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Review article

Nutritive value, biological properties, health benefits and applications of *Tetrapleura tetraptera*: An updated comprehensive review

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ABSTRACT

Due to the health benefits that medicinal plants present, they are applied in traditional healthcare in developing and developed countries alike. *Tetrapleura tetraptera,* a flowering plant mostly found in the western part of Africa has an essential chemical composition that gives it nutritive value and medicinal capacities. This review aims to highlight the nutritional attributes, biological properties, health benefits, and applications of *T. tetraptera*. The fruit of the plant has been revealed to possess about 58.48–63. 86% carbohydrates, 251.22–288.62 mg/g potassium, 182.11–200.02 mg/g calcium, 322.00–342.00 mg/g manganese, and 0.02–4.69 mg/g vitamins. Also, active phytochemical compounds including phenols (3.51 ± 0.03 mgGAE/g), flavonoids (0.87 ± 0.03 mgQE/g), saponins (4.27 ± 0.03 mgDE/g), tannins (23.87 ± 0.44 mg/100 g), and alkaloids (5.03 ± 0.15% w/w) have been discovered in the fruit of *T. tetraptera*. The plant's abundant phytochemicals account for its antioxidant, antimicrobial, anti-inflammatory, anti-diabetic, anti-parasitic, and anti-proliferative activities. These biological properties in turn translate to health benefits including lower blood pressure, enhanced immune system, malaria treatment, diabetes and hypertension management, and cancer prevention. The health-promoting assets of *T. tetraptera* underscore its applications in beverage production, food preservation and flavoring, feed supplementation, and pharmaceutical formulations. The data gathered in this piece is crucial for industrial food processing and the creation of potent pharmaceutical products and functional foods with superior health attributes.

1. Introduction

In both developed and developing nations, medicinal plants are employed in healthcare because they present health benefits and as such are known as natural healers. These plants are traditionally identified as harmless and are usually applied in the fight against long-standing diseases [1]. Since the ancient days, the preventive role of medicinal plants has been known to mankind and has been

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passed to generations within human communities [1]. Some commonly known medicinal plants are chamomile, echinacea, feverfew, garlic, ginkgo, and ginseng. Plants such as *Tetrapleura tetraptera* and *Moringa oleifera* can also be classified as such because they exhibit medicinal properties [2,3].

Tetrapleura tetraptera is a flowering-medicinal plant belonging to the Leguminosae family. It is a deciduous tree mostly found in the western part of Africa and is usually referred to as Aidan fruit in English [4]. Countries such as Ghana and Nigeria are common places where *T. tetraptera* can be obtained. It is known as "Prekese" and "Aridan" in the Twi and Yoruba languages of Ghana and Nigeria respectively [5]. *T. tetraptera* has a variety of chemical compositions that translate into its nutritive value. Significant amounts of various nutrients such as ash, fiber, proteins, carbohydrates, vitamins, and fats are present in *T. tetraptera* [4,6]. The chemical composition of the plant may vary at different parts of its fruit. For example, the carbohydrate and mineral contents of *T. tetraptera* fruit among the seeds, pulp, and woody coats are significantly different [7].

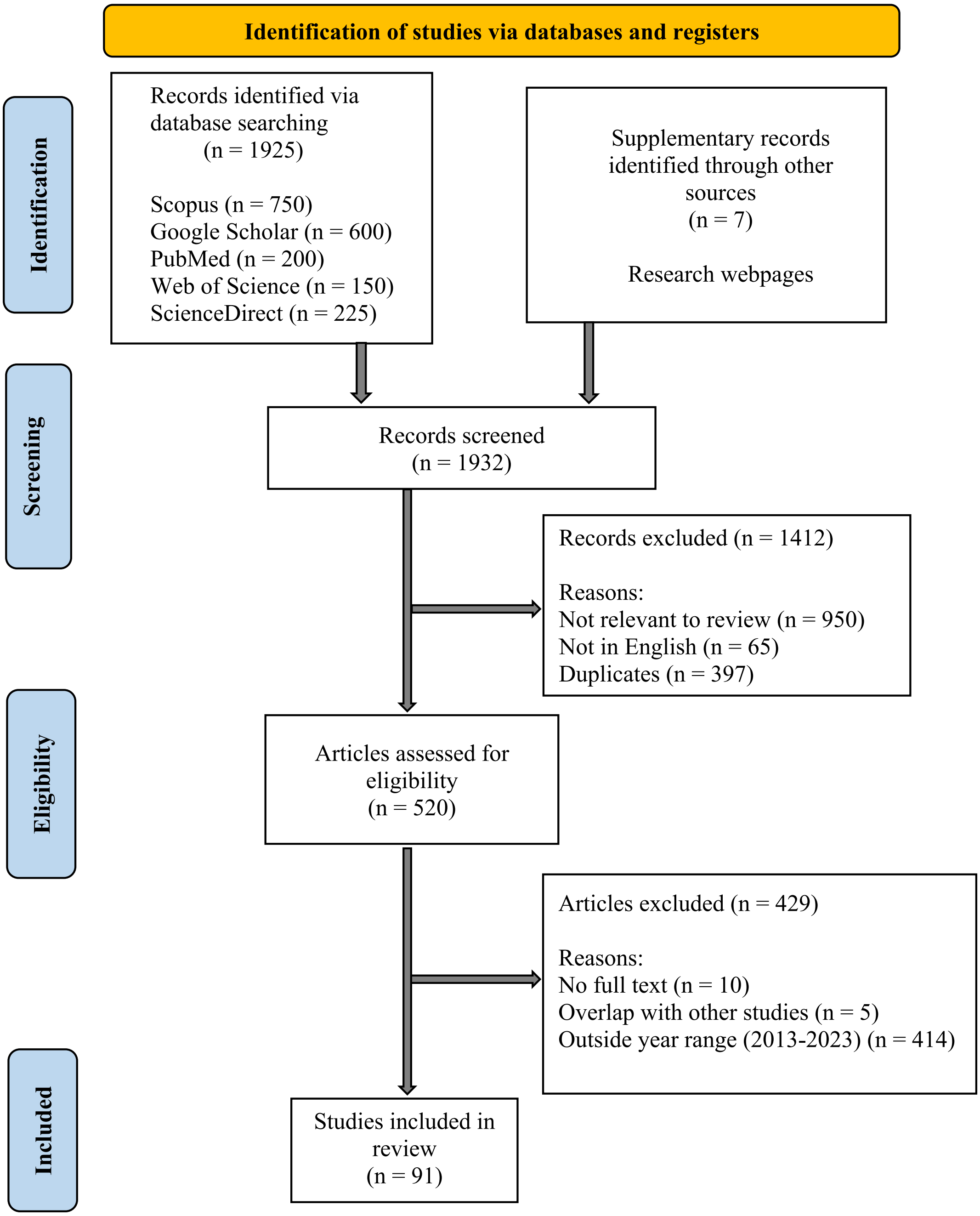

Fig. 1. Flowchart demonstrating data collection procedure for the study.

Similar to the nutritional composition, *T. tetraptera* possesses an essential concentration of phytochemicals such as tannins, alkaloids, steroids, flavonoids, triterpenoids, and phytate [5,8]. These bioactive naturally occurring organic compounds induce health benefits in humans compared to micronutrients and macronutrients [5]. The rich source of the aforementioned phytochemicals in *T. tetraptera* confers its pharmacological activities such as antimicrobial, hypoglycaemic, neuromuscular, molluscicidal, trypanocidal, and anti-ulcerative [9].

Due to the potential medicinal qualities and aroma exhibited by *T. tetraptera*, it is used in a variety of culinary delights. It is also applied in perfumes, pomades, alcoholic beverages, and biscuit production as a flavoring agent [5]. Extracts from *T. tetraptera* possess some biological properties such as antioxidant and anti-inflammatory properties that equip it with inhibitory effects towards some pathogens. *T. tetraptera* is employed in the regulation of convulsion, asthma, hypertension, rheumatic pains, leprosy, inflammation, and the relief of malaria fever [10]. The world health organization reported that 80% of people are still reliant on traditional medicine like herbs for the treatment of several diseases [11,12]. As such, it is germane to have information on the compositions of medicinal plants such *T. tetraptera* and how it confers different health benefits on consumers.

Given the chemical composition and biological properties of *T. tetraptera*, it has the potential to be used in ethnomedicine, pharmaceutics, and industrial food productions such as functional food formulations. Functional foods improve human health by combating malnutrition as well as acute and chronic ailments including cardiovascular diseases, cancer, and diabetes [13,14]. They can be used as a food supplement providing essential nutrients to the human body. Established that *T. tetraptera* contains many phytochemical compounds, essential functional nutrients, and numerous biological activities, the plant has a huge potential to serve as potent functional food inducing functional actions in a host biological system. This review thus seeks to explore the nutritive value, biological properties, health benefits, and applications of *T. tetraptera* in essential fields of mankind.

2. Methodology

This review study was conducted following the accepted PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analysis) standards [15]. Five major scientific databases comprising Scopus, Google Scholar, PubMed, Web of Science, and ScienceDirect were employed to thoroughly search for relevant literature. Keywords such as *Tetrapleura tetraptera*, medicinal plant, nutrition, pharmacology, health benefits, and biological properties were utilized in the search for existing peer-reviewed journal papers published within the last ten years (2013–2023). By using the EndNote X9 citation tool (Thomson Reuters, Toronto, Canada), the various citations gathered were combined. The PRISMA flowchart highlighting the data collection procedure for this study is presented in Fig. 1.

3. Result and discussions

3.1. Botanical description of T. tetraptera

T. tetraptera thrives naturally in rainforests, reaching heights of 20–25 m, and widths of 1.2–3 m [3]. The plant's leaves are sessile and sparsely hairy and have a common stalk that is 15–30 cm long and mildly siphoned on top [16]. The flowers are pinkish cream

Fig. 2. Distinct parts of *T. tetraptera* and their applications.

turning orange and arranged in spikelike panicles 5–20 cm long, typically in sets in the top leaf axils. Each flower has a slender stalk, 10 short stamens, and anthers with a gland at the tip [16]. Fruit hangs persistently at the ends of the branches on strong, 25 cm-long stalks. It measures 15–25 cm in length, and 5 cm in width, and has four longitudinal, wing-like ridges that are nearly 3 cm wide. It is shiny, glabrous, dark purple-brown, and is typically slightly curved [3]. The seeds that rattle in the pods are small, black, hard, flat, and about 8 mm long. The rattle-producing seeds are entrenched in the body of the pod, without a split opening [3]. The individual parts of *T. tetraptera* utilized in various applications are displayed in Fig. 2.

3.2. Nutritive value of *T. tetraptera*

T. tetraptera is rich in many essential nutrients. These nutrients are deposited in various parts of the plant including fruit, pulp, and seed. The nutritional possessions of *T. tetraptera* have been demonstrated in several studies, justifying the plant's usage in nutrition. However, the majority of these studies frequently focus on the dry fruit (a combination of the pulp and seed), which is the most utilized part of the plant. In nutritional studies of the plant, the proximate, mineral, and vitamin contents are typically covered. Table 1 presents the nutritive value of *T. tetraptera* in the plant's dry fruit.

3.3. Biological properties of *T. tetraptera*

The presence of phytochemicals and other bioactive compounds of *T. tetraptera* gives the extracts of the plant essential biological properties that play a crucial role in ethnomedicine. Reported biological properties of *T. tetraptera* extracts are antimicrobial (e.g. antifungal, and antibacterial) properties, antioxidant properties, anti-inflammatory properties, anti-diabetic properties, antiparasitic properties (e.g. anti-trypanosomal, anti-helminthic, molluscicidal activity), antiproliferative properties (anticancer), antiprotozoal (e.g. antimalaria), and antiviral [22]. Fig. 3 shows some common biological activities displayed by *T. tetraptera*.

3.3.1. Antimicrobial properties

The use of medicinal plants like *T. tetraptera* in the treatment of various human ailments such as respiratory infections, convulsions, and rheumatism has gained medical concern for the past few years especially in Africa [23,24], owing to the increasing cost and resistance of pharmaceutical antibiotics [19]. Parts of the plant, thus the leaf, the stem bark, and the fruits play crucial roles in antimicrobial activity due to the presence of phytochemicals [19,23,25]. Leaf extract of *T. tetraptera* has been known to have antimicrobial activity against *Pseudomonas aeruginosa, Staphylococcus aureus, Escherichia coli,* and *Candida albicans* [25]. On the other hand, the stem bark extract of *T. tetraptera* has also been reported to have higher antimicrobial activity against *S. aureus, Streptococcus pneumonia,* and *Candida* spp. as compared to the leaf [23]. This means the intermittent use of the parts of the plant could be employed

Table 1
Proximate, mineral and vitamin compositions of the fruit of *T. tetraptera.*

Proximate	Content (%)	Reference
Moisture	5.06–8.22	[17]
Ash	2.65–4.02	[17–19]
Protein	5.61–6.69	[17,18]
Carbohydrate	58.48–63.86	[17,18]
Fat	11.19–24.71	[17,18]
Fiber	3.14–4.11	[17,18]
Mineral	**Content (mg/g)**	**Reference**
Magnesium	92.56–98.66	[17]
Potassium	251.22–288.62	[17]
Calcium	182.11–200.02	[17]
Sodium	19.95–26.80	[17]
Copper	8.20–10.11	[18]
Zinc	10.25–16.24	[18]
Phosphorus	36.22–43.11	[17]
Iron	16.11–18.22	[18]
Manganese	322.00–342.00	[17]
Selenium	2.97–4.56	[6]
Cobalt	44.00–47.26	[6]
Vitamin	**Content (mg/g)**	**Reference**
Vitamin A	3.22–4.69	[17,18]
Vitamin B	2.66–3.69	[18]
Vitamin C	0.88–1.20	[17,18]
Vitamin E	2.66–3.69	[17,18]
Thiamine (Vitamin B1)	0.01–0.04	[18]
Niacin (Vitamin B3)	0.11–0.04	[18]
Riboflavin (Vitamin B2)	0.01–0.03	[18]
Beta-carotene	0.02–0.07	[6,20,21]

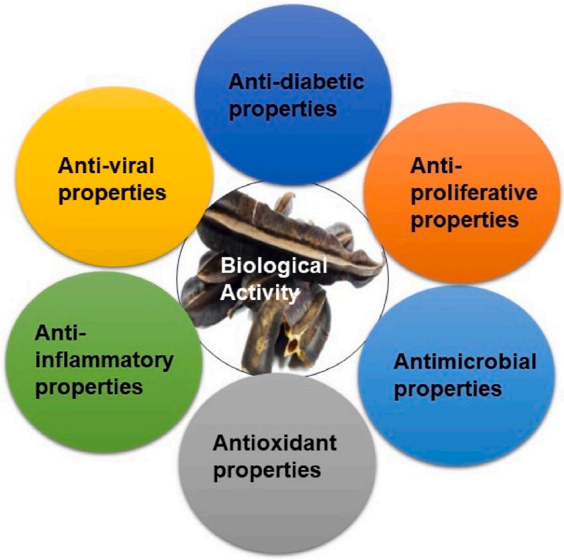

Fig. 3. Some common biological properties demonstrated by the extracts of *T. tetraptera*.

in the treatment of several bacterial and fungal infections due to its antimicrobial activities [23]. Several studies have reported the antibacterial activity of *T. tetraptera* extracts against different bacteria. This effect may vary depending on the type of solvent employed in the extraction of the active compounds of the plant and the type of bacteria subjected to the treatment. Studies from Enabulele and Ugha [26] revealed that aqueous extracts of the fruit and seed of *T. tetraptera* can inhibit *Klebsiella pneumoniae* and *S. aureus* compared to ethanolic extract. Similar to antibacterial activity, extracts of *T. tetraptera* exert antifungal action on various pathogenic fungi. This effect may also be dependent on the parts of the plant as well as the solvent used for extraction. Anyamele et al. [22] revealed that aqueous fruit extract of *T. tetraptera* can inhibit *Aspergillus* and *Mucor* but is ineffective against *Rhizopus*, yet petroleum ether and ethanol extracts could inhibit the growth of *Rhizopus* [19]. This biological property of the plant makes it unique, and its usage should be encouraged in ethnomedicine.

3.3.2. Antioxidant properties

Antioxidant activity is one of the most active biological properties of *T. tetraptera* which contributes to its usage in ethnomedicine since it acts as a reducing agent, preventing cell damage by neutralizing free radicals and inhibiting further oxidation [5]. This function is interplayed by the stem bark, fruit, and leaf of the plant. Famobuwa et al. [27] established that the stem bark of the plant has a lot of antioxidant activities. In addition, Koma et al. [23] also reported that the stem bark of the plant exhibits stronger free radical scavenging activity than the leaf. This property of *T. tetraptera* agrees with the assertion that the efficacy of the fruit and the stem bark of *T. tetraptera* in its bioactivities may be attributed to its potential antioxidant activity [27]. That notwithstanding, Adusei et al. [5] revealed that the pulp of *T. tetraptera* has more antioxidant activity when compared to the whole fruit and the seeds. The presence of phenolic compounds in plant materials is one of the chief contributors to the antioxidant properties shown by plant products. By

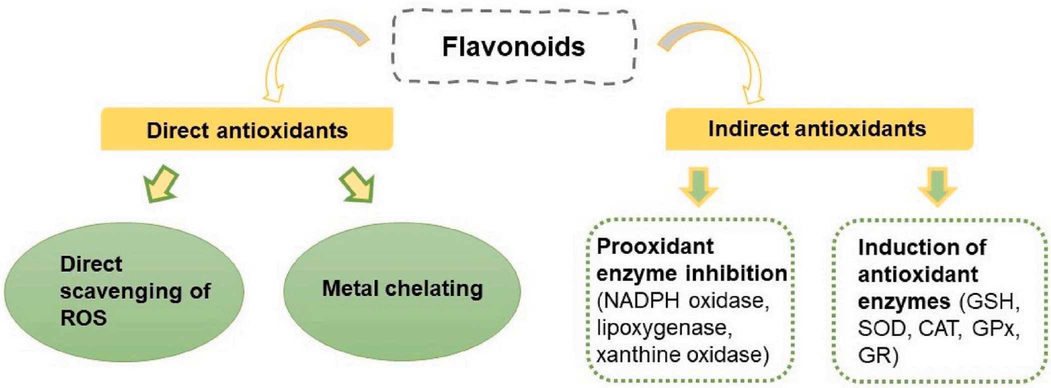

Fig. 4. Antioxidant activity by flavonoids in *T. tetraptera.* A modification of the diagram by Khan et al. [29] and Kopustinskiene et al. [30]. **GSH** = glutathione, **SOD** = superoxide dismutase, **CAT** = catalase, **GPx** = glutathione peroxidase, **GR** = glutathione reductase.

employing HPLC/LC-MS analysis on ultrasound-assisted *T. tetraptera* dry fruit extract, Dzah [28] determined twenty-four (24) phenolic compounds. Highest amongst these compounds include orientin Epigallocatechin (310.22 μg/g), (366.00 μg/g), caffeic acid (344.91 μg/g), ferulic acid 4-*O*-glucuronide (493.02 μg/g), ferulic acid 4-*O*-glucoside (370.58 μg/g). The extract exhibited a high cellular antioxidant capacity in a dose-dependent manner when compared to gallic acid in HepG2 cells. The minimum inhibition concentrations of *T. tetraptera* extract and gallic acid were 171.79 and 242.70 μg/mL respectively [28]. Given that the extract of *T. tetraptera* has a cocktail of phenolic compounds compared to the pure gallic acid, such an effect was expected. Fig. 4 displays how flavonoids can exhibit antioxidant activity.

3.3.3. Anti-inflammatory properties

One other important biological property of *T. tetraptera* is its anti-inflammatory activities since its use has been very vital in the management of arthritis, inflammation, and rheumatic pains [31]. Different solvent fraction of the leaf carries varying anti-inflammatory activity [31]. In addition, the anti-arthritics property of *T. tetraptera* fruit is owed to the anti-inflammatory activity of the fruit [24]. The composition of carvacrol in *T. tetraptera* may be a crucial factor for the anti-inflammatory features displayed by the plant extract [22]. Carvacrol is a monoterpene that is available in the essential oil of different plants [32]. Because of the therapeutic effect of carvacrol, it is used in traditional medicine. Carvacrol has a positive effect in a dose-dependent manner in the reduction of IL-1β and IL-8 when assessed against the aforementioned pro-inflammatory cytokines [32]. Studies have also shown that carvacrol inhibits the expression and inflammatory cytokine levels of cyclooxygenase-2 and nitric oxide synthase [33]. Other compounds available in *T. tetraptera* such as menthol, methyl eugenol, α-copaene, and octadecanoic acid are known to possess anti-inflammatory activities [22]. Ojewole and Adewunmi [34] examined the anti-inflammatory effects of *T. tetraptera* fruit extract on egg albumin-induced inflammation of hind paw edema in rats. The results indicated a 50–800 mg/kg dose-dependent reduction of the inflammation induced [34]. These findings substantiate *T. tetraptera* as a potent medicinal plant that could be exploited in ethno-health care services. Fig. 5 demonstrates the mode of anti-inflammatory action by flavonoids.

3.3.4. Anti-diabetic properties

Diabetes mellitus (DM) is a metabolic disease that occurs as a result of insulin deficiency [35]. According to the World Health Organization (WHO), about 180 million people worldwide have diabetes [35]. Treatment of diabetes has gained a lot of public attention for the past few years due to the increasing number of diseases. The WHO projects that over 180 million people worldwide will be diabetic by 2030 [35]. Allopathic drugs have been mainly used for the management of DM but recent studies have established the role of *T. tetraptera* in the management of hyperglycemic cases [35]. The generation of free radicals and reduction of antioxidant capacity have been linked to diabetes mellitus in several studies. In diabetic patients, the decrease in antioxidant parameters is determined [36]. Thus, studies have suggested the application of phytochemicals in the management of diabetes since they can exert free radical scavenging actions and antioxidant potential [36]. Phytochemicals such as flavonoids are found to fight the complexities of

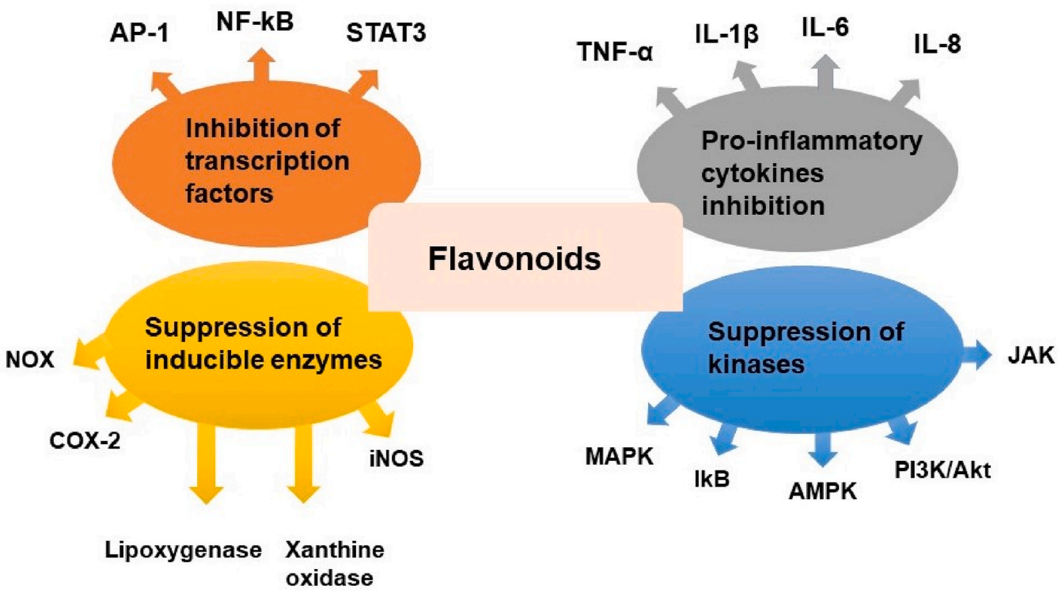

Fig. 5. Targets of flavonoids during inflammation processes. **TNF** = tumor necrosis factor, **IL** = interleukin, **AP-1** = activator protein 1, **NF-kB** = nuclear factor kappa-light – chain-enhancer of activated B cell, **STAT3** = signal transducer and activator 3, **NOX** = NADPH oxidase, **COX-2** = cyclooxygenase-2, **iNOS** = inducible nitric oxide synthase, **AMPK** = activated protein kinase, **PI3K** = phosphatidylinositide 3-kinase, **Akt** = protein kinase B, **MAPK** = mitogen-activated protein kinase, **JAK** = Janus kinase, **IkB** = IkB kinase. A modification of the diagram by Kopustinskiene et al. [30].

diabetes [36] and given that *T. tetraptera* has a significant concentration of flavonoids, it explains the potential in the management of diabetes [28]. The stem and leaf extract of *T. tetraptera* is identified to contain limonene, a cyclic monoterpene [22]. The compound limonene possesses both antihyperglycemic and antioxidant effects and in turn, can meliorate the effects of diabetic intricacies [36]. Furthermore, a study by Adesina et al. [3] showed that the fruit extract of *T. tetraptera* has a better glucose-lowering activity relative to the diabetes mellitus standard drug, glibenclamide. In addition, the root bark extract of *T. tetraptera* has been recommended as a remedy for diabetes mellitus management [35].

3.3.5. Anti-parasitic properties

One of the medicinal plants that have evolved as possible alternatives to chemical-based insecticides (with harmful effects on the environment and non-target organisms) is *T. tetraptera* [37]. *T. tetraptera* extract has been considered very useful in the control of malaria infection due to its strong larvicidal activity against the larvae of *Anopheles gambiae* [37]. In addition, the fruit extract of *T. tetraptera* has been reported to exhibit schizonticidal activity in early infection of *Plasmodium falciparum* as well as having a strong anti-plasmodia activity [3]. Moreover, African trypanosomiasis and helminthiasis are neglected tropical diseases (NTDS) that mostly affect people in remote areas of Sub-Saharan Africa [38]. Control and elimination of these diseases have been a challenge but Obeng et al. [38] revealed that *T. tetraptera* fruits and stem bark have anti-trypanosomal and anti-helminthic activities which encourage its usage in the control and management of parasitic infections. Also, *T. tetraptera* extracts have been reported to have the highest molluscicidal activity amongst some indigenous plants against freshwater snails which helps to control Schistosomiasis or Bilharzia [39]. Moreover, Adesina et al. [3] reported that most parts of the plant including the stem bark, the fruit, and the root carry molluscicidal activity. This makes the use of *T. tetraptera* in controlling schistosomiasis very promising and needs further investigation.

3.3.6. Anti-proliferative (anti-cancer) properties

Chemotherapeutic substances that have been involved in the management and treatment of cancer have been developed from medicinal plants [10] since recent cancer therapeutics have unbearable side effects like hair loss, toxicity, and chemo-resistance [10, 40]. The effects of cancer drugs have called for less toxic and more effective ways of managing cancer [40]. As a medicinal plant, *T. tetraptera* has been reported to be cytotoxic to carcinoma cells and reduce tumor burden [10]. In addition, the methanolic extract of the fruits of the plant has been reported to have an anti-proliferative ability against leukemia and human breast cancer [40]. Dzah [28] studied the cytotoxicity of various concentrations of *T. tetraptera* extract on the human liver cancer cell line HepG2. In all the concentrations of the extract used (50 μg/mL – 350 μg/mL), *T. tetraptera* extract had a high cytotoxic effect relative to the same concentrations of gallic acid [28]. The concentration of the extract was proportional to the anti-cancer effect, with a minimum inhibition concentration of 168.06 μg/mL. Polyphenols have been associated with the induction of cellular apoptosis through various mechanisms. Polyphenols may become prooxidants under oxidative stress and produce significant concentrations of free radicals which can induce cancer cell apoptosis [28,41]. In different cancer cells, aqueous extract of *T. tetraptera* displayed prooxidant action to induce changes in mitochondrial membrane potential [42]. Plant polyphenols can also induce conditions to mimic caloric restriction mimetics in cells, thus inducing molecular mechanisms governing mitochondrial biogenesis and mitophagy [43]. Such effects are some reasons behind the antiproliferative and antitumor characteristics of polyphenols and their potential in cancer management and treatment. This property of *T. tetraptera* fruit extract is very encouraging and calls for further isolation and categorizing of potential anti-cancer agents from the plant to enhance its use in ethnomedicine [40].

3.3.7. Anti-viral properties

Tetrapleura tetraptera contains significant concentrations of piperazine, 2-hydroxy-gamma-butyrolacetone, 6-octadecenoic acid, octadecanoic acid, and thymol [44–46]. Such compounds possess antiviral properties against certain viruses. Studies have shown that piperazine can inhibit the growth of the highly pathogenic chikungunya virus. The treatment of chikungunya virus with 6 mM piperazine efficiently inhibits the growth of the virus after 72 h [45]. Thymol (2-isopropyl-5-methylphenol) has been long applied as an antiviral agent in traditional medicine. Thymol like camphene and menthol shows significant binding affinity to the spike glycoprotein of SARS-CoV-2, even though it lacks hydrogen binding interaction with the protein. In the preparation of disinfectant against COVID-19, thymol was part of the active ingredients listed by the United States Environmental Protection Agency and the Canadian Government [47]. Thus, the presence of such compounds in *T. tetraptera* presents a potential use of the plant for combating some viruses. Also, studies have shown that compounds such as octadecanoic acid can produce essential synergistic antiviral effects when combined with a commercial drug like ribavirin with a low cytotoxic effect [48]. With *T. tetraptera* containing some concentration of octadecanoic acid [22], its combination with other compounds could produce effective antiviral action prior to significant studies.

3.4. Health benefits of T. tetraptera

Tetrapleura tetraptera offers a wide range of health benefits. The presence of many active phytochemical compounds such as alkaloids, flavonoids, saponins, tannins, phenols, and steroids gives it therapeutic properties [49]. The basic chemical structures of the major phytochemical compounds in *T. tetraptera* are presented in Fig. 6. According to Adusei et al. [5] there are about 3.51 ± 0.03 mg GAE/g phenols, 0.87 ± 0.03 mg QE/g flavonoids, 4.27 ± 0.03 mg DE/g saponins and 5.03 ± 0.15 %w/w alkaloids present in the ethanolic extract of the pulp of *T. tetraptera*. Erukainure et al. [44] also reported the presence of 23.87 ± 0.44 mg/100 g tannin, 20.48 ± 1.18 mg/100 g flavonoids, 2.76 ± 0.15 % saponins, and 1.43 ± 0.43 % alkaloids in the ethanolic extract of the peels of *T. tetraptera*. Other bioactive compounds such as piperazine, octodrine, glycidol, n-decanoic acid, 2-hydroxy-gamma-butyrolacetone, and 6-octadecenoic acids are also traces of bioactive compounds available in *T. tetraptera* with limited information on their bioactivity [44]. The inherent therapeutic properties presented by the available bioactive compounds account for the application of *T. tetraptera* in traditional herbal remedies to treat illnesses and infections [50]. The treatment of jaundice using decocted *T. tetraptera* pods is an example of such an application [51]. In traditional West African medicine, *T. tetraptera* is used as a remedy to treat a range of illnesses such as gastric ulcers, rheumatism, fevers, rash, convulsions, smallpox, malaria, diarrhea, inflammation, hypertension, jaundice, leprosy, diabetes, arthritis, as well as coughs and hemorrhoids [52]. The fruit is mostly used to treat and regulate adult-onset type 2 diabetes mellitus as well as seizures, leprosy, inflammation, rheumatism, flatulence, jaundice, and fevers [53]. Some other important health benefits exhibited by *T. tetraptera* are discussed below.

3.4.1. Lowering of blood cholesterol

Tetrapleura tetraptera contains saponins, a naturally occurring compound widely found in the cells of plants. Saponins improve the immune system by decreasing blood lipids and blood glucose response [54]. High levels of saponins diets can inhibit platelet aggregation [54]. Bile acids are released into the intestine when food is consumed [18]. The presence of saponins in *T. tetraptera* offers detergent properties that enable their attachment to release bile and halt the reabsorption of bile acids produced by the body [18]. Hence, lowering body cholesterol levels, and reducing the risk of a heart attack.

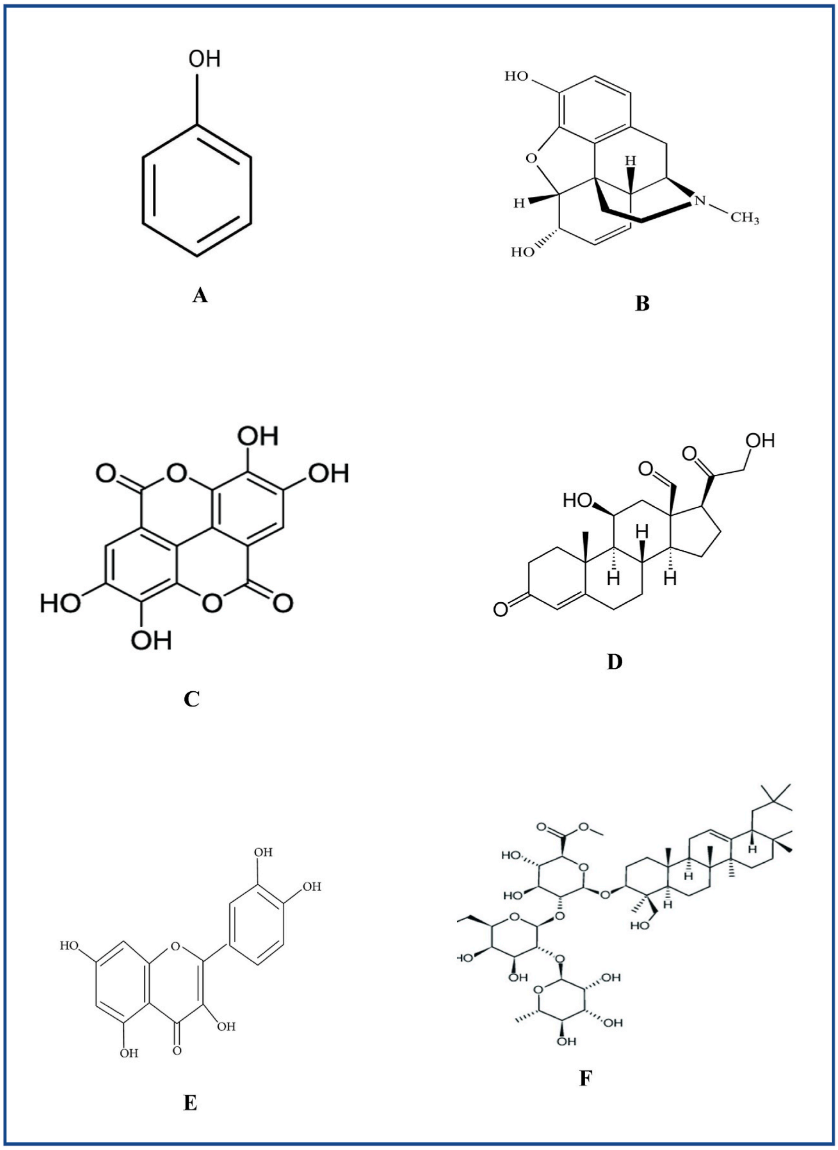

Fig. 6. Basic chemical structures of major phytochemical compounds in *T. tetraptera.* Phenol (A); Alkaloid: Morphine (B); Tannin: Ellagic acid (C); Steroid (D); Flavonoid (E); Saponin (F).

3.4.2. Enhance the immune system

Saponins possess the ability to activate the mammalian immune system [54]. The significant concentration of saponins in *T. tetraptera* provides the plant with its immunomodulatory effects. The presence of saponins can help with immunoregulation and the reduction of inflammation and oxidative stress in various disease models [55]. The production of serum antibodies can be promoted by saponins [55]. The chemical composition of *T. tetraptera* with such an essential component grants the human body capacity to combat viruses and some fungi such as *Candida albicans* and thrush [18].

3.4.3. Treatment of malaria

Extract of *T. tetraptera* is employed in the treatment of various ailments in traditional medicine. Its use in malaria treatment is no exception, as it possesses antiplasmodial activity [18]. [56,57] reported the use of *T. tetraptera* extract in treating malaria in Gabon and Cameroon ([56,57]. Methanolic extract of the bark and roots of *T. tetraptera* inhibited the growth of *Plasmodium falciparum* 3D7 at 83.6 and 76.3% respectively [57]. Different groups of phytoconstituents are known to possess antimalarial properties. This includes alkaloids, flavonoids, steroids, and terpenes. Alkaloids in particular are considered essential and potent because of their powerful antimalarial properties. The fruit extract of *T. tetraptera* contains between 1.88% and 2.22% of alkaloids [18]. This demonstrates the plant's antimalarial actions and utilization in African traditional medicine for malaria therapy.

3.4.4. Treatment of diarrhea

Tetrapleura tetraptera tumbles amongst 25 different plant species employed in diarrhea treatment [58]. *T. tetraptera* is used as the basis for several herbal remedies because of the astringent properties of tannins present in the plant. Tannin-rich plant fruits can be used to alleviate intestinal inflammation, reduce diarrhea, and relieve nausea [18]. *T. tetraptera* possesses some of the major groups of tannins, including gallotannins (e.g., gallic acid) [59], Ellagitannins (e.g., ellagic acid) [60], and proanthocyanidins or condensed tannins [61] (e.g., catechin, epigallocatechin) [28,62]. These types of tannins have significant effects in the treatment of diarrhea. For instance, the supplementation of gallic acid (400 mg/kg) in piglets reduces diarrhea occurrence [63]. Similarly, ellagic acid is a natural polyphenol drug known to have anti-diarrhea effects. Studies by Chen et al. [64] revealed that the administration of 0.3 mL (10 mg/mL) of ellagic acid in mice protected the ileum against castor oil-induced diarrhea through the activation of the peroxisome proliferator-activated receptor (PPAR) signaling pathway. The presence of ellagic acid in *T. tetraptera* (151.00 μg/g) with other forms of tannins provides the biological activity of *T. tetraptera* against diarrhea. Furthermore, other studies have shown that the administration of Actitan-F (a natural molecular complex of tannin) can truncate the duration of acute diarrhea in children [65]. Likewise, the use of chestnut tannins, for example, can reduce neonatal calf diarrhea [65]. Compared to subjects not fed with chestnut tannins, calves treated with tannins experienced a reduction in diarrheic episodes by almost 4 days [66]. The effects of the various types of tannins in the control of diarrhea explain why *T. tetraptera* has traditionally been utilized to treat diarrhea and gastrointestinal inflammation [18].

3.4.5. Management of diabetes and hypertension

Extracts of *T. tetraptera* have proven significant glucose binding capacity in a concentration-dependent manner. In a study by Eyenga et al. [67], any given concentration from the extract of *T. tetraptera* showed substantial glucose-binding ability. The glucose adsorption capacity of *T. tetraptera* is attributed to the high fiber content of the fruit (>40%) (Eyenga et al. [67]. The binding of fibers to free glucose has been one of the mechanisms employed in inducing glucose reduction [67]. Traditionally, the fruit of *T. tetraptera* is utilized as a culinary spice to cure diabetes and hypertension by locals in Ghana, the Yoruba tribe of Nigeria, and indigenes of the southern and western parts of Cameroon [9]. Many physiological characteristics of phytochemicals are advantageous to the health of humans. Through enhancing lipid metabolism, antioxidant status, capillary function, reducing blood pressure and cholesterol, and boosting glucose metabolism, phytochemicals in plant-based meals can benefit diabetes patients' overall health [50]. Also, the zinc content of *T. tetraptera* demonstrates its importance in the control of diabetes [68]. Zinc has several benefits for both type-1 and type-2 diabetes [69]. Its usage as a supplement in diabetic patients enhances glycemic control and improves lipid parameters [69].

3.4.6. Prevention of cancer

Through various modes of action such as inhibition of proliferation, invasion, metastasis, inflammation, and activation of apoptosis, cancer can be prevented by flavonoids such as epigallocatechin-3-gallate [70]. Epigallocatechin-3-gallate (EGCG) can induce apoptosis of hypophosphorylated retinoblastoma and avoid invasion and metastasis in pharyngeal carcinoma cells. EGCG can decrease the expression of vascular endothelial growth factor (VEGF) expression and prevent gastric tumor cell proliferation [70]. The availability of EGCG in *T. tetraptera* endows it with potential antiproliferative activity. Similarly, bioflavonoid like rutin is known to counteract several cancers through mechanisms like oxidative stress, angiogenesis modulation, malignant cell growth inhibition, and cell cycle arrest [71]. *T. tetraptera* has about 295.97 μg/g of rutin available in the fruit [28] presenting the plant with significant anticancer activity. Also, scopoletin (a coumarin available in various edible plants) presents anticancer activity via multiple mechanisms like modulating cell cycle arrest, inducing apoptosis, and regulating multiple signaling pathways [72]. *T. tetraptera* possesses scopoletin, which is significant in conferring anticancer properties [72,73]. People susceptible to certain types of cancer may benefit from scopoletin obtained from the application of *T. tetraptera* extracts. A study by Yuan et al. [74] revealed the inhibitory activity of scopoletin against small-cell lung cancer. Similarly, Shi et al. [75] showed that a derivative of scopoletin exhibits an anti-tumor effect against breast cancer MDA-MB-231 cell lines. The basic chemical structures of some key phytochemicals in *T. tetraptera* with health properties are shown in Fig. 6.

3.5. Applications of *T. tetraptera*

3.5.1. Beverage production

In the brewing process of sorghum beer (locally known as "Pito"), an alcoholic beverage commonly available in the northern part of Ghana and other West African nations, *T. tetraptera* is added to the boiled wort. It helps in the extraction of available bioactive compounds and aroma, thus, enhancing the nutritional content and flavor of the brewed "Pito" [7]. Studies have suggested that the extracts from *T. tetraptera* could ensure smooth and rapid fermentation by increasing yeast nutrition in the wort. To improve yeast nutrition, calcium chloride, gypsum, and other minerals are used in brewing processes to enhance yeast nutrition. Such an approach is not practiced by local brewers of "Pito", it thus suggested that based on the chemical composition of *T. tetraptera* its addition indirectly provides the needed minerals for the yeast to ensure ideal fermentation [7,76].

Besides its application in local alcoholic beverage fermentation, *T. tetraptera* in addition to honey is used to produce a non-alcoholic beverage known as "Natu Prekese drink" [7]. It is claimed that this beverage aids in preventing menstrual pain, boosts the immune system, and improves blood circulation. However, its application as a dietary supplement has not been evaluated by the FDA, and as such the product is not intended to diagnose, treat, cure, or prevent disease or health condition. Similarly [77], produced a non-alcoholic "prekese" beverage extracted syrup from *T. tetraptera.* The production of the non-alcoholic drink involved milling and boiling the fruits of *T. tetraptera*. The obtained filtrate was concentrated into a syrup that could be reconstituted by mixing with water and sugar into a ready-to-drink product. Given that the efficiency of most functional fruit drinks in the market is antioxidant level dependent, the produced drink's antioxidant level was determined. Compared to drinks rich in polyphenols available in the USA such as pomegranate juice, red wine, blueberry juice, black cherry juice, and orange juice, the "prekese" drink possessed higher antioxidant activity [77]. Individuals cognizant of the taste, aroma, and color of beverages produced from *T. tetraptera* have shown a significant penchant for such drinks. The quality of produced "prekese" drinks show a range of properties acceptable by the Ghana Standards Authority for beverages [77].

In addition to the possibility of producing beverages from *T. tetraptera*, it has the potential to preserve other sources of beverages upon its incorporation as a preservative. The addition of extracts from *T. tetraptera* (100 mg/mL) to a freshly prepared watermelon juice saw a reduction in fungal and bacterial load compared to unpreserved juice for 7 days [78]. There is increasing market demand for nutritious food free of chemical preservatives and microbially safe. Freshly prepared juices are usually consumed in non-chemically and non-thermally treated forms, thus maintaining most of the nutrients needed by the consumer. Notwithstanding, there is the challenge of controlling potential spores-forming microbes such as *Bacillus* sp. In such foods.

T. tetraptera extract has a minimum inhibition concentration of 50 mg/mL against *Bacillus cereus*, a common fruit juice spoilage microbe. This effect thus suggests that the incorporation of *T. tetraptera* extracts can potentially enhance the shelf-life of freshly prepared fruit juice while maintaining its nutritive value [78]. The growth of microorganisms such as *Staphylococcus aureus*, *Bacillus cereus*, and *Saccharomyces cerevisiae* can also be reduced upon the addition of essential oil from *T. tetraptera*. The minimum inhibition concentration against these microbes as determined by Ref. [79] were 42, 46, and 36 mg/mL respectively. Essential oil from *T. tetraptera* can be applied as a natural fruit juice preservative owing to its bactericidal capacity.

Hot water and organic solvent extracts from *T. tetraptera* can increase the sugar content of fruit juice. The addition of *T. tetraptera* extracts to pineapple and pawpaw juices saw an increase in the sugar content from 19.5% to 20.0% and 15.0%–16.0% respectively using hot water extraction. Similarly, *T. tetraptera* extracts using ethanol enhanced the sugar content of pineapple and pawpaw juice by 2% and 1.5% respectively [80]. The increase in sugar content of the fruit juices by the addition of *T. tetraptera* stems from the high content of glucose (3.25 mg/mL), sucrose (2.62 mg/mL), and fructose (1.82 mg/mL) present in the extracts of *T. tetraptera* [80]. Given the flavor, antimicrobial potential, and sugar content of *T. tetraptera*, it stands as a promising candidate in the application of beverages as natural additives instead of synthetic flavoring agents.

3.5.2. Food preservation and flavoring

T. tetraptera is usually used in traditional dishes mainly because of its flavor. Together with vegetables such as garlic, pepper, and palm fruits, it is used to prepare a Ghanaian local delicacy known as "palm nut" soup [81]. In the southeast region of Nigeria, the pod of *T. tetraptera* is employed as a spice for seasoning [81]. Owing to the significant antimicrobial properties of *T. tetraptera*, it can be applied in the preservation of foods such as pork and chicken. By applying root extracts of *T. tetraptera* (1%v/v) on pork loaded with 1×10^4 CFU/mL of *Escherichia coli* and *Staphylococcus aureus* for 6 days, about 99.99% of the microbial load was reduced [82]. The minimum inhibition concentration (MIC) and minimum bactericidal concentration (MBC) of 12.5 and 25.0 μg/mL were observed against *E. coli* and 3.125 and 6.25 μg/mL against *S. aureus* respectively [82]. It such effect, *T. tetraptera* has a prospect in its usage as a natural preservative in the meat industry.

Frying is one of the major cooking methods widely used around the globe. Coconut oil is a common example of oil mostly employed in frying. A challenge associated with food prepared with oil is rancidity. Rancidity is related to the odor and off-flavor of oil over a period [83]. This is usually caused by lipid oxidation (reaction of oil and fat with molecular oxygen). Thus, an integral property applied in considering the use of oil in foods is their oxidative stability. To ensure oxidative stability, synthetic antioxidants such as butylated hydroxytoluene (BHT) are used in enhancing the oxidative stability of cooking oils. The use of *T. tetraptera* in coconut and palm kernel oils can serve as a natural antioxidant in the prevention of oxidative rancidity [83]. After treating both coconut and palm kernel oil with 0.01% of *T. tetraptera* for 12 days [83], observed a reduction in the *p*-anisidine value to 4.47 ± 0.65 from 6.45 ± 2.83 and 3.12 ± 0.47 from 5.27 ± 0.55 respectively. *p*-anisidine values like oxidative stability and peroxide value are indicators of oil quality. It suggests oil deterioration during frying and relates directly with the presence of aldehydes and ketones presence (organics compounds responsible for the rancid taste and flavor of fatty substances). Thus, a lower *p*-anisidine value of coconut and palm kernel oil after treatment with *T. tetraptera* shows its capacity to be employed in oil preservation.

T. tetraptera has the capacity to augment the shelf-life of perishable vegetables such as tomatoes and pepper after treatment with aqueous extracts of *T. tetraptera*. The addition of different concentrations of the extract (0.25 mg/mL - 1 mg/mL) correlated with the increased shelf-life of pepper and tomatoes with increasing concentration [84]. Treatment of tomatoes and pepper with an extract concentration of 1 mg/mL resulted in almost double the shelf life of untreated vegetables. Such effects of aqueous extract from *T. tetraptera* are attributed to the presence of antimicrobial, phytochemical, and antioxidant properties [84].

3.5.3. Medical and pharmaceutical applications

Traditionally, *T. tetraptera* is used in the treatment of cancer, diabetes, and other diseases. As such studies have explored the application of extracts of *T. tetraptera* against various cancer cell lines to validate the cytotoxic effects. Dichloromethane methanol extract of *T. tetraptera* fruits, exhibited cytotoxic effects against B16–F1 murine melanoma cells, SKMel-505 BRAF wildtype melanoma cells, MaMel-80a BRAF-V600E homozygous mutant melanoma cells, and SKMel-28 BRAF-V600E homozygous mutant melanoma cells [85]. The lethal dose (LD_{50}) determined from this extract was above 5000 mg/kg body weight. Furthermore, the methanolic extract of *T. tetraptera* has been employed as an antiproliferative agent against cancer cell lines [40]. evaluated the antiproliferative properties of *T. tetraptera* against MCF-7, Chang liver cell, and Jurgkat cell lines and observed a positive cytotoxic effect on these cells at a concentration above 100 μg/mL using whole fruit extract. Various fractions of the extract may exhibit different degrees of antiproliferative activity on the applied cell lines [40]. The aforementioned studies show the potential of *T. tetraptera* extracts as an anticancer agent.

Hyperuricemia is a condition related to an elevated level of uric acid in the blood. The increase in the concentration of uric acid in the body is associated with higher activity of xanthine oxide [86]. Application of *T. tetraptera* fruit extracts showed inhibitory effects against Fe^{2+} and xanthine oxidase (XO) induced lipid peroxidation. Treatment of induced lipid peroxidation in the lungs, liver, and kidney of rats with different concentrations of *T. tetraptera* extracts saw a reduction in XO activity with increasing concentrations of *T. tetraptera* fruit extracts. By using 60 μg/mL of *T. tetraptera* extract, about 80%, 60%, and 55% of xanthine oxidase inhibition was observed by Ref. [86] in the lungs, kidney, and liver respectively of induced lipid oxidation rats. Higher lipid peroxidation inhibition was reported in rats induced with Fe^{2+}. Inhibition of about 82%, 81%, and 60% was observed for the kidney, lungs, and liver respectively. A similar dose-dependent inhibition effect on lipid oxidation of hepatic tissue can occur upon treatment with ethanolic extract of *T. tetraptera* fruit peel, as reported by Ref. [44]. The presence of phytochemicals, DPPH radical scavenging ability, and nitric oxide radical scavenging ability of the extracts of *T. tetraptera* is suggested to impact the inhibition of lipid peroxidation. Compared to gallic acid and ascorbic acid, *T. tetraptera* exhibits low scavenging capacity and in turn low lipid oxidation inhibition [44]. The lipid peroxidation inhibitory capacity of *T. tetraptera* fruit extract indicates the therapeutic application of *T. tetraptera* against hyperuricemia and related conditions in a dose-dependent manner [86].

Plants in general have extensive applications in the traditional African setting for the treatment or management of cognitive dysfunction. The presence of significant amounts of *p*-coumaric acid, rutin, catechin, quercetin, ellagic acid, gallic acid, and chlorogenic acid of *T. tetraptera* extracts has been linked to the enhanced cognition of host organisms [87]. Studies from Ref. [87] suggest that the administration of *T. tetraptera* extracts can improve memory indices and prevent scopolamine-induced memory deficits in rats. Scopolamine is a psychoactive drug applied to induce amnesia experimentally. Its application can reduce spatial and non-spatial memory in rats, however, pretreatment of rats with 300 mg/kg aqueous *T. tetraptera* extracts can reverse declined memory indices caused by scopolamine. This shows the prophylactic ability of *T. tetraptera* against cognitive impairment in amnesia-induced rats.

By decreasing the elevated activity of Alanine Transaminase (ALT), Aspartate Transaminase (AST), and phenylalanine ammonia-lyase (PAL) in serum, *T. tetraptera* can be used for the prevention of liver damage. Subjecting rats to CCl_4 treatment results in reduced glutathione, superoxide dismutase (SOD), and catalase (CAT) levels. Oral administration of *T. tetraptera* extract in liver injury-induced rats saw an increase in the glutathione, SOD, and CAT activity whereas decreasing the malondialdehyde (MDA) levels compared to the untreated subjects. A microphotograph of the rats' liver showed a reversal to the normal state of the injured rats after *T. tetraptera* treatment of 100 mg/kg for 48 h [88]. The significant concentrations of phytochemicals available in *T. tetraptera* extracts and their corresponding oxidation scavenging ability give it treatment and preventive capacity against several ailments.

3.5.4. Feed supplementation

Other than the extensive applications of *T. tetraptera* in food and medicine, it can also be used to supplement feeds for farm animals and pets for various reasons [89]. Owing to the challenges of the use of antibiotics in feeds for animals, *T. tetraptera* can be employed as a feed supplement in place of antibiotics. By fortifying broiler chicken feed with 0.2% *T. tetraptera* fruit powder [89], observed an increase in body weight relative to chickens fed with a diet containing 0.4% *T. tetraptera* and a diet with no supplementation. The said study observed a similar feed conversion ratio (FCR) for chickens fed with an antibiotic-supplemented diet (FCR = 2.02) and 0.2 % *T. tetraptera*-supplemented diet (FCR = 2.03). With a lower cost of production and improved growth performance, *T. tetraptera* powder could be employed as an antibiotic growth promoter in producing chicken meat free of antibiotic residues and preventing the creation of antibiotic resistance.

Similarly, the employment of *T. tetraptera* as a feed additive in rabbit bucks' diet resulted in a reduction in the feed conversion ratio relative to percent dosage. The Lowest feed conversion ratio (2.43 $\pm$ 0.03) was recorded when the subjects were fed with 1% of *T. tetraptera* compared to FCR (3.76 $\pm$ 0.50) of subjects without the addition of *T. tetraptera* [90]. High livestock production efficiency is associated with lower FCR [90]. Thus, the reduction in FCR in the rabbits after the inclusion of 1% of *T. tetraptera* reveals the potential of *T. tetraptera* as a natural feed additive for livestock. *T. tetraptera* can also serve as a feed additive for a diet of West African Dwarf rams. Supplementation of *Panicum maximum* with varying concentrations of *T. tetraptera* increased glutathione peroxidase and superoxidase after the feeding trial. The diet formulation containing up to 2% of *T. tetraptera* improved the thermo-physiological responses (pulse rate and breathing rate) in the rams and decreased the level of oxidative stress [91].

3.6. Future perspectives of T. tetraptera

T. tetraptera is promising in combating undernourishment and improving ethnomedicinal practices, owing to its essential micro and macronutrients, active bioactive ingredients, and great pharmacological possessions. The plant's various nutritional assets, predominantly in the fruits, hold promise for the production of healthy functional foods. Therapeutically, the plant's numerous biological actions have the potential to generate potent pharmaceutical products. As a result, *T. tetraptera* merits rigorous investigation to tap into the full potential of the food and medicinal plant.

4. Conclusions

This review study documented the nutritive attributes, biological properties, health benefits, and applications of *T. tetraptera*. Protein, vitamins, and minerals have been established to be present in the fruit of the plant. Likewise, *T. tetraptera* possesses antimicrobial, antioxidant, anti-inflammatory, anti-diabetic, anti-parasitic, and anti-proliferative properties, justifying its usage in ethnomedicine for combating diabetes, hypertension, cancer, malaria, and diarrhea. Industrially, the plant has demonstrated relevance in food processing and pharmaceutical formulations. Hence, *T. tetraptera* holds a global impact in the domains of health, nutrition, and pharmaceutics. To guarantee the safety and efficacy of its exploitations, extensive toxicological studies on the plant are recommended in future research.

Ethical approval

As the current study was a secondary reanalysis of publicly available data, no ethical approval was required.

Data availability statement

Data will be made available on request.

CRediT authorship contribution statement

Richard Q. Mensah: Writing – review & editing, Writing – original draft, Data curation, Conceptualization. **Stephen Adusei:** Writing – review & editing, Writing – original draft, Data curation, Conceptualization. **Samuel Azupio:** Writing – review & editing, Writing – original draft, Data curation. **Richmond Kwakye:** Writing – review & editing, Writing – original draft, Data curation.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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