

Potential health benefits of conventional nutrients and phytochemicals of *Capsicum peppers*

Abstract

Capsicum peppers are great herbal medicine bestowed with natural pharmacological bioactive compounds majorly Phytochemicals, capsaicin, essential oils and a rich mix of organic micronutrients with potential health benefits. They play nutritional roles in diets and possess medicinal properties. These bioactive agents manifest their usefulness over mono-therapy by working in consortium and exert synergistic, polyvalent and pharmacological effects in humans as nutraceutical that serve as functional foods; as crude drugs for health benefits including prevention and treatments of chronic metabolic diseases such as coronary heart disease, diabetes and obesity. The synergistic effects of the phyto-nutrients of *Capsicum peppers* are thought to make them potentially effective anti-microbial, anti-inflammatory, anti-cancerous, anti-tumor, anti-mutagenic and possess good antioxidants with scavenging ability for singlet oxygen, free radical inhibitors, peroxide decomposers and metal chelating agents which are implicated in favoring of the onset of degenerative diseases including mucosa degeneration. While capsaicin imparts the ability for *Capsicum peppers* to function as topical agents, for the relief of various forms of pains as pain medicine; its activity as neurotoxic and cytotoxic agent is suggested to give various potential environmental health benefits and also benefiting man as a potential effective anesthesia. The presence of Phytochemicals in *Capsicum pepper* makes them not only useful and much cheaper alternatives to synthetic drugs but the Phytochemicals can be harnessed as crude drugs for the production of novel drugs. However, clinical studies on the consumption of *Capsicum peppers* are insufficient and needed to confirm some of the findings from animal studies.

Keywords: *Capsicum peppers*, phytochemicals, essential oils, capsaicin, synergy, health benefits

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Introduction

Plants have been the main source of all types of medicines. Knowledge of the use of such plants has helped sustain the populace from time immemorial. While, cruciferous, green leafy vegetables and other fruits have been given much attention, the *Capsicum peppers* have been relegated to the background even with its rich bountiful and diverse nutrients. Meanwhile, the *Capsicum peppers* as medicinal plants contain many pharmacologically active compounds that may act single handedly in modulation or in synergy to improve health. Capsaicin serves as a major secondary metabolite in *Capsicum peppers*. It is the principal bioactive agent in *Capsicum peppers*. This bioactive agent in pepper plants is implicated as a chemical lead for the synthesis of drugs and for therapeutic purposes.¹ Along with the rich antioxidants and essential oils and promising rich constituent of conventional nutrients in *Capsicum pepper*, capsaicin gives *Capsicum pepper* its numerous medicinal values in alternative medicine. The major groups of Phytochemicals in *Capsicum pepper* also enhance their classification as herbal plant and pain medicine.

These Phytochemicals are pharmacological/biologically active compounds and herbal products which exert their medicinal actions without serving as nutrients in human diets. They are bioactive compounds which serve as nutraceuticals/functional foods. They play important nutritional roles in diets, confer numerous health benefits to man, relief pains and prevent chronic, metabolic diseases because of their inherent wide range of medicinal properties including antioxidant, anti-microbial, anti-mutagenic, anti-tumor, anti-cancerous and

cardio-protective activities. As functional foods, *Capsicum peppers* make up good nutrition which can help prevent illness. And as herbal medicines and aromatic plant, they may be useful in the treatment of existing health problems. Generally, herbal medicines are not only effective but are useful and much cheaper alternatives compared to synthetically produced drugs. Again, *Capsicum pepper* can be easily grown and used domestically for common complaints at local levels.

The establishment of bioactive natural products is the oldest chemical lead in the development of new medicine in the pharmaceutical industries. Rich bioactive compounds inherent in medicinal plants can be refined to give more specifically acting novel drugs. Currently, there is an increasing acknowledgement that herbal medicines can be a very effective and much cheaper alternative to modern medicines which are synthetically produced.² The potential health benefits of *Capsicum peppers* are considered in this paper. Their level of pungency, Phytochemicals and essential oils are related and equated to reported observed effects as medicinal drugs on human-beings in an attempt to suggest and link them to medicinal/drug purposes. It is believed that the study will expose the numerous and divergent uses of *Capsicum peppers* and increase the awareness of this potent plant as an important herbal plant.

Capsicum peppers

Capsicum pepper has always been one of the most important spices with amazing healing powers since ancient time but seems to be under-rated as a natural medicine in the modern pharmaceutical drug

age. *Capsicum peppers* belong to the family Solanaceae and the genus *Capsicum*. The *Capsicum annum* (chilli pepper and sweet pepper) and *Capsicum frutescens* (bird eye pepper) are two of the commonest species and three of the commonest varieties of *Capsicum peppers* found in the southern part of Nigeria, West Africa.³ The bodies of the bird eye pepper fruits of the *C. frutescens* capsicum peppers are smaller and narrower than those of the *C. annum*; varying between a length of 2.5cm to 9.1cm and width of between 0.5cm and 3.8cm. *Capsicum peppers* are used economically for nutritive, ornamental, environmental and medicinal purposes. They are used as vegetables for flavoring, as food additives, as preservatives and for medicinal/crude drug purposes.^{4,5} Whatever values pepper has as medicinal plant is due to the presence of essential oils which gives it a characteristic aroma, the carotenoids and to the aromatic pungent principle called capsaicin.^{1,6}

Nutrients and phytochemicals of capsicum peppers

Capsicum peppers are promising sources of rich mix of conventional nutrients and also offer an equally rich mix of phytonutrients. Phytochemicals found in medicinal plants are products of secondary metabolism.⁷ Primary metabolites including carbohydrates, proteins, lipids, nucleic acids, heme and chlorophyll take part in primary metabolic processes of maintaining/building tissues and plant cells. However, plants synthesize a diverse array of secondary metabolites/Phytochemicals⁸ which do not play vital biochemical roles in plants but rather exhibit ecological functions like plant defense against microbial and fungal pathogens and insect pests. Empirical studies have indicated that the consumption of fruits and vegetables imparts health benefits example reduced risk of coronary heart disease, stroke and cancer. These health benefits are mainly attributed to organic micronutrients such as carotenoids, polyphenols, vitamin C and others⁸ which scavenge and deactivate reactive free radicals and make them harmless.

Capsicum peppers are good sources of vitamin K, C, B and carotene (pro-vitamin A) in addition to lycopene, flavonoids, Phytochemicals and trace metals; the unripe, green and yellow fruits contain considerable lower amounts of these substances. The level of carotenes like lycopene is nine times higher in red peppers. Also, their vitamin C content is two times higher than those of the green ones.⁹ *Capsicum peppers* generally are rich sources of antioxidants and vitamin C. However, these carotenes are still present in good amounts and even retained after some months of freezing.¹⁰ A 100g of red *Capsicum* contains energy (8.8g), sugars (5.3g), Fiber (1.5g), fat (0.4g), proteins (1.9g), about 173-240% of vitamin C (ascorbic acid), 39% of vitamin B6 (pyridoxine), 32% of vitamin A, 13% of iron, 14% of copper, 7% of potassium, magnesium 6%. They also contain manganese and are rich sources of B-complex group of vitamins such as niacin, pyridoxine (vitamin B6), riboflavin and thiamin.¹¹ The combination of these rich nutrients and antioxidant properties of the phytochemicals inherent in the *C. peppers* may subscribe to their abundant health benefits.

Antioxidants in *Capsicum peppers*

One of the health benefits of *Capsicum pepper* would be the rich effects of its antioxidant nutrients provided by its numerous Phytochemicals. These antioxidants are protective agents against Reactive Oxygen Species (ROS). ROS are highly reactive harmful free radicals which include super-oxides, singlet oxygen and hydroxyl radicals; they move round the body and cause oxidative damage to

macromolecules like proteins, lipids, carbohydrate, nucleic acid and cells and thus involved in the initiation phase of the degenerative diseases.⁸ ROS and their oxidative damage are implicated in several diseases including cancer, aging, heart disease, stroke, diabetes mellitus, rheumatism, arthritis, osteoporosis and ulcers.¹² In diabetes mellitus particularly, ROS impairs insulin receptors, inactivates the glycolytic enzyme, glyceraldehyde-3-phosphate dehydrogenase and ultimately leads to hyperglycemia. Insulin resistance increases weight gain because fats are accumulated in the adipose tissue. The elevated levels of free fatty acids lead to obesity which is a factor in the development of insulin resistance which in turn causes diabetes mellitus. The consumption of *Capsicum peppers* with its good source of antioxidants can scavenge and significantly deactivates the harmful free radicals and prevent oxidative damage to cells and hence, the resultant diseases.

As vegetables, the red sweet pepper contains twice the pro-vitamin A as carrot and twice the vitamin C contents of green pepper.⁹ Sweet (bell) peppers are excellent source of antioxidant and anti-inflammatory phytonutrients.¹⁰ The presence of antioxidants -vitamin C and pro-vitamin A carotenoids (α - and β - carotenes) in *Capsicum peppers* may be able to support immune function and anti-inflammation making them useful in the treatment of asthma, arthritis, rheumatism. Vitamin C is well known for its antioxidant action. It may help lower blood pressure and cholesterol levels. Uboh & Umoru¹³ found a correlation between vitamin C and iron chelating ability which may suggest that vitamin C chelates heavy metals, reduces free radicals and reduces the risk of atherosclerosis, cardiovascular disease and cancer. They also suggested that high content of phenolics may also be responsible for the high free radical scavenging capacity. Vitamin C helps to form connective tissues, keep capillaries healthy to help prevent easy bruising and keeps the gum healthy.¹⁴ β -carotene particularly, offers protection against cataract. The presence of vitamin A is also implicated in the maintenance of epithelial cells, normal bone and teeth development in children and prevention of osteoporosis in adults. It supports spermatogenesis, estrogen function and tissue differentiation as well as maintenance of normal skin health and prevention/treatment of acne. The level of pro-vitamin A carotenoids (α - and β - carotene) depends on the type of pepper. Some cultivars have as much as 12mg/kg total carotenoids while others are below the detectable level.¹¹

Vitamin C is water soluble and is able to scavenge free radicals and prevents damage inside and outside the cells' aqueous environment. Vitamins A and C both reduce inflammation like those in arthritis and asthma while high intake of vitamin C and β -carotene may prevent atherosclerosis, diabetes, colon cancer and asthma.¹⁵ Amongst the carotenoids in *Capsicum peppers*, lycopene is present in good amount and gives pepper and tomatoes red coloration. However in tomatoes, lycopene appears to be stable even during food processing and its bioavailability enhanced by processing, heat, presence of dietary lipids and other carotenoids like β -carotene.¹⁴ On the other hand, carotenoids in *Capsicum peppers* like vitamin C and vitamin B6 are susceptible to heat but lycopene, beta carotenoids and lutein are retained even after some months of freezing.¹⁰ The increase in the carotenoids content during the development of tomatoes from immature green to ripe is related to the increase in the lycopene content.¹⁶ This may also be the case in the in the *Capsicum peppers*. The presence of lycopene in *Capsicum peppers* as a potent antibody will promote health.

Lycopene induces cell-cell communication via gap junctions and

growth as well as peroxy radical scavenging. It is the most effective singlet oxygen quencher amongst the biological carotenoids¹⁷ probably because lycopene is not converted to α - and β - carotenes and so predominates as a potent antioxidant with anti-proliferative/anti-cancerous activities. Lycopene is much more potent in inactivating singlet oxygen than β -carotene even though its structure resembles that of beta carotene.¹⁶ The antioxidant property of lycopene is protective against cell damaged from gamma-radiation when cancer patients undergo radiotherapy. High intake of lycopene reduces the risk of prostate, cervical, breast cancer and cancer of the pancreas, lung, stomach, esophageal and bladder by inhibiting several pathways linked to cancer cells growth and acting on mitogenic pathway of IGF-I. Lycopene lowers LDL cholesterol and the risk of heart disease possibly by inhibiting cellular HMG-CoA reductase- the rate-limiting enzyme in cholesterol synthesis. It is also useful in treating asthma and boosting the immune system. The high ability of lycopene in scavenging ROS may be due to its high lipophilic nature this allows it to function maximally in lipophilic environments. Some empirical studies in an attempt to explain the activity of lycopene postulates that as lycopene lowers ROS, there is a concomitant lowering of oxidative damages to lipoproteins, membrane lipids, proteins, enzymes, DNA, disruption of cellular homeostasis and accumulation of damaged molecules thereby inhibiting oxidative stress. This way, the reduced oxidative stress helps decrease the risk of chronic diseases.

Quercetin and luteolin are the two most abundant flavonoids found in peppers. Flavonoids are the most important phenolic antioxidants with great pharmacological effects. Their protective properties include antioxidant, antimicrobial, anti- cancer and cardiovascular protective activities.⁸ Their favourable structure-function configuration makes them efficient peroxy radical scavengers. Their structure gives them the ability to lower cellular oxidative stress; they can chelate iron thereby preventing metals from taking part in the initiation of lipid peroxidation and oxidative stress through enzyme (metal) catalyzed reaction¹³ for example high level of iron in the blood can cause oxidation and may lead to cancer. Quercetin like lycopene may interfere with IGF-I signaling *in vitro* and prevent cell proliferation; the antioxidant property is majorly due to their redox activities. The presence of the functional group OH⁻ in the structure and its position on the ring of the flavonoid molecule determine the antioxidant capacity. The addition of -OH⁻ groups to the flavonoids nucleus will enhance the antioxidant activity while substitution by -OCH₃ group diminishes the antioxidant activity. The higher the degree of polymerization, the higher the antioxidant activity.

Red sweet pepper is said to have an impressive amount of the carotenoids, lutein and zeaxanthin which are found in high concentration in the macula of the eye, around the retina.¹⁰ In the retina, they aid in protection against oxygen related damage. In event that the macula is degenerated, vision can become poor or even lost. It is expected that future studies on *Capsicum pepper* intake would demonstrate health benefits in this area of macular degeneration risk due to the high concentration of lutein and zeaxanthin content of this pepper. Other major carotenoids prevalent in *Capsicum* genus are capsantin and capsorubin.¹⁸ These carotenoids add colors to the food besides adding flavor to the food. They may also contribute to the overall antioxidant properties of peppers. With the rich array of antioxidant phytonutrients in the *Capsicum peppers*, health benefits expected would be a reduction of chronic diseases arising from oxidative stress. Such chronic diseases like coronary heart disease, obesity and diabetes commonly arise from oxidative

stress which generally causes damages to biomolecules such as proteins, nucleic acids and lipids which leads to most degenerative diseases. Carotenoids have protective effects against these diseases. Particularly, for coronary heart disease, obesity and diabetes it can prevent the oxidation of LDL because of its singlet oxygen quenching ability. It is expected therefore that the increased consumption of the phytonutrients would reduce the risks of these diseases. Regardless of the seemingly importance of antioxidants in preventing diseases, very few work has been done on their occurrence and activities in *Capsicum peppers*. Especially limited is research on human studies to confirm results of *Capsicum pepper* intake from animal studies.

Essential oil of capsicum peppers

Essential or volatile oil is extract from the plant. It is a concentrated hydrophobic liquid having volatile aromatic compounds. Oil from the pepper is essential because it has the essence of the pepper plant's characteristic fragrance. The characteristic fragrance is as a result of the presence of varied composition of organic substances mostly hydrocarbons having the general formula (C₅H₈)_n. Prominent functional groups present typify the terpenes and their derivatives, esters, phenols, carotenoids, aldehydes and other organic compounds. The organic compounds confer the characteristic aroma and flavor to *capsicum peppers* which may be the reason for their usefulness in enhancing flavors of many fresh and cooked foods, these essential oils may make them useful as food additives and condiments for stimulating appetite. The essential oil gives pepper its characteristic aroma and fragrance. Chilli pepper has a high oil content which may be the reason for its characteristic aroma. This may form the basis for its popularity in giving variety to monotonous staples and preservative of unfresh meat. The preservative function of the oil may be from the well-known fact that volatile oils of several plants possess antimicrobial activity which acts as chemical defense against plant pathogens. The existence of antimicrobial activity in pepper oil would be of considerable health benefit.

Volatile terpenes and aldehydes have drawn the attention of researchers and food industries recently as excellent food preservatives as antimicrobial additives with very little amount of residue.¹⁹ Using the essential oil component of *Capsicum peppers* for inhibition of food micro-organisms may find a wider application in food processing industries. However, essential oils are lipophilic and hydrophobic in nature; their poor solubility in water coupled with the possession of piquancy obtained in the course of extraction may limit their use and preservative ability in certain foods. The establishment of an effective dose is, therefore, important to cancel the effect of over-spicing in terms of piquancy. Overcoming these Challenges, essential oil from *Capsicum peppers* may counter the use of antibiotics and chemical preservatives and serve as natural preservatives and replacement to synthetic additives. However, the pepper oils are non-saponifiable lipids implying that they are non-saturated fatty acids and so can be persevered for some time without spoilage or peroxidation if there is a successful separation of water or an extraction done using acetone.^{20,21} This way they may be useful for industrial purposes such as in the production of cosmetics, insecticides, flavoring, beverages, candies and drinks.

Capsicum pepper oils do not contain capsaicin but during maceration some capsaicin are incorporated into the oil. These oils from both bird-eye and chilli peppers may find useful applications in the production of cream to reduce pains in amputees, pains from arthritis, for quick relief of headache, back and muscular pains and

as counter irritant balm²² because they are lipophilic they possess the ability to react with the lipid parts of the cell membranes and modify the activity of the calcium ion channels when the volatile oil is applied. At a particular dosage, the membranes become saturated with the volatile oils. This interaction influenced by their physiochemical properties and shape of the molecules is able to affect the enzymes, carriers, ion channels and receptors on the cell membrane and the resultant effects would make them resemble those of local anesthetics.

Capsicum peppers produce warmth in the body meaning that they have the ability to act as rubefacients.²³ This may be achievable by opening the capillaries to aid blood circulation. By dilating small capillaries and increasing circulation, they warm the body such that the skin reddens but not burnt when topically applied. This ability to cause increased circulation increases body warmth, stimulates the lungs as well as increase smooth blood circulation through the arteries and veins, this coupled with their high vitamin C content, help reduce cholesterol and triacylglycerols. Also, as non-saponifiable lipids, the oil is naturally low in cholesterol and triglycerides content and so may benefit a person's health by contributing to the prevention of heart disease. According to Lejeune et al.,²⁴ they may be useful as blood thinners for heart disease and high blood pressure; and as internal stimulants and carminatives.

Dietary fiber in capsicum peppers

Sweet pepper has a 'slightly woody' and fibrous nature which may constitute sources of dietary fiber. This fiber could help *Capsicum* pepper remove cholesterol and sugar better from the body and bloodstream, respectively. The removal of sugar helps in fighting diabetes. In terms of cardiovascular benefits, we have seen studies showing bile acid binding by fiber-related nutrients in bell peppers. Because this binding process prevents absorption of bile acids up into the body, our liver will seek to replace them by breaking down cholesterol into its component parts - namely, bile acids. So the net result here can be a reduction in our blood cholesterol level.¹⁰ However, more research is still needed to draw conclusions.

Capsaicin contents of *Capsicum* peppers

Capsaicin is an aromatic pungent principle, non-volatile phenolic compound with molecular structure: (C₁₈H₂₃NO₃)-8-methyl-N-Vanilyl-1,6-nonenamide.²⁵ It is hydrophobic, odorless, colorless, and waxy to crystalline when in pure state. The pungent principle of the *Capsicum* species commonly known as red pepper is the major component that makes red pepper 'hot' and spicy. It is the major health benefit possessed by the *Capsicum* peppers. The pungency of the flavonoids of the *Capsicum* pepper is produced by the capsaicinoids, alkaloid compounds, often called capsaicin after the most pungent and prevalent one.²⁶ The total content of both capsaicin and its analogues are referred to as capsaicinoids. Other analogues include norhydrocapsaicin, dihydrocapsaicin, homocapsaicin and homodihydrocapsaicin which are not found in abundance in plants and so are minor. Capsaicin is the most intense and known to be the basic chemical that is tested for when determining the piquancy of pepper. It is what determines the Scoville scale of any pepper. It is very potent to the taste and nerves. It is found on the epidermal cells of the septa that separate the chambers of the fruit that the seeds are attached to. Capsaicin is further accumulated in the placenta and found in the fruits of capsicum pepper.^{27,28}

While seeds are not the source of pungency, they occasionally

absorbed capsaicin because of their closeness to the placenta. No other part of the plant produces capsaicinoids.¹⁸ Cultivated plant cells and tissues derived from hot pepper fruits have been used in an attempt to produce high quantities of capsaicin for the pharmaceutical and food industries.²⁹ The content of capsaicin varies significantly according to specie. The hotter species are useful as medicinal/drug. Peppers are hotter if they are smaller against popular belief that the bigger the 'hotter'.¹ Sweet pepper has only trace amount of capsaicin and these domesticated non-pungent (sweet) varieties are mostly developed in *C. annum*.³⁰ A popular medical belief is that pepper should not be included in the diets of ulcer patients. Aside recommending the less pungent specie for such patients with strong attachment to it, empirical studies show that it may reduce the risk of stomach ulcers by destroying the bacteria causing ulcer in the stomach.¹¹ Capsaicin may thus possess antimicrobial property. The phenolic compound, capsaicin, has been found to inhibit the germination of bacterial spores. This compound plays an important role in the protection of the plant against pathogenic agents by entering the cells of the pathogens and cause cell lysis. Virulent attack of pathogenic bacteria using capsaicin may provide a means of nontoxic control of bacterial infections that has been customarily treated with synthetic antibiotics.

Peppers are hotter as they ripen meaning that their capsaicin concentration increases during ripening. Pungency is also affected not only by the genetic composition of the cultivars but also by the environment, biotic and abiotic factors in which the plant grows including:

- Weather and changes in temperature. Same species grown in temperate regions may have more capsaicin than those grown in cooler regions.
- Growing conditions including water status, light level, uv exposure and availability of mineral elements.
- Age of fruits.
- Level of stress the plant is subjected to. High level of environmental stress will increase pungency.

Though the bird-eye and chilli peppers have high capsaicin content and hence, high Scoville units, the *C. frutescens* are generally more pungent than members of the *C. annum*; the high pungency of the *C. frutescens* would classify them as major drug or medicinal *Capsicum*¹ found in the Southern part of Nigeria. Though the chilli pepper of the *C. annum* species is not as pungent as bird-eye but with its notable pungency it could also be used as a substitute for similar functions performed by the bird-eye pepper of *C. frutescens*.¹ The high pungency of the *C. frutescens* would classify them as hot spices, drug/medicinal. The usefulness of bird-eye and chilli pepper as medicinal drugs also has been reported by Geppetti et al.³¹ and Kissin.⁴ Traditional medicinal practices utilize the bioactive component, capsaicin, as herbal remedy for the treatment of degenerative diseases including cancer. Cale³² reported that capsaicin was found not only to retard the growth and expansion of cancer cells but also increased the degree of apoptosis (the death of cancer cells) and that capsaicin demonstrated the ability to arrest the growth of prostate cancer cells. However, the effectiveness for the treatment of different cancers may be varied and may also be dependent on the stage of the cancers. However, supporting researches on treatment for cancer exist only in the laboratory and animal studies. According to the American Cancer Society, most human studies into capsaicin focus mainly on

its effectiveness as an oral treatment for pain relief in cancer patients with side effects from chemotherapy and radiation therapy.³² Human studies are important to find out if these potential benefits of capsaicin extend to human.

The pharmaceutical industry uses capsaicin as counter-irritant balm for external application. Capsaicin is used as an analgesic in topical ointments, nasal sprays and dermal patches to relieve pain, typically in concentrations between 0.025% and 0.1%.³³ It may be applied in cream form for the temporary relief of minor aches and pains of muscles and joints associated with arthritis, backache, strains and sprains, often in compounds with other rubefacients.²³ It is suggested that these two species (bird-eye and chilli peppers) may be best used externally as counter-irritant for the treatment of arthritis, relief of pains and aches rheumatism, lumbago and neuralgia as analgesics and/or anti-inflammatory by selectively binding to a protein (TRPV1) -a heat activated calcium channel that resides on the membranes of pain and heat sensing neurons.³⁴ Its sensation overwhelms the nerves through calcium influx thus blocking pain sensation from the nerves for some time. The mechanism of action involves capsaicin acting on efferent sensory neurons involved in pain receptors which are used for analgesics purposes. This also makes them useful for the treatment of headaches and counter-irritant. By binding to the TRPV1 receptors also, capsaicin molecule produces similar sensations to those of excessive heat, explaining the reasons for the spiciness of capsaicin being described as a burning sensation. This way, capsaicin acts like hormones, signal transduction molecules and neurotransmitters.³⁵

Chronic exposure to capsaicin causes reduction of neuro-transmissions by the neuron leading to decrease pain sensation and blockade of neurogenic inflammation. The nerve endings release a neurotransmitter known as substance P. In the presence of capsaicin with its painful sensation, the amount of substance P transmitted to the brain increases informing the brain of the pain, this causes further release of substance P transmitted to the brain increases informing the brain of the pain, this causes further release of substance P. After some time, the substance P decreases and further release from the nerves is also decreased. This lends its usefulness as an analgesic in the treatment of pains in general including post-surgical, oestro-arthritic pain and toothache.³⁶ Thus, capsaicin acts like naloxone and other compounds that compete for receptor sites with endorphins and opiates and cause blockade. There is an experience of pleasure and even euphoria from ingesting capsaicin attributed to pain-stimulated release of endorphins, a different mechanism from the local receptor overload that makes capsaicin effective as a topical analgesic.³⁷ The alkaloid content could be used as a source of synthetic heliotrope, as a therapeutic agent particularly as a chemoreceptor against mutagenesis or tumor genesis.³⁸

Capsaicin might actually protect against peptic ulcer by stimulating the hormone that increases blood flow and nourishes gastric mucosal membrane.³⁹ They may be useful as laxative for indigestion because of their ability to stimulate the flow of saliva and gastric juices and also recommended for treatment of fever since they promote perspiration when in excess. This ability to promote perspiration makes them useful in cooling the body, especially in the tropics. Among the health benefit attributed to the phytochemical capsaicin of *Capsicum* peppers is the usefulness in regulation of blood sugar levels.²⁴ By breaking down carbohydrate it may ultimately enhance the regulation of blood sugar. It acts as an anti-diabetic agent probably by increasing the pancreatic secretion of insulin from beta cells or by increasing

the release of bound insulin. Furthermore, the enhancement of carbohydrate breakdown helps in weight loss. Additionally, capsaicin increases body heat production and oxygen consumption which helps in burning calories and losing weight.⁴⁰ There is, however, insufficient clinical evidence to determine the role of ingested capsaicin on a variety of human disorders, including obesity, diabetes, cancer and cardiovascular diseases.²³

Capsaicin forms blisters throughout the pepper pods which helps in defense against pathogens by being cytotoxic to them. They serve as deterrent against invading animals by exhibiting neurotoxic activity against them. Capsaicin is very much the major secondary metabolite responsible for the deterrents' activities of bird-eye and chilli peppers against certain animals and micro-organisms; these two species of pepper could be biochemically considered as bio-pesticides. They are suggested for environmental use as pest deterrents because of their high pungency against browsing animals (like cockroaches) and herbivorous insects. They could be used as a bio-repellant for ants and for keeping attacking dogs away. They could be used to deter rodents, rabbits and squirrels and even elephants.⁴¹ In fact, the capsaicinoid elements of hot chilli pepper extract is the principle component of household and garden insect-repellent formulas⁴² probably because of their neurotoxic effects. Part of the proposed environmental usefulness of capsaicin is to combine it with lidocaine oenatonium capsaicinate and both be added to paint as a repellent to barnacles since it is non-toxic to aquatic life. These bio-pesticide activities forms environmental health benefits to man. On the other hand, these cytotoxic and neurotoxic properties of capsaicin against insects becomes beneficiary to man as pain medicine particularly as an anesthesia by their action on the central nervous system and as muscle relaxants.

Future consideration of synergistic, polyvalent and polypharmacological application of the *Capsicum* peppers

Medicinal plants contain many pharmacologically active compounds that may act individually, additively or in synergy to improve health.^{43,44} *Capsicum* peppers serve nutritional and phyto-therapeutics principally due to their rich content of phytonutrients and phytochemicals. Individually, these components possess effective biological activities. Sometimes, however, there are situations whereby biological effects is brought about by a combination of other biological agent(s) that enhance the activities of other active component(s) just like in conventional medicine where a combination of drugs is applied in the prevention and treatment of complex diseases. For instance, the essential oil and capsaicin are both effective in inflammatory arthritic conditions and general neurotransmission. Thus, in combination they could be more effective in combating related health conditions rather than the use of just one component. This brings to the fore the concept of synergism.⁴⁵

Synergism means working in consortium; 'working hand-in hand' or simply put, working together. It results in greater positive effects arising from the combinations of more than one phytochemical and/or phytonutrients.⁴⁶ In synergy, the resultant effect is greater than that of a mono-therapy. There are general instances where a total herb extract shows a better effect than an equivalent dose of an isolated compound.⁴⁷ The entire fruits of *Capsicum* pepper are likely to contribute to overall health benefit. Epidemiological studies have pointed out that the consumption of fruits and vegetables imparts health benefits from

degenerative diseases. These health benefits are usually attributed to their organic micronutrients content. The mixture of the constituent phytochemicals in *Capsicum pepper* may be an advantage due to the synergistic effect exhibited by the constituents. There is increasing advocacy towards the modification of a single agent, in a medicinal plant, as a sole factor for the correction of disease conditions.

The phytochemicals-phenols, flavonoids with carotenoids, Quercetin, luteolin, lycopenes -have high capability of removing free radicals, chelate transition metal catalysts, activate antioxidant enzymes, and reduce alpha tocopherol radicals and inhibit oxidase.⁴⁸ The flavonoids have antioxidant capacity; they can inhibit cellular oxidative stress. Carotenoids and vitamin A are good singlet oxygen quenchers. Similarly, vitamin C is a good reducing agent and so acts as a good electron donor. Oboh & Umoru¹³ found positive correlations between phenols, flavonoids, vitamins A and C and attributes which indicate that all have good redox properties and hence antioxidant activities. The correlation between vitamin C and iron chelating ability may point to the fact that vitamin C chelates heavy metals and reduces the risk of cardiovascular diseases and cancer⁴⁹ and other degenerative diseases. In synergy, a high free radical scavenging ability would be conferred to the utilization of the whole *Capsicum pepper* as against the utilization of any of its single active agent. The concept of polyvalence is defined by Houghton⁵⁰ as the range of biological activities that an extract may exhibit which contribute to the overall effect observed clinically or *in vivo*. In polyvalence, active agents may have individual biological activity or it could be a situation with an agent having several biological activity related to the disorder or that of agents that can modulate the activity of the major component responsible for the actual biological effect.

Polyvalence exhibited in a combination of vitamin C and K, capsaicin and flavonoids in pepper could promote proper blood clotting, reduction in the risk of heart attack and stroke. The vitamins check likely damage from oxygen radicals while the flavonoids reduce the level of lipid peroxidation in the blood which would otherwise lead to atherosclerosis and cause blockage to the arteries and ultimately lead to heart attack and stroke. The rich phytochemicals and antioxidants in *Capsicum peppers* suggest that they may help reduce the risk of complications associated with diabetes. Excessive blood platelets and platelet aggregation occurs frequently with diabetics, the bioactive agents in peppers thin the blood, prevent blockages in the blood vessels and reduce the risk of heart attack. Dallatu et al.⁵¹ suggested that supplementation with antioxidant micronutrients have positively influenced blood glucose regulation. The combination of the capsaicin and antioxidants of the *Capsicum peppers* would provide reduction of oxidative stress and inflammatory effects and eventually result in lowering of blood glucose level. Both oxidative stress and inflammation are both diabetic complications. Most phytonutraceuticals with antioxidant properties may work directly by quenching free radicals or indirectly in cell signaling pathway linked to redox balancing.⁵²

Capsicum peppers would provide reduction of oxidative stress and inflammatory effects and on its own, capsaicin exerts anti-diabetic effects. This may arise from its anti-glycemic and anti-hyperlipidaemia activities that produce the overall anti-diabetic effect. In this case, exhibits the concept of polyvalence. As an anti-glycemic and anti-hyperlipidaemia agent, it may be that capsaicin is able to bind to more than one therapeutic target; increase therapeutic potency and reduce the probability of developing drug resistance. This is the concept of poly-pharmacy. By this mechanism, they may enhance safety and efficacy in the treatment of disease in this case, diabetes.

Conclusion

The health benefits of *Capsicum peppers* as medicinal attributable to the presence of phytochemicals and antioxidants arises from the presence of phyto-nutrients particularly vitamin C, vitamin A and the variety of secondary metabolite phytochemicals majorly, capsaicin and others including α - and β - carotenes, lycopene, flavonoids, quercetin, luteolin which may have more than one biological functions. Most of these nutrients and phytochemicals are likely to work in synergy and contribute to the abundant health benefits of *Capsicum peppers*. Capsaicin content determines the pungency of *C.peppers* and is particularly pivotal in the use of *Capsicum peppers* as drug.⁵³ The plant offers a safe, effective and inexpensive source with great economic and potential health benefits for the control of the development of various metabolic and anti-oxidant associated diseases as against the modes of treatment with synthetic drugs which are not only expensive but have side effects with increasing drug resistance with prolonged usage.

Additionally, the essential oils may be able to counter the use of anti-biotic and chemical preservative and serve as natural preservatives and a replacement to synthetic additives. The secondary metabolites could serve as sources of pesticides, important chemicals in food preservation and many valuable drugs, or work in synergy with other bioactive agents. While capsaicin shows promise in some laboratory and animal studies, results from human studies remain unavailable. Therefore, large scale human studies are needed to confirm some of these suggested health benefits and some of the same benefits of *Capsicum pepper* intake suggested in animal studies. On the overall, *Capsicum peppers* with their rich phytochemicals and organic micronutrients mix of constituent bioactive agents are promising towards the development of novel therapeutic strategy.

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Conflict of interest

Author declares that there is no conflict of interest.

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