme activities and bilirubin level.

5.10 Nephroprotective effects

Nephroprotective effects have also been explored with the use of *T. portulacastrum* extracts. In one study, the protective effect of a methanolic extract of *T. portulacastrum* against atherosclerotic diet-induced renal damage was investigated. It was found that the experimental diet resulted in glomerulosclerosis/nephropathy, which was ameliorated by the extract at 100 or 200 mg/kg[63]. Balamurugan *et al*[64] administered gentamicin, an aminoglycoside, to albino Wistar rats to induce nephrotoxicity. The authors explored the nephroprotective effect of an ethanolic extract of *T. portulacastrum*, which was administered to the animals at a dose of 200 mg/kg and a concomitant dose of 100 mg/kg gentamicin for 14 d. Histopathology and biomarkers of kidney injury were compared between the untreated control group and the group that received the extract. Urine creatinine, serum creatinine, blood urea, BUN and kidney weight were found to be significantly increased in the gentamicin only treated group compared to the extract treated group. Urine volume output was also significantly increased in the group treated with the extract, indicating properly functioning kidneys. Additionally, *in vitro* antioxidant activities, such as DPPH-free radical-scavenging and nitric oxide radical-scavenging activities, were compared to that of ascorbic acid. While the ethanolic extract demonstrated antioxidant and DPPH-free radical-scavenging activity, the 50% effective concentration was significantly higher than that of ascorbic acid[64]. The authors therefore concluded that the nephroprotective effects observed were likely due to antioxidant and free radical-scavenging activity.

Finally, Karim *et al*[65] explored the nephro-protective effects in an experimental model of adriamycin-induced nephrotic syndrome. In this study, rats were divided into groups of 10 animals each, with groups consisting of untreated controls, an adriamycin-treated (7.5 mg/kg) group, and adriamycin-exposed groups that received treatment with an ethanolic extract of *T. portulacastrum* at two different doses, 450 and 900 mg/kg, pre- or post-adriamycin administration for 20 d. Compared to untreated controls, adriamycin administration produced histopathological changes in the kidney, and proteinuria, increased the serum cholesterol, creatinine, and BUN, and decreased the serum albumin and protein . Administration of the ethanolic extract of *T. portulacastrum* at both doses reduced the serum cholesterol, creatinine and BUN, and increased the serum albumin and serum protein levels. Histopathological examination of kidneys demonstrated significant changes in adriamycin-treated groups compared to untreated controls, such as increase of mesengial cell proliferation, glomerular inflammation, atrophy, interstitial congestion, and ischemia. *T. portulacastrum* treatment reduced these histopathological changes in both the pre- and post-treatment groups.

5.11 Cancer-preventive and therapeutic properties

Since *T. portulacastrum* exhibited potent hepato-protective activities against hepatic damage induced by various hepatotoxins, several studies investigated its chemopreventive potential against chemically induced hepatocarcinogenesis in animals (Table 4). Bhattacharya

and Chatterjee[66] demonstrated for the first time that an aqueous, chloroform and ethanolic extract of aerial parts of *T. portulacastrum* reduced the incidence, multiplicity, size and volume of macroscopic hepatic nodules in rats exposed to diethylnitrosamine (DENA), a dietary and environmental carcinogen. In the same study, the morphometric analysis of focal lesions revealed that all extracts reduced the incidence and growth of microscopic altered liver cell foci in DENA-initiated rats. Interestingly, a maximum protection against DENA-induced hepatocellular carcinogenesis was achieved with the chloroform extract. The same authors reported that the aforementioned extracts depressed GSH level and GST activity, reduced lipid peroxidation (based on lower malondialdehyde level) and increased the activities of cytochrome P-450 and uridine diphospho glucuronyl transferase in the livers of DENA-treated animals compared to DENA control[67]. Once again, the chloroform extract was found to be the most effective in preventing microsomal oxidation and accelerating detoxification during experimental hepatocarcinogenesis. The same laboratory also investigated the chemopreventive efficacy of the chloroform extract against a two-stage rat liver carcinogenesis model employing DENA as the initiating agent and phenobarbital as a promoter. Dietary administration of the extract throughout the experiment (before and after DENA initiation), before initiation only or during promotional phase inhibited the appearance and growth of hepatic nodules and foci. The extract administered during the entire term of the experiment produced statistically significant results with aforementioned morphologic and morphometric parameters and also reversed DENA-induced hepatic histopathological alterations[68].

Recently, our laboratory has undertaken a comprehensive research initiative to explore chemopreventive potential of *T. portulacastrum* against 7,12-dimethylbenz(a)anthracene (DMBA)-induced rat mammary gland carcinogenesis, an experimental tumor model that mimics human breast cancer. We recently provided compelling evidence for the first time that dietary administration of an ethanolic extract of *T. portulacastrum* afforded a striking reduction of DMBA-initiated breast tumor incidence and total tumor burden with a simultaneous improvement of intratumor histopathological characteristics (Figure 3). The *T. portulacastrum* extract dose-dependently suppressed abnormal cell proliferation and induced apoptosis mediated through alteration of Bax/Bcl2 ratio. Mechanistically, the extract was capable of diminishing activated canonical Wnt/ β-catenin signaling to exhibit antiproliferative, proapoptotic and tumor-suppressive effects during DMBA-inflicted early stage breast cancer[69]. Very recently, Mandal and Bishayee[70] reported that the same extract down-regulated the expression of cyclooxygenase-2 and heat shock protein 90 (HSP90), blocked the degradation of inhibitory κBα,

Table 4 Biological effects of *Trianthema portulacastrum* in preclinical *in vivo* models of cancer

Test material	Animal model	Biological endpoints	Dose; duration	Route	Reference
Aqueous, ethanolic and chloroform extracts of aerial parts	DENA-induced hepatocarcinogenesis in male Sprague-Dawley rats	↓Nodule incidence and multiplicity; ↓nodular volume; ↓focal incidence and area	100 mg/kg; once daily for 22 weeks	p.o.	Bhattacharya *et al*, 1998[66]
Aqueous, ethanolic and chloroform extracts of aerial parts	DENA-induced hepatocarcinogenesis in male Sprague-Dawley rats	↓GSH; ↓GST; ↓lipid peroxidation; ↑CYP; ↑UDPGT	100 mg/kg; once daily for 22 weeks	p.o.	Bhattacharya *et al*, 1998[67]
Chloroform extract of aerial parts	DENA-initiated and phenobarbital-promoted hepatocarcinogenesis in male Sprague-Dawley rats	↓Nodule incidence and multiplicity; ↓nodular volume; ↓focal number and area	100 mg/kg; once daily for 4–20 weeks	p.o.	Bhattacharya *et al*, 1999[68]
Ethanolic extract of aerial parts	DMBA-induced mammary carcinogenesis in female Sprague-Dawley rats	↓Tumor incidence and weight; ↓PCNA; ↓cyclin D1; ↑apoptosis; ↑Bax; ↓Bcl-2; ↓β-catenin; ↓COX-2; ↓HSP90; ↓IκBα; ↓NF-κB; ↓Nrf2	50, 100 and 200 mg/kg; once daily for 18 weeks	p.o.	Bishayee *et al*, 2014[69]; Mandal *et al*, 2015[70]

COX-2: cyclooxygenase-2; CYP: cytochrome P-450; DENA: diethylnitrosamine; DMBA: 7,12-dimethylbenz(a)anthracene; GSH: glutathione; GST: glutathione *S*-transferase; HSP90: heat shock profein 90; IκBα: inhibitory κBα; NF-κB: nuclear factor-κB; Nrf2: nuclear factor erythroid 2-related factor 2; PCNA: proliferating cell nuclear antigen; UDPGT: uridine diphosphoglucuronyl transferase.

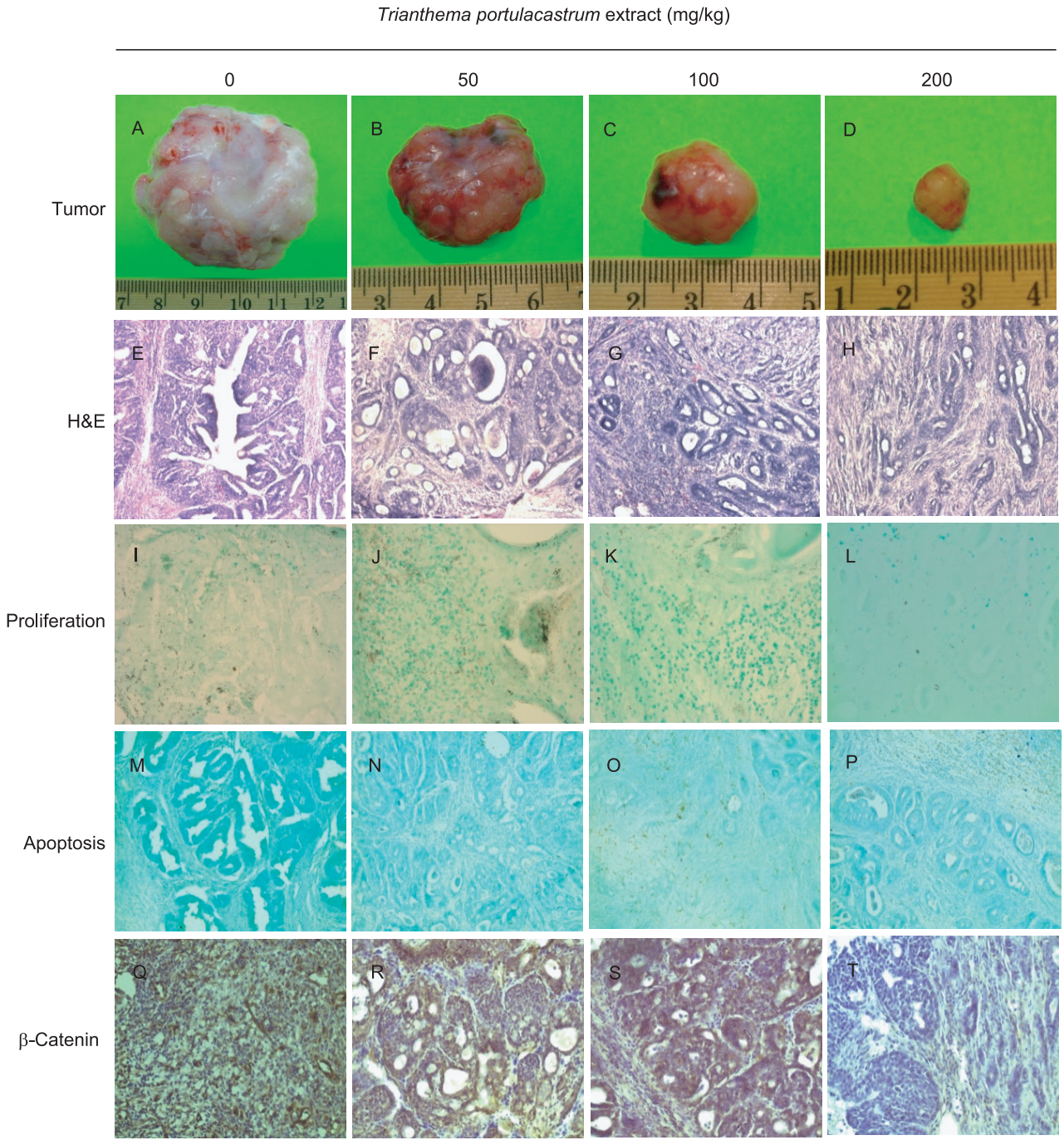

Figure 3 Chemoprevention of 7,12-dimethylbenz(a)anthracene-initiated rat mammary tumorigenesis by *Trianthema portulacastrum* extract

Effects of the extract on the size of mammary tumors (A–D), intratumor histopathological profiles (E–H), cell proliferation (I–L), apoptosis (M–P) and β-catenin protein expression (Q–T). The rats were treated with the extract orally two weeks prior to and 16 weeks following 7,12-dimethylbenz (a) anthracene administration. All animals were sacrificed 16 weeks following 7,12-dimethylbenz(a)anthracene exposure. The mammary tumors were subjected to morphological observation as well as histopathological (H&E) and immunohistochemical analysis using anti-proliferating cell nuclear antigen and antiβ-catenin antibodies. Apoptosis was detected by DNA fragmentation assay. Magnification: × 100 for H&E and apoptosis and × 200 for proliferation and β-catenin. Reproduced from reference 69 with permission.

hampered the translocation of NF-κB from cytosol to nucleus and upregulated the expression and nuclear translocation of nuclear factor erythroid 2-related factor 2 (Nrf2) during DMBA mammary carcinogenesis. These results suggest anti-inflammatory mechanisms of *T. portulacastrum* extract which may be mediated through simultaneous and differential modulation of two interconnected molecular circuits, such as NF-κB and Nrf2 signaling pathways

6 Toxicities

A number of studies have explored toxicities associated with large doses of various extracts of *T. portulacastrum*. Overall, toxicities were not observed in rats and mice in tested doses of up to 3 000 mg/kg. This was observed by two separate investigation[21,26]. It should also be noted that this dose is well beyond doses necessary to elicit any of *T. portulacastrum*'s physiological activities that were being explored in the studies described above. While the few studies discussed here demonstrated that *T. portulacastrum* to be nontoxic at high doses in rodent models, the limited number of studies exploring the area of toxicity represent a drawback and future exploration is encouraged.

7 Conclusion and future perspectives

Traditional/ethnomedicine is still a major modality by which much of the world populations treat ailments. However, for many of these herbal treatments, scientific evidence supporting their use is lacking and is thus warranted. Investigations into the mechanisms of natural remedies will have two benefits. One is producing evidence to support their use, and the other is providing potential for using identified active phytochemical compounds as leads for new drug discovery and development. *T. portulacastrum* is one of a number of plants being used as a natural remedy that has been investigated for its many perceived health benefits. In this article a number of different studies exploring the biological and therapeutic effects of *T. portulacastrum* have been described (Figure 4).

These studies describe the multitude of biological effects both *in vitro* and *in vivo* of *T. portulacastrum*. While in some cases, for example anti-infective effects, the activities of extracts are not particularly exciting as the concentrations needed to achieve activity are likely unachievable with conventional dosing. However, this opens the door to the possibility of isolating the active compound(s) and further developing it as a potent therapeutic drug. In other cases, such as diabetes, the extract demonstrated even greater activity in blood

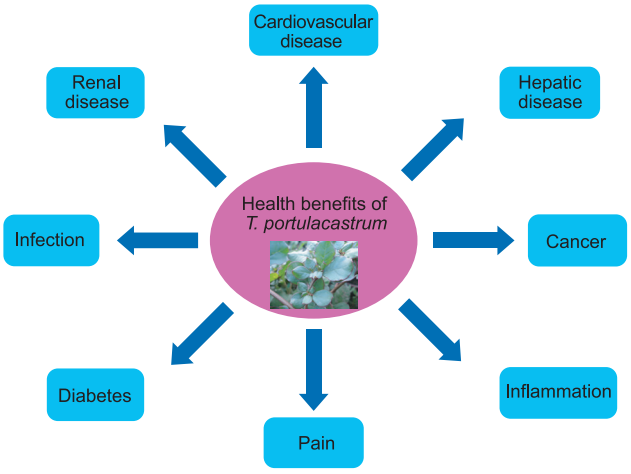

Figure 4 An overview of various biological and pharmacological activities of *Trianthema portulacastrum*

glucose reduction in mice than the commonly prescribed therapeutic, namely glibenclamide.

Perhaps the most intriguing research has occurred in the areas of organ protection and oncology. The antioxidant properties of *T. portulacastrum* have demonstrated beneficial effects in the protection against free radicals and damage to both kidneys and liver in *in vivo* rodent models. In a model of breast cancer *T. portulacastrum* was capable of diminishing activated canonical Wnt/β-catenin signaling to exhibit antiproliferative, proapoptotic and tumor-suppressive effects. Further exploration into the specific phytochemicals within *T. portulacastrum* extracts used may potentially lead to more potent and commercially produced therapeutics for the prevention of these disease states. However, without definitive well-designed clinical trials, recommending *T. portulacastrum* for specific ailments is not possible. Nonetheless, these studies have provided preliminary evidence in support of the ethnomedicinal uses of *T. portulacastrum* and demonstrated a need for well-designed clinical trials.

8 Competing interests

The authors declare that they have no competing interests.

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