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Phytochemical, Pharmacological and Toxicological Aspects of *Capparis erythrocarpos* Isert.: A Review

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Abstract

Capparis erythrocarpos is a shrub plant with a large natural distribution used in traditional medicines to cure various illnesses. The study sought to review and compile all data available on this medicinally important plant, which will help inform scientists and researchers the gap needed to be filled in studying the plant. The present review summarizes information concerning the ethnopharmacology, morphology, phytochemistry, toxicology and biological activities of *C. erythrocarpos*. Scientific databases such as NCBI/PubMed, Google scholar, Sci finder, Science direct were searched for published article on the plant. The active phytochemicals; flavonoids, alkaloids, terpenoids, phytosterols, glycosides, tannins, coumarins and saponins have been identified from various parts of the plant. Pharmacological and biological studies on the plant have revealed its antimicrobial, analgesic, anti-inflammatory, antipyretic, anti-diabetic and anti-dyslipidemia activities, with no reported toxic effect.

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It is recommended that future studies should focus on identification, separation, purification and quantification of the most bioactive constituents of *C. erythrocarpos* due to the paucity of information in this area.

Keywords: Capparis erythrocarpos; flavonoids; alkaloids; anti-inflammatory; ethnopharmacology.

1. Introduction

The large diversity of medicinal plant species is a huge source of potentially active phytochemicals with novel structures that can be harnessed. According to Newman and Cragg, out of a total of 1881 new approved drugs in the last four decades, 929 originated from natural sources and fall into the class of biological molecules, unaltered natural products, botanical drugs, or derivatives of natural products, while the remaining 952 drugs are classified as synthetic drugs or synthetic drugs with natural product pharmacophores[1]. As such, the importance of medicinal plants cannot be over emphasized.

Capparis erythrocarpos Isert. is an important medicinal plant with known potent ethno-pharmacological properties, and can be very useful in modern drug discovery. Plants of genus Capparis are trees or shrubs with stipular thorns [2], comprising of about 700 species, of which only five have been identified in Ghana [3, 4]. These species are *Capparis seperia* L., *Capparis brassii*, *Capparis fascicularis*, *Capparis tomentosa*, and *Capparis erythrocarpos* Isert [5,6]. *C. erythrocarpos*, is commonly used locally for the management of pain, inflammation, chronic diarrhoea and other several ailments in Ghana and sub-Saharan Africa [7]. Based on its traditional use a number of researches have been carried out to scientifically prove its anti-inflammatory [8], analgesic [7,8], anti-nociceptive[9], anti-pyretic [10], anti-microbial [11,12], anti-diabetic [13] and anti-dyslipidaemic [14] activities. Some studies have also been conducted to identify the phytochemical constituents that may be contributing to these reported activities. Even though there are a number of reported pharmacological and biological activities of *C. erythrocarpos*, there is currently no review that puts together all the data on the various reported activities. The present review seeks to compile all available data on the plant, comprising its identification, ethno-pharmacological uses, secondary metabolites, pharmacological activities and toxicological assessment. Although, there are not many published works involving this plant, which is the main limitation of this study, the available literature was utilized for this work. The review will also help reveal research areas which need to be investigated on the plant, as well draw scientific focus for strategic planning to optimize its sustainable use.

2. Traditional uses

Ayurveda mention of this plant reveals the use of the stem bark and root for its analgesic and inflammatory diseases [15]. The roots are used across Africa for the treatment of headache, conjunctivitis and chronic diarrhoea [16,17]. Tropical Africans also use the leaves of the plant to treat child convulsive fever, pounded roots are applied on severe abscess and vapour from the pounded roots are used to treat inflammation of the connective tissue of the eye [18,19].

In Tanzania, the roots are used to treat skin rashes, tuberculosis, cryptococcal meningitis, oral candidiasis, herpes zoster, herpes simplex and chronic diarrhoea [17].

The whole plant is used in Uganda for the management of menstrual pains, infertility and anemia [20]. In Ethiopia, *C. erythrocarpos* is used traditionally for the management of symptoms of cyst and skin infections. Kenyans also use the plant as an anti-diarrhoea and anthelmintic agent [7]. In Ghana, it is used as an aphrodisiac, for the management of pain, arthritis and other forms of inflammatory conditions [21]. Various parts of the plant have been processed into different dosage forms as commercial products on the Ghanaian market (Table 1). Table 2 contains the various vernacular names by which the plant is referred to in different localities.

Table 1: Commercial products on the Ghanaian market containing *C. erythrocarpos*

Product name	Manufacturer	Dosage form	Type	Indication
Sirrapac [22]	Center for plant medicine research	Powder	Monoherbal	Treatment of rheumatoid arthritis
Alomo bitters [23]	Kasapreko Ltd.	Tincture	Polyherbal	Appetizer
Class bitters [24]	Class herbal Centre	Decoction	Polyherbal	Backache, general body pains and sexual weakness

Ltd: Limited

Table 2: Vernacular names of *C. erythrocarpos*

Country	**Tribe**	**Vernacular name**	**Reference**
Ghana	Ewe	Lalenui, Anngo	[21]
Ghana	Ashante	Woresenakyiame	[21]
Ghana	Fante	Okyerubrcm	[21]
Ghana	Ga	Aqmaqma	[21]
Uganda		Muzingani omwelu	[25]
Uganda		Kitunku ekitono	[25]
Tanzania		Oluvuranganga	[17]

3. Plant description

C. erythrocarpos which emerges from the kingdom Plantae, also falls under the clade Tracheophytes. It is an Angiosperm, Eudicot and Rosid. It is found among the members of the order Brassicales, in the family Capparaceae, commonly known as the caper family, genus *Capparis* and species *erythrocarpos* [21,26,27].

C. erythrocarpos is usually described as a scandent shrub or climber, armed with sharp, paired hooked thorns (Figure 1). Branches slightly zigzag, greyish-velvety when young. The stem of the plant can be described as weak, light green when young and brown when old. The leaves are fleshy with a glossy appearance. The striking difference between the young and old leaves is the light green lanceolate shaped young leaves as opposed to dark green elliptical to ovate old leaves [28]. The leaf base is cuneate to rounded. The apex is sharply acuminate to obtuse with dimensions of 3-14 cm long and 1.5-5 cm broad. Its flowers or stout pedicels (2-2.5 cm long) are clustered at the end of a leafy shoot, petals are mostly emarginated, ovary ribbed and the fruit scarlet is 5 cm long [21]. The flowers are solitary, axillary, white in colour but often pink at the base of the stamens. Iner sepals are petaloid greenish white, 3-4 times longer than outer sepals [29]. Stamens 40-50, up to 2.8 mm long [29]. Fruits ellipsoid, 4 × 2.5 cm, strongly 6-8 ridged and deep-pink when ripe (Figure 2) [29]. Seeds are brown in colour and usually 15-20 per fruit.

Figure 1: Pictures of root, root bark and full plant of *C. erythrocarpos*. Source: CPMR arboretum Mampong-Akuapem, Ghana.

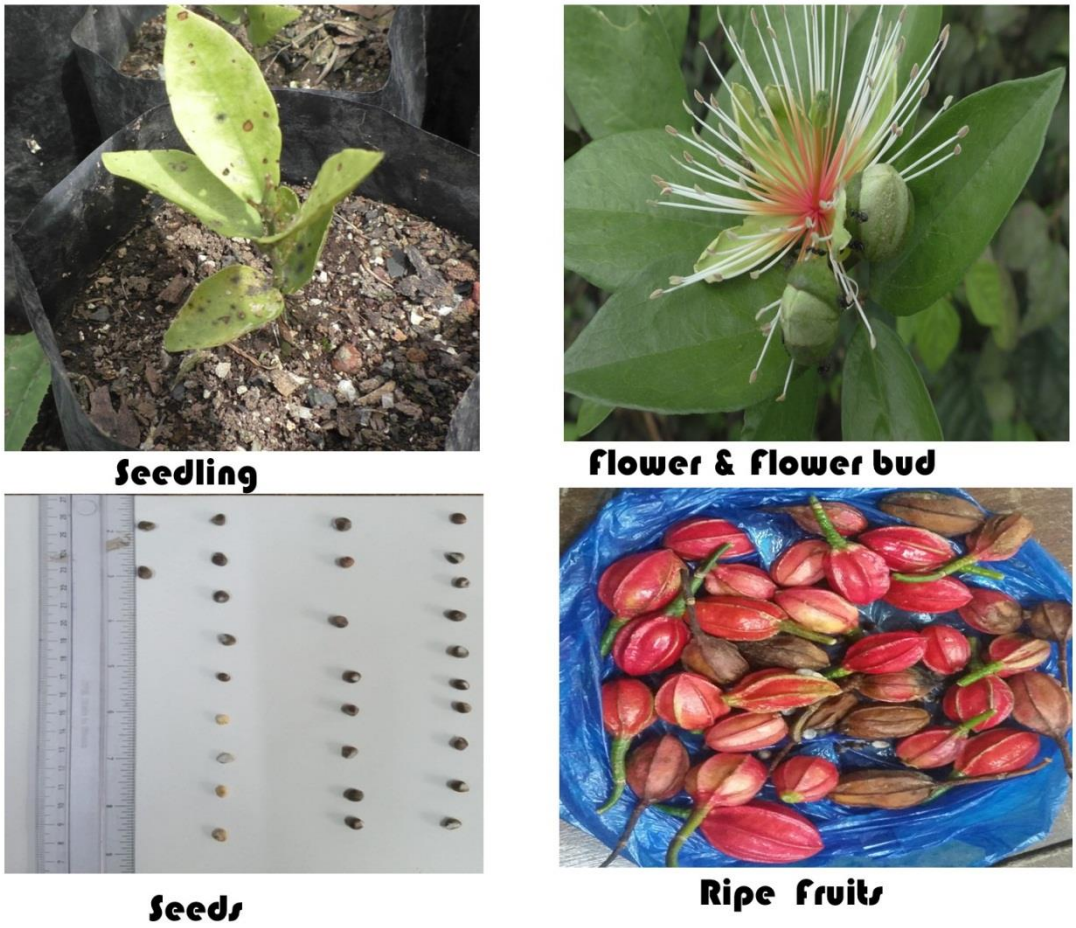

Figure 2: Pictures of Seeds, seedlings, inflorescence and ripe fruits of *Capparis erythrocarpos.* Source: CPMR arboretum, Mampong-Akuapem, Ghana.

4. Pharmacognostic Characterization of *Capparis erythrocarpos*

4.1 Leaf

The fresh matured leaves are green in color, elliptical to ovate shaped, bitter to taste and musty in odor. The leaves are alternately arranged with pinnate venation, sinuate margin, acute apex, short stalked petiole with two spiny stipules on its symmetrical base [30]. *C. erythrocarpos* has small amphistomatic leaves 18-19 which shorten travel distance of carbon dioxide to the mesophyll cells in the leaves [31]**.** This feature enhances photosynthesis in *C. erythrocarpos* [32,33]. Thick outer epidermal walls, a feature of xerophytes which was confirmed in *C. erythrocarpos* [34,30]. These observed features are essential for easy identification and authentication of the plant. Safranin, a stain for detecting different types of cells; lignified, cutinized or suberized cell wall confirmed the presence of lignin and suberin in *C. erythrocarpos* leaves [30]. For leaf surface determination, the stomata of *C. erythrocarpos* is shorter (0.018 ± 0.004 mm) but broader (0.019 ± 0.003 mm) than other member of the genus [30]. Another distinctive feature about *C. erythrocarpos* leaves is its hyperstomata. Anomocytic stomata is the main type of stomata present on both surfaces of the leaf. Other types of stomata present include anisocytic and actinocytic [30].

4.2 Stem

Twumasi and her colleagues also reported on the morphological features of the stem of *C. erythrocarpos.* The young stems are green, matured stems are greenish brown and the inner parts are creamish white. The stem showed white patches, lenticels and wrinkles which are well distributed all over the outer bark [28]. *C. erythrocarpos* stem possesses thorns [3,34]. It also has thick fibre vessels arranged within the collateral vascular bundle and small, compact parenchymatous cells. *C. erythrocarpos* has cortical sclereids but not pericyclic fibres. A transverse section of the stem of the plant reveals a lot of branched and stellate trichomes attached to a thick layer of cuticle. There is only a single layer of epidermal, isodiametric parenchyma cells and a pith containing prismatic calcium oxalate crystals with numerous starch grains. The vascular bundle has lignified vessels with outer phloem. The powdered stem contains a lot of starch grains, numerous vessels and lignified sclerenchymatous cells [28,35].

4.3 Root

The root of *C. erythrocarpos* has a bitter taste with macromorphological features of the root similar to the stem. The root has one to two layer(s) of epidermal cells overlaid with a cork with no trichome and four to seven layers of cortical collenchyma cells. Highly dispersed through the isodiametric parenchyma cells are large starch grains and stone cells. Present is a collateral vascular bundle and lignified medullary rays consisting of 15-25 rows of parenchyma. In the middle lies a pith. All throughout the cells in the section (from the epidermis to the pith) are oil deposits. The powdered root showed similar structures as the stem but it lacked trichomes and had smaller secretory cell [28]**.**

5. Ecology

The plant thrives in the thickets of coastal scrub and islands. The plant can be found in Congo, Angola, Sudan, Uganda, Ghana and East Africa. In Ghana, it can be found in and around Tema of the Greater Accra region and on the Accra plains in the Eastern Region [21]. *C. erythrocarpos* survives in a wide range of climatic conditions but seem to prefer dry humid semi-savannah regions. It also has savannah adaptive features such as deep tap root that enable it to survive in its habitat and drought periods.

6. Phytochemical screening

Qualitative and quantitative analysis of phytochemicals of a particular plant defines its biological, nutritional, and pharmaceutical attributes. Hence investigating the profile of biochemicals and bioactives in a medicinal plant is considered as a vital parameter to exploring its nutraceutical and or pharmaceutical applications [36]. Unfortunately, there is no literature record of any quantitative phytochemical evaluation and active compounds isolated from the *C. erythrocarpos.*

In a qualitative phytochemical analysis, Danquah and his colleagues (2011) reported the presence of flavonoids and alkaloids as the predominant chemical constituents in the ethanolic root extract of *C. erythrocarpos* [10]**.** Similarly, Woode and his colleagues (2009) also reported the presence of high amount of alkaloid, and

flavonoid with traces of triterpenes in the crude ethanolic root extract [9]. A more recent study revealed that, the root bark of the plant contains the highest number (five) of phytochemical constituents whiles the stem and the leaf contains equal numbers (four each). Reducing sugar, triterpenes and phytosterols were presents in all the three extracts. In addition, saponins were present in the root bark and leaf but absent in the stem. Alkaloids were also present in the root bark and stem extracts but not in the leaf [8].

Twumasi and her colleagues also investigated the phytochemical constituents in an aqueous extract of *C. erythrocarpos*. Saponins, tannins, glycosides, flavanols, triterpenoids, coumarins and alkaloids were detected in the powdered leaves, stem and roots of the plant [37]. All the above researchers employed standard techniques such as Mayer's tests for alkaloids, Fehling's test for reducing sugars, Liebermann-Burchard's test for phytosterol and triterpeness, froth test for saponins, Shinoda's test for flavonoids, Borntrager's test for free anthraquinones and Ferric chloride solution test for phenolics for the phytochemical analysis.

7. Biological/ Pharmacological activity

C. erythrocarpos has been reported to exhibit a number of pharmacological and biological activities, which have been discussed below and summarized in Table 3.

7.1 Anti-inflammatory (anti-arthritic) and Analgesic activity

C. *erythocarpos* is widely known for its anti-inflammatory and pain-relieving properties. Infections, physical and chemical agents can stimulate acute inflammatory response, which when unresolved lead to chronic inflammation that can cause major threat to human health and lead to development of various diseases. Carrageenan is commonly used to induce acute inflammation, characterized by oedema, which serves as a model for assessing the acute anti-inflammatory property of medicinal agents. Various studies on different parts of the plant have been carried out and reported to confirm the anti-inflammatory, anti-nociceptive and analgesic activity of the plant. A study by Danquah and his colleagues (2011), to assess the acute anti-inflammatory activity of C. erythrocarpos revealed that, the ethanolic root extract (10-300 mg/kg) administered before inducing carrageenan foot oedema in chicks, significantly reduced induced foot oedema with maximal inhibition of 48.86±20.41% and ED_{50} value of 59.37±18.83 mg/kg. Kumatia and his colleagues (2019), further proved the acute anti-inflammatory and analgesic activities of C. erythrocarpos, by comparing the stem and leaf to the root bark, in order to get a substitute for the commonly used root bark which is making the plant go on extinction, using the carrageenan induced paw oedema, hot plate and acetic acid induced writhing assays. The root bark and leaf extracts at 200 mg/kg p.o. significantly ($p<0.05$) exhibited anti-inflammatory activity of 48.93% and 37.42% respectively. The extracts again produced significant ($p<0.05$) analgesic activity (178.20 – 248.70 %) which was higher than morphine (136.70%) at 5 mg/kg in the hot plate assay. The stem extracts (200 mg/kg) showed the highest analgesic activity of 54.61% in the writhing assay [38].

Table 3: Summary of the Pharmacological activities of C. erythrocarpos

Pharmacological activity	**Plant part**	**Type of extract**	**Dose range (mg/kg)**	**Minimal active dose (mg/kg)**	**Experimental model / method**	**ED_{50} (mg/kg)**	**Reference**
Anti-inflammatory	Root	Ethanol	10 – 300	10	Carrageenan foot oedema	59.37 ± 18.83	[10]
	Root bark Leaves	Hydro-ethanol Hydro-ethanol	5 – 200 5 – 200	5 5	Carrageenan induced paw oedema test Carrageenan induced paw oedema		[8]
Analgesic	Stem Leaves Root bark	Hydro-ethanol	5 – 200	5	Hot plate Assay and Acetic acid induced writhing assays		[8]
	Stem Leaves Root	Aqueous	30 – 300	30	Von-Frey filament of bending force of 9 g		[37]
Anti-arthritic	Root Stem Leaves	Ethanol	30 – 300	30	Freund's adjuvant arthritis model	35.59 ± 15.73	[38]
	Stem leaves Root	Aqueous	30 – 300	30	Freund's adjuvant arthritis model	181.5 182.5 36.4	[37]
Anti-nociceptive	Root	Hydro-ethanol	10 – 300	10	Formalin-induced nociceptive test		[9]
Anti-pyretic	Root	Hydro-ethanol	30 – 300	30	Baker's yeast induced pyrexia		[10]
Anti-dyslipidaemia	Root back	Hydro-ethanol	20 – 200	20	Atherogenic indices assay Blood pressure determination		[14]
Anti-diabetic	root	Hydro-ethanol	100 – 1000	100	Streptozotocin-induces diabetes Oral glucose tolerance test		[13]

The analgesic activity of the extracts may be due to their ability to suppress the cyclooxygenase enzyme and decrease the biosynthesis of prostaglandins, and as a result of the presence of secondary active metabolites. These metabolites act by eradicating inflammatory pain mediators and block the experience of pain [39,40]. These secondary metabolites also prevent mitochondrial leakage, free radical outflow, damage of the mitochondrion and pain associated with oxidative stress which occurs as a result of mitochondrial redox reaction [41,42,43].

A model for chronic inflammation, adjuvant-induced arthritis in rats, which mimics rheumatoid arthritis in humans, was employed by Danquah and his colleagues (2011) to provide scientific confirmation for the use of the plant locally as an anti-arthritic agent. Complete Freund's Adjuvant (CFA) was injected into the right paw of rats to induce arthritis which was measured using water displacement plethysmography. It was reported that the ethanolic root extract (30 mg kg-1; p.o.) administered in therapeutic treatment, significantly ($F_{3,16} = 4.25$, $p = 0.02$) reduced adjuvant-induced arthritis with maximal inhibitions of 34.19±15.73% and also significantly ($F_{3,16} = 4.28$, $p = 0.02$) prevented the spread of arthritis from the ipsilateral to the contralateral paw [10]. However, higher doses of the extract (100 and 300 mg kg-1; p.o.) had no significant inhibition on the induced arthritis. Twumasi and his colleagues (2019), compared the anti-arthritic and analgesic effects of three different parts (leaves, stem and root) of C. erythrocarpos, employing the complete Freund's adjuvant arthritis model and measuring responses to Von Frey filament number 9, respectively [37]. Also, the mechanism of anti-inflammation was determined. It was reported that extracts from all the parts, leaves, stem and root reduced paw volumes significantly, with ED50 values of 182.5, 181.5 and 36.4 mg kg-1 respectively. Results obtained for the roots were in agreement with findings from previous studies where the least dose was the most active against inflammation [8,10]. The higher doses of all extracts gave a lower potency and this could have resulted from the presence of other secondary metabolites in the extract that mask the anti-inflammatory activity when they are present in sizable quantities. The leaf extract (100 mg kg-1) showed analgesic activity with a decrease in percentage response to Von Frey filament 9. Lower doses of all extracts reduced Tumor Necrosis Factor-alpha (TNF-α) levels, with that of stem extracts reducing Interleukin-6 (IL-6). The extracts also reversed elevated White blood cells (WBC) and platelets levels. The observed anti-arthritic activity of the leaf, stem and root bark may be due to the inhibition of the release of inflammatory mediators at the various phases of arthritis.

In a mouse formalin test, Woode and his colleagues (2009) assessed the antinociceptive effect of ethanol root extract, the extract (10-300 mg kg-1) dose dependently reduced pain scores in both phases of the formalin-induced nociception, indicating both central and peripheral effects. Morphine (1- 10 mg kg-I; i.p.) was used as positive control. Morphine, an opioid agonist was antinociceptive and inhibited both phases of the formalin response which clearly depicts that it is a centrally acting analgesic drug. At dose 100 mg kg-1, the formalin-induced pain was significantly reduced in the first and second phases of nociception by 47.54±5.65 and 80.01±3.77%, respectively by the extract. The analgesic effect was further investigated to determine the possible mode of action(s) of the extract by using the non-selective opioid receptor antagonist naloxone and non-selective adenosine receptor antagonist theophylline. The results showed that, naloxone reversed the effect of morphine as expected but naloxone however, did not reverse the antinociceptive effect of the extract in both phases, suggesting that opioid receptor activation was not involved in the antinociceptive effect of the extract. The antinociceptive effect of the plant was completely reversed in the first phase and significantly reversed in

the second phase by theophylline, which suggest that, adenosine is involve in the antinociceptive effect of C. erythrocarpos [9].

7.2 Antipyretic activity

Pyrexia is a sign associated with a number of diseases including infections and inflammatory conditions. Yeast induced fever is an efficient and consistent technique employed to investigate and search for new antipyretic drugs [44]. A study by Danquah and his colleagues (2011a) to assess the antipyretic activity of the plant's ethanol root extract (30-300 mg kg-1) employed the baker's-yeast induced pyrexia in rats. The antipyretic activity of the extract showed that C. erythrocarpos caused a significant reduction in rectal temperature however, the effect was not as pronounced and sustained as compared to the standard used (paracetamol). The authors concluded that, the results support the view that the extract has some influence on Protaglandin-biosynthesis, since prostaglandin is believed to be a regulator of body temperature. The extract produced a significant and dose-dependent ($F\ 4, 15 = 51.85$, $P<0.0001$) reduction in the rectal temperature whiles paracetamol (10-100 mg kg-1) caused a reduction in rectal temperature of the rats in a dose dependent manner ($F\ 4, 15 = 78.87$, $P<0.0001$). The antipyretic effect began from the first hour after the drug administration and was sustained for 4 hours [10].

7.3 Anti-dyslipidaemic Activity

The anti-dyslipidaemia effect of Sirrapac, a milled root bark of C. erythrocarpos, investigated in male adult Sprague-Dawley rats over a three-month period, assessed the rats' body weight, food intake, Serum triglycerides (TG), total cholesterol (TC), high density lipoprotein-cholesterol (HDLC), low density lipoprotein-cholesterol (LDLC), leptin levels and effect on blood pressure [14].

The hydro-ethanol extract of Sirrapac (20, 100 and 200 mg kg-1), dose dependently and significantly ($p < 0.05$) reduced body weight, food intake, serum levels of TC, LDLC, TG and serum leptin with significant ($p < 0.05$) increase in levels of HDLC. There was also a significant decrease in rat systolic blood pressure with no effect on the diastolic blood pressure, indicating its anti-lipidaemic effects and ability to manage cardiovascular diseases and other associated problems, like obesity [14]. The reduction in body weight may be due to loss of appetite in the animals. The milled root bark directly acts to reduce appetite and fats circulation, which prevents the deposition of fats as energy stores in the adipose tissues.

7.4 Anti-diabetic activity

Diabetes mellitus which is a chronic endocrine and metabolic condition results when the pancreatic beta-cells are not able to maintain sufficient secretion of insulin or when the cells of the body are unable to fully utilize the produced insulin. It is associated with persistent hyperglycemia and dyslipidemia which can lead to cardiovascular diseases and other metabolic conditions. The anti-dyslipidaemic activity of *C. erythrocarpos* therefore makes it a potential anti-diabetic agent.

The in-vivo anti-diabetic activity was investigated by Nyondo and his colleagues (2020), employing the

streptozotocin (STZ)-induced diabetes in mice. Also, the oral glucose tolerance test (OGTT) was employed to investigate the acute anti-hyperglycemic activity in normal mice. The hydro-ethanolic root extract of C. erythrocarpos after 14 days of daily oral administration in STZ-induced diabetic mice, significantly at doses 250 mg kg-1 ($p = 0.0267$), 500 mg/kg ($p = 0.0002$) and 1000 mg kg-1 ($p = 0.0011$), reduced the level of fasting blood glucose. After 2 hours of oral glucose load in OGTT, the extract significantly lowered the blood glucose levels at doses of 100 mg kg-1 ($p = 0.0322$), 200 mg kg-1 ($p = 0.0118$) and 500 mg/kg ($p = 0.0222$) [13]. Diabetes mellitus which is a chronic endocrine and metabolic condition results when the pancreatic beta-cells are not able to maintain sufficient secretion of insulin or when the cells of the body are unable to fully utilize the produced insulin. It is associated with persistent hyperglycemia and dyslipidemia which can lead to cardiovascular diseases and other metabolic conditions [45]. The anti-dyslipidaemic activity of C. erythrocarpos may therefore contribute to its anti-diabetic potential.

8. Antimicrobial activity

Antibacterial and anti-fungal activity of C. erythrocarpos leaf extracted successively with ether and methanol was tested against Staphylococcus aureus (ATCC 25923), Escherichia coli (ATCC 25922), Pseudomonas aeruginosa (ATCC 27853) and Candida albicans (clinical isolates) using the agar well diffusion and the broth serial dilution assays. The ether leaf extract exhibited activity against all the test microorganisms with mean zones of inhibition of 26.3±2.03mm (C. albicans), 26.3±0.58mm (S. aureus), 25.3±1.53mm (E. coli) and 13.0±0.00mm (P. aeruginosa), the methanol extract had no activity against E. coli and P. aeruginosa. However, E. coli was most susceptible to the ether extract with the least MIC of 320µg mL-1, followed by C. albicans, S. aureus and P. aeruginosa with MICs of 330, 400 and 500 µg mL-1, respectively. The methanol extract showed activity against C. albicans and S. aureus with MIC of 500 and 530 µg mL-1, respectively [11]. The anti-fungal efficacy testing of the dichloromethane root extract was also assessed in-vivo using the mice infection model. Immunocompromised mice were infected with 0.3 mL of 0.5 McFarland standard inoculum of C. albicans and then treated with 100, 200 and 400 mg kg-1 of the extract. The extract dose dependently reduced the fungal load with respective mice survival. The extract at the test doses showed significant anti-fungal activity with organ burden clearance ranging from 64.0%–99.9% ($P < 0.0001$). The highest dose (400 mg kg-1) of the root extract was the most effective with mice survival of 60% [12].

9. Toxicological assessment

The first reported acute and sub chronic toxicity study was by Woode and his colleagues (2009). The researchers administered high doses of ethanolic extract (300-3000 mg kg-1 p.o) to mice, followed by close monitoring for signs of toxicity for 24 hours and 14 days, respectively. The results showed no remarkable signs of toxicity either immediately or during the post – treatment period even at the highest dose of 3000 mg kg-1 of body weight. Also, there were no changes in behavior, activity, posture, or external appearance that were considered to be test drug related. All the animals also survived throughout the 24 hours and the 14 days study period, respectively. There were generally no statistically significant changes in the hematological indices and biochemical parameters taken, suggesting that the extract has a high safety profile [9]. Martey and his colleagues (2013) also researched on the safety of the root bark of C. erythrocarpos, in male Sprague-Dawley

rats by evaluating the effects of C. erythrocarpos on the function and/or morphology of key organs such as the liver, kidney, lung, heart and the bone marrow. After 6 months of chronic administration of C. erythrocarpos at 18 and 180 mg kg-1 body weight to the rats, the effects of the plant on certain serum biochemical, haematological, urine and histopathological determinations were used as indices of organ specific toxicity. The results indicated that C. erythrocarpos had no effect on urine, hematological and serum biochemical indices at termination of treatment with the exception of serum ALT level which was significantly ($p<0.05$) attenuated in a dose-dependent fashion (21-35%), an indication that the plant extract or its metabolite(s) inhibits ALT activity. This therefore, indicates that these organs were not adversely affected by C. erythrocarpos treatment. Histopathological studies showed that C. erythrocarpos did not adversely affect the morphology of the liver, kidney and heart tissues. However, lungs of the animals showed slight but insignificant inflammatory response in alveolar areas and Clara cell hyperplasia without the thickening of alveolar septa and bronchiolar epithelial wall. C. erythrocarpos did not affect any of the hematological indices which suggests that it did not suppress or damage the bone marrow or directly affected the blood cells. The lack of effect of the plant extract on blood clotting time suggested that it does not affect vitamin K levels or inhibit the synthesis of blood clotting proteins. The latter is supported by the fact that serum albumin levels were not affected by C. erythrocarpos treatment, suggesting that hepatic protein biosynthetic activity was not impaired. However, there were significant ($p<0.05$) changes in weight of C. erythrocarpos-treated animals with duration of treatment compared to control [22]. This phenomenon was later investigated by Saka and his colleagues and the authors concluded that, the reduction of body weight of the test animals may be through the suppression of appetite with subsequent reduction in fat uptake and deposition [14]. These results suggest that there is no organ specific toxicity associated with chronic administration of C. erythrocarpos in rats.

10. Conclusion and Recommendation

From the review of the existing works, it may be concluded that C. erythrocarpos has been used in the treatment of various diseases and reported to have anti-inflammatory, analgesic, anti-dyslipidaemic, anti-diabetic, antipyretic and antimicrobial activities. Despite the many pharmacological activities shown by this plant, some other activities like aphrodisiac and use of the plant for treatment of chronic diarrhoea which are traditionally known has not yet been confirmed through research yet.

Finally, we recommend that future studies should focus on identification, separation, purification and quantification of the most bioactive constituents of C. erythrocarpos. Pharmacological evaluation of its aphrodisiac and anti-diarrhoea activities must be studied. The effective dose must also be ascertained for future clinical trials on the pharmacological action of C. erythrocarpos.

11. Conflict of Interest

Authors declare that there are no conflicts of interest

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