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A Review on the Nutraceutical Potentials of *Daucus Carota* in the Management of Sickle Cell Anaemia

Abdulkadir Mohammed Danyaro*[1], Bello Aminu Bello[1,2], Zinat Suleiman Mohammed[1], Adam Abdullahi Adam[2], and Khadija Aliyu Nuru[1].

[1]Department of Biochemistry,
Sa'adu Zungur University,
Gadau, Bauchi State,
Nigeria.

[2]Department of Biochemistry,
Federal University Dutse (FUD),
Dutse, Jigawa State,
Nigeria.

Email:amidkana03@gmail.com

Abstract
Daucus carota (carrot) is a widely distributed and cultivated root crop that is consumed as vegetable for human nutrition and as therapeutic agent because of its rich phytochemical compositions as well as minerals and fatty acids essential for many biochemical processes. It possesses enormous nutritional values as well as antioxidant, anti-inflammatory, antidiabetic, anticancer and antimicrobial activities among other pharmacological properties. The medicinal values of this vegetable hinge on these pharmacological properties, which in turn are due to the numerous bioactive compounds it possesses. There is presently no evidence of the antisickling activity of carrot, even though literatures revealed some of the bioactive compounds responsible for sickling inhibition or reversal, pain relief as well as prevention of endothelial dysfunction and haemolysis of red blood cells, are also contained in carrot. Therefore, this review aimed to explore the nutraceutical potentials of carrot in the management of sickle cell anaemia.

Keywords: Antisickling, Daucus carota, Nutraceutical, Pharmacological Properties, Sickle Cell Anaemia.

INTRODUCTION
Daucus carota is a widely distributed and cultivated member of the A*piaceae* family that is consumed as vegetable for human nutrition and therapeutic agent because of its minerals, essential and edible oils, steroids, antioxidant pigments (carotenoids), flavonoids, tannins and other phytochemicals (Prajna & Hedge, 2018; Tijjani *et al.*, 2022).

It is an economically important crop with diverse range of phenotypic and genotypic variations and with increased domestication because of its rich carotenoid, anthocyanin and sugar contents that determine its different colours (white, yellow, orange, red, purple and black) (Figure 1) and flavours as well as its biennial growth habit, increased size and variation of root shape (Riaz *et al.*, 2022).

Author for Correspondence

Figure 1: Various types of Carrots (Reddit, 2019)

It is cultivated globally as a biennial root vegetable and has many nutritional benefits because of its numerous components that work together to improve the overall health of individuals (Stefl, 2017).

Apart from its nutritional value, it is also a good therapeutic agent because of its numerous pharmacological properties that include antioxidant, anti-inflammatory, antidiabetic, anticancer and antimicrobial activities among others, brought about by the presence of antioxidants and other bioactive compounds (Arun *et al.,* 2021; Rafiq *et al.,* 2022). These pharmacological properties confer medicinal values to it and make it a good medicinal and vitamin containing food (El-Saber e*t al.,* 2020).

However, there appears to be limited or no study on its antisickling activity in-spite of the fact that, it contains the bioactive compounds that have been proven to be useful in either inhibition of sickling of red blood cells (RBCs) or their reversal, prevention of endothelial dysfunction and RBCs' haemolysis, or even in the relief of nociceptive pain, all of which form the pathophysiology and symptoms of sickle cell anaemia (SCA), a genetic autosomal disorder of RBCs characterized by painful swelling of mostly the chest, arms and legs (caused by the blockage of blood flow to bodily tissues and organs) as well as jaundice (the yellowing of the skin, eyes and mouth caused by the piling up of bilirubin from destruction of RBCs that happen faster than the liver can filter them) and other symptoms (Inusa *et al*., 2019; Hernandez *et al*., 2021; Acharya *et al*., 2023).

Hence, this review was carried out to explore the nutraceutical potentials of carrot in the management of SCA by revision of existing literatures and aimed to provoke interests for researches toward development of carrot antisickling nutraceuticals.

Nutritional Value of *Daucus carota*

Daucus carota or carrot is a popular vegetable with many nutritional benefits. It is ranked 10th in nutritional value among 39 most nutritious fruits and vegetables (Stefl, 2017). Its nutritional value is largely due to its dietary fiber, carotene and sugar contents, all of which are abundant in the phloem that constitutes about 60% of the root crop, which is the frequently used part of the plant in human diet, even though the leaves, which are also rich in vitamins A, C and K as well as potassium (K) can be used in soups, salads and pesto (Krivokapić *et al.*, 2020).
The summary of the nutritional value of carrot per 100 g along with the percentage daily value (DV) based on a 2,000 calorie diet, is given in table 1 below, the values of which may vary from one literature to another, probably due to different plants used, soil characteristics and environmental factors (Mandrich *et al.,* 2023).

Table 1: Summary of the nutritional value of *Daucus carota*

Nutrient	Amount/100 g	% Daily Value (DV)
Calorie	41 kcal	2
Moisture	-	-
Carbohydrate	9,600 mg	3
Protein	900 mg	2
Fat	200 mg	0
Fiber	2,800 mg	10
Vitamin A (as β-Carotene)	835 µg	93
Vitamin C	5.9 mg	7
Vitamin K	13.2 µg	11
Vitamin B	19 µg – 1.0 mg	5
Vitamin E	0.7 mg	4
Ash Content (Minerals)	900 mg	-

United States Department of Agriculture (USDA), 2018; Mandrich *et al.*, 2023.

Pharmacological Properties of *Daucus carota* and Key Bioactive Compounds

Carrot is regarded as a vitamin containing food and medicinal plant with numerous pharmacological properties and offers considerable therapeutic effects against conditions such as diabetes, cancer, gastrointestinal problems and cardiovascular conditions, all because of the presence of antioxidants and other bioactive compounds (Arun *et al.,* 2021; Rafiq *et al.,* 2022).

The bioactive compounds, which are produced through secondary metabolic processes, include carotenoids, phenolic compounds, polyacetylenes, ascorbic acid and tocopherols (Ahmad *et al.,* 2019). They are responsible for the nutritional and pharmacological properties of this wonderful food crop. Some of the key pharmacological properties and the responsible bioactive compounds are highlighted in table 2 below.

Table 2: The pharmacological properties and bioactive compounds of *Daucus carota*

Pharmacological Property	Bioactive Compounds	Mechanism of Action	References
Antioxidant activity	Carotenoid (β-Carotene, Lutein, Zeaxanthin), Phinolic compounds	Neutralize free radicals and reactive oxygen spaces (ROS). Inhibit lipid peroxidation and enhance antioxidant enzymes activity.	Boileau *et al.*, 2000; McNulty & Murphy, 2011.
Anti-inflammatory effect	Polyacetylene (Falcarinol) and Carotenoids	Inhibit pro-inflammatory cytokines and enzymes like Cyclooxygenase -2 (COX-2). Reduce NF-$_K$B activation, and modulate inflammatory pathways	Schmeda-Hirschmann & Yu, 2005; Pandey & Rizvi, 2009
Antidiabetic activity	β-Carotene, polyphenols, dietary fiber, Falcarinol, Falcarindiol and Vitamin A.	Inhibit enzymes involved in glucose metabolism, increase cellular uptake of glucose from blood and reduce oxidation or formation of ROS.	Karkute, 2018; Tijjani *et al.,* 2022;
Antihypertensive activity/cardiovascular benefit.	Coumarin glycosides (DC-2 and DC-3).	Blocking of Calcium ion (Ca^{2+}) channel, potassium-mediated vasodilation, lower cholesterol level and reduce oxidative stress to decrease arterial blood pressure.	Arun *et al.,* 2021

Anticarcinogenic/Cytotoxic effect.	β-Caryophylene, Caryophylene oxide, α-Humulene and β-2-Himachalen-6-ol, β-Carotene and Falcarinol.	Induce apoptosis and cause cell cycle arrest in cancer cells, prevail DNA damage through antitoxin activity.	Arun *et al*., 2021. Isma'il *et al*., 2024;
Antimicrobial effect.	Geranyl acetate and α-Pinene.	Inhibition of fungal growth and destruction of fungi	Al-snafi, 2017; Ismail et al 2024
	(E)-methylisoeugenol, Elemicin, Luteolin and luteolin derivatives.	Bacteriacidal activity against *E. coli*, *S. aureas*, *B. cereus* and *L. plantarum.*	Rokbeni *et al.*, 2023.
Central nervous system (CNS) activity/memory enhancing effect	Choline	Inhibits brain cholinesterase activity and elevates brain acetylcholine levels. Prevents depression to improve memory	Bahrami *et al*., 2018 Babu *et al.*, 2014.
	β-Carotene and Lutein	Protects brain cells from oxidative stress and reduce the risk of cognitive decline	

* $NF_{-K}B$ = Nuclear factor kappa-light-chain-enhancer of activated B cells.

Carrot is also known to have benefits to the eyes, skin, hair, fertility, gastrointestinal tract and the immune system as well as confers protective effects to the liver and kidney (Sodimbaku *et al.*, 2016; Al-Snafi, 2017; Bahrami *et al.*, 2018; Arun *et al.*, 2021)

Nutraceutical Potential of *Daucus carota* inSickling Inhibition and Reversal

Carrot is rich in aromatic amino acids like phenylalanine, tryptophan and tyrosine as well as antioxidants like Rutin and Quercetin, and phenolic compounds like polyphenols and derivatives (Tchoulegheu *et al.*, 2023). These compounds have been demonstrated to be good sickling inhibition and reversal agents and are usually components of antisickling formulations (Imaga, 2013; NatureClaim Team, 2024). They act by modulating bisphosphoglycerate mutase (Figure 2) to lower the level of 2,3-bisphosphoglycerate in RBCs and increase haemoglobin's affinity for oxygen thereby inhibiting or reversing sickling (Muhammad *et al.*, 2019a) or by preventing oxidative stress to minimize the production of ROS thereby improving RBCs' function and alleviating sickling (Muhammad *et al.*, 2019b).

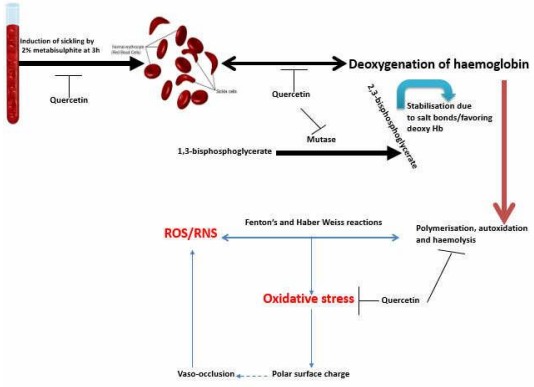

Figure 2:Mechanism of Quercitin sickling inhibition and reversal (Muhammad *et al.*, 2019a).

Antihaemolytic Potential of *Daucus carota* inSCA Condition

It also contains vitamin C as well as Kaempferol (0.20mg/100g), Quercitin (0.20mg/100g), and Luteolin (0.10mg/100g) (Carlos & Dias, 2014; NatureClaim Team, 2024), which have been reported to hinder haemolysis in RBCs by inhibiting the hepatic expression of Hepcidin [a peptide hormone produced in the liver that is crucial in Iron (Fe) homeostasis] and spleenic Fe

levels. Rutin also present in carrot has the ability to restore the integrity of RBCs' membranes by preventing or reversing the formation of ROS (Figure 3) (Cotoraci *et al.,*2021).

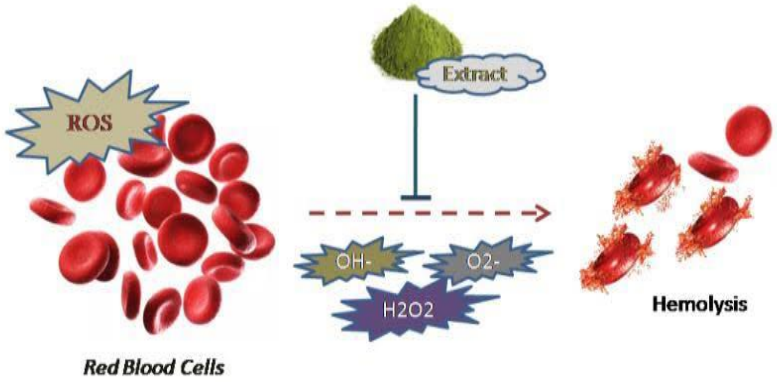

Figure 3: Inhibition of the formation of ROS to prevent haemolysis of RBCs (Bhat *et al.,* 2019).

Nutraceutical Potential of *Daucus carota* inPreventing Endothelial Dysfunction

Carrot contains Lycopene (0.05mg/100g), Anthocyanin (10-30mg/100g), Quercetin and Chlorogenic acid (20-30mg/100g) (Lee *et al.,* 2017; Smith & Jones, 2018; Williams & Patel, 2019). The compounds have been shown to be beneficial to preventing oxidative-induced endothelial dysfunction by increasing Nitric Oxide (NO) bioavailability and inhibiting the NF_KB signaling of inflammatory pathway to prevent oxidants-induced endothelial dysfunction (Monsalve *et al.,* 2017). Chlorogenic acid particularly inhibits the production of ROS, translocation of NF_KB and expression of adhesion molecules to protect against endothelial dysfunction (Monsalve *et al.,* 2017).

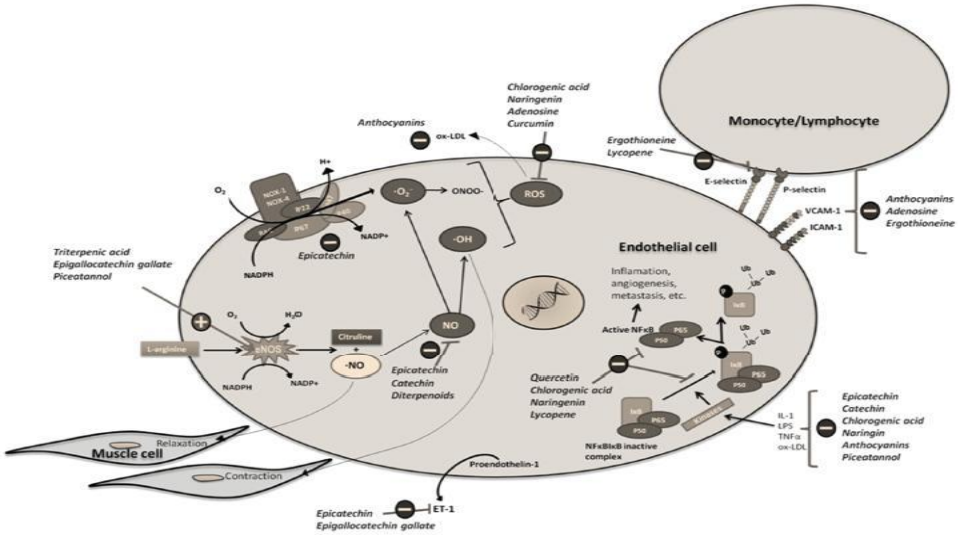

Figure 4: Mechanisms of endothelial function protection by natural bioactive compounds (Monsalve *et al.,* 2017)

Nutraceutical Potential of *Daucus carota Against* Nociceptive Pain

Carrot also contains β-Caryophyllene (0.2-0.5mg/100g) (Garcia *et al.,* 2020), Chlorogenic acid, Lycopene, Quercitin and many other bioactive compounds that have been identified as naturally occurring anti-nociceptive compounds (Lim & Kim, 2016). They target the cannabinoid receptors type 2 (CB2), Gamma-amino butyric acid (GABA) receptors, Connexin 43 (Cx43) Gap-junction protein and Opioid receptors (OPR) (Ameh *et al.*, 2012; Lim & Kim, 2016). This makes it potentially beneficial in the management of SCA.

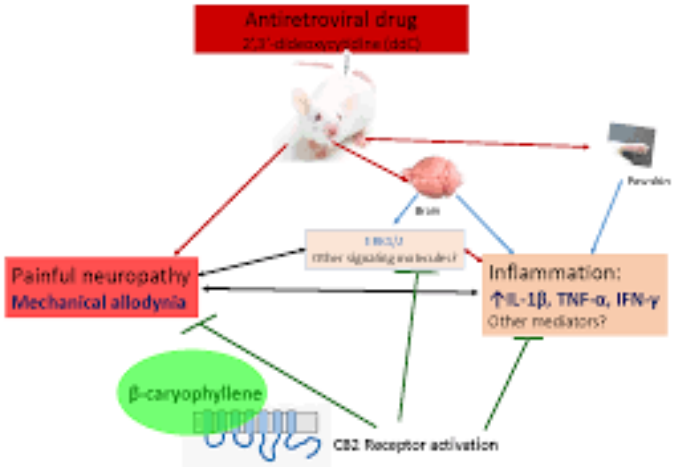

Figure 5: Mechanisms of action of β-Caryophyllene in reducing pain (Monsalve *et al.,* 2017)

Conclusion and Future Prospects

The pharmacological properties offered by carrot's bioactive compounds confer medicinal values to it and makes it a good medicinal and vitamin containing food. It may certainly have the nutraceutical potentials for the management of SCA because it also contains the phytochemicals that have been proven to be useful in either inhibition of sickling of RBCs or their reversal, prevention of endothelial dysfunction and RBCs' haemolysis. As such, future researches should exploit it in the development of antisickling nutraceuticals.

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