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Garlic and Its Effects on Health with Special Reference to the Reproductive System

Carlo Valente, Guillaume Aboua and
Stefan S. Du Plessis

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1. Introduction

Garlic is widely used around the world for its pungent flavour as a seasoning or condiment. From the history, it is known that garlic has been used for more than 7,000 years by humans. Originally the plant was native to central Asia [1], but it has long been used for consumption (raw or cooked) as seasoning in many other parts of the world such as the Mediterranean region, Africa, and Europe. It has specifically been used for its medicinal purposes in ancient Egypt. [2].

The garlic plant's bulb is the most commonly used part of the plant. As mentioned, garlic or more specifically the cloves is believed to have many medicinal properties ranging from positively affecting anything such as high blood pressure (BP) and lowering cholesterol to using it as a treatment for the common cold [3]. Even Hippocrates, Galen, and Dioscorides all mention the use of garlic for many conditions, including parasites, respiratory problems, poor digestion, and low energy [4].

Plants have always been the sources of important medicines since time immemorial. Currently there is a huge movement and emphasis towards scientifically and clinically unlocking the value of traditional phytomedicines in the service of humanity. With this in mind the scope of this chapter is to investigate garlic's effects on human health with special reference to the effect on the reproductive system. The chapter will furthermore aim to explain the mechanisms via which garlic can exert its effect.

2. Garlic: Overview and properties

Allium sativum, or commonly known as garlic, is a vegetable species that can be classified as either a food or a medicinal herb. It is a widely used plant product that is cultivated all over the world. Garlic falls into a family of *Amaryllidaceae* or the genus *Allium*. Its closest relatives in the onion genus include the onion, shallot, leek, rakkyo and chive [4].

The bulbs are mainly composed of water (approximately 84.09%), organic matter (13.38%) and inorganic matter (1.53%). The leaves consist of more or less the same components with slightly different ratios (water 87.14%, organic matter 11.27% and inorganic matter 1.59%) [5, 6].

The organic matter is mostly carbohydrates while the inorganic matter is compounds such as sulphur and iron. The large number of sulfur compounds contributes to the smell and taste of garlic. Allicin has been found to be the compound most responsible for the "hot" sensation of raw garlic (RG) [7]. Allicin, along with its decomposition products diallyl disulphide and diallyl trisulphide, are major contributors to the characteristic odour of garlic, while other allicin-derived compounds, such as vinyldithiins and ajoene show beneficial *in vitro* biological activity [4].

Despite having a minimal amount of ions and other compounds, those that are present play a very important role in the composition and overall beneficial effects that garlic potentially possesses [8].

When crushed, *Allium sativum* yields allicin, an antibiotic [9] and antifungal compound (phytoncide) discovered by Cavallito and colleagues in 1944. Fresh or crushed garlic also has enzymes, B vitamins, proteins, minerals, saponins, flavonoids, and Maillard reaction products. Furthermore, a phytoalexin (allixin) was found, a nonsulfur compound with a γ -pyrone skeleton structure with antioxidant effects, antimicrobial effect [10] antitumor promoting effects [11], inhibition of aflatoxin B2 DNA binding and neurotrophic effects [11].

There are different variants of the garlic root and each has its own properties that aid with good health. The white (natural) and black (fermented) garlic are just derivatives of how it is prepared, although each has its own unique effects. The white garlic is said to have medicinal properties while the black fermented garlic is more commonly used for cooking. Garlic can further be divided into two main subspecies being *Ophioscorodon* or hard necked garlic and *Sativum* or soft necked garlic [12]. Garlic can often be found in 4 forms namely; RG homogenate, garlic powder, aged garlic extract (AGE) and garlic oil.

- The RG homogenate is prepared by collecting garlic cloves and removing several outer layers. The cloves are then blended with distilled water and left for half an hour at 25°C. The solution is then filtered and a homogenate sample is obtained [13].
- Garlic powder is prepared by pulverising crushed and dehydrated garlic cloves. This is mainly used for cooking purposes.

- AGE is obtained by placing garlic cloves in ethanol for a minimum of 20 months at room temperature. This reduces the concentration of allicin [13]. Which could reduce the medicinal properties of garlic as allicin is said to play a significant role.
- Garlic oil is obtained through a complex steaming and distillation process and is used in cooking or as medicinal oil.

The preparation of the garlic bulb is probably the most important factor in its effectiveness. Fresh garlic is often described as the best preparation to use to get superlative medicinal value out of the herb. Dried or cooked garlic often loses its potency because the amount of allicin present is significantly decreased in the cooking process [3]. Although the active ingredient in garlic is said to be unknown there is a lot of speculation around allicin as being the main constitutive/candidate [3]. More studies on sulphur are currently being done as this could also play a significant role, especially in organically grown garlic. Other studies state that the active ingredients are more directly associated with sulphur-containing amino acids, such as allicin, S-allylcysteine (SAC), S-allylmercaptocysteine (SAMC) S-methylcysteine, diallyl disulphide and sulfoxides [14].

Allicin is a very unstable molecule and breaks down very easily. This is why it is recommended to eat fresh garlic as it contains the highest amount of allicin. It is also the reason for the strong odour that garlic possesses. The more prominent this odour is the higher levels of allicin and beneficial values the bulb is said to have [15]. Due to this instability medical companies have now started to develop garlic supplements that contain Alliin - a stable precursor to allicin. It is only released upon digestion meaning the body will have the added benefit of having a sufficient amount of the favourable metabolite along with the safer more stable option [15].

The preparation of the garlic is of vital importance and studies have shown that each preparation has its own beneficial effects and more importantly its own threshold to when it starts becoming detrimental to the body. 2-5g of RG and 10-15g of boiled garlic provide beneficial effects with regard to prevent cancer development [16]. Likewise a certain amount of garlic supplementation would be beneficial in the male reproductive system. Unfortunately this amount is still unknown.

3. Garlic and human health

Garlic has been considered as a disease preventative food and its effects on the human health have been studied. Garlic infused medicine is on the increase due to the proposed beneficial effects on human health. The effects of garlic on both plant and animal models is best known for its ability to decrease the amount of lipids or free fatty acids, as well as its anti-atherogenic effects in both models [8].

Garlic supplements are now also being widely developed and recent studies have shown just that by mimicking the effect garlic has on the body. Allium products have the potential to reduce the risk of developing cancer or the potential to decrease the risk factors associated

with cancers [17]. Research has been done on this and some evidence has been found that it has beneficial effects but there are also studies that show no effect at all [18].

Garlic has shown to have therapeutic effects, but the side effects are poorly investigated. The medicinal effects of garlic on certain diseases and specific systems will subsequently be discussed.

3.1. Effects on cardiovascular system

Cardiovascular disease (CVD) also known as heart disease is becoming an increasingly alarming problem in developing countries as it is the most common form of mortality [14]. Countries such as Spain and the USA have always been associated with heart disease, but developing countries are now showing an increasing trend in developing heart conditions [19]. With risk factors such as hypertension and hypercholesterolemia present, the onset of heart disease becomes more likely [20].

The effects of garlic on the cardiovascular system have been attracting a lot of interest in recent times with the development of modern medicine in particular [3]. An increase in the amount of cholesterol in the body can lead to the formation of atherosclerotic plaques and this is a risk factor for both heart attacks and strokes. Low-density lipoprotein (LDL) cholesterol levels can greatly be reduced without affecting the good High-density lipoprotein (HDL) cholesterol levels. The mode of action is said to be that garlic blocks the liver from making too much LDL because of its bio-active ingredients [15]. The high levels of cholesterol result in an increase in free-radical producing peptides. Reactive oxygen species (ROS) and oxidative stress (OS) levels are also key markers in CVD and by decreasing these levels the onset of heart disease can be delayed. Unfortunately the likeliness of developing heart disease increases with age and decreasing the amount of harmful oxidation in the body would be beneficial.

Garlic can delay the onset of heart disease due to its antioxidant properties. The type of extract used is of vital importance as it will influence the beneficial effects. Garlic reduces the amount of cholesterol in the body and by doing this the heart becomes more protected. Garlic also plays an important role in maintaining the structure and efficacy of endothelial cells and endothelial function [21]. The administration of AGE inhibits the progression of coronary-artery calcification and reduces the risk of a myocardial infarction or a heart attack [20]. Similarly, Allicor (a garlic powder tablet) was given to people suffering from coronary heart disease (CHD). This resulted in decreasing the risk of myocardial infarction, more significantly noted in males as opposed to females [14]. Studies have shown that the most effective way to reduce CVD is to try and reduce all the risk factors. Garlic-based preparations is thought to be promising agents for multifunctional risk reduction, but the mode of action remains slightly obscure [14].

With an increase in age the metabolic parameters of an individual is likely to change and this is evident in the onset of menopause in females. The end of the fertile phase in a woman's life is known as menopause and generally occurs during midlife or typically between the ages of 40 and 50. Together with diabetes, excessive weight, hypertension and endothelial dysfunction, menopause is a well-known risk factor for CVD which could lead to an increase in

metabolic parameters. Evidence shows that the vascular function in postmenopausal women could be affected by the changes in the reproductive hormones. One of the main precautionary measures for postmenopausal women with an increased CVD risk is exercise, however since ancient times garlic has been used as a treatment for CVD. It is said that AGE combined with exercise resulted in greater body weight loss than either AGE or exercise on its own. With the onset of menopause, fat and cholesterol levels are increased as well as the degree of oxidative stress. AGE has shown to reduce all these factors and is more easily absorbed in the body than other garlic preparations [21].

3.2. Effects on blood pressure

Blood pressure or arterial BP is the pressure exerted by circulating blood upon the walls of blood vessels [22]. BP can fluctuate from person to person depending on the individual and their health. A healthy patient should have an ideal BP of 120/80. If the BP exceeds 140/100 the patient is said to be hypertensive and if it is below 90/60 the person is hypotensive [23].

Hypertension and diabetes is said to be lifestyle-related diseases that has become a serious issue for countries previously not associated with it. Asian countries have now started to show a large increase in the amount of people suffering from high BP, with Japan having an estimated total of seven million people living with the disease [24]. Moreover one billion adults worldwide are affected by hypertension with about sixty-five million of them residing in the USA. This has led to approximately 40% of cardiovascular related deaths [25]. Hypertension has been considered to be the most important bio-marker in the onset of CVD.

Anti-hypertensive treatment has not always resulted in the desired effect of reducing the BP and alternative means of medication have now been developed. Garlic supplements and garlic derived products are becoming more and more popular in western medicine. AGE and RG showed to have the highest effect on lowering BP [24]. Interestingly, it is well known that AGE contains less allicin than RG. This has led to more studies being performed in order to establish the compound specifically responsible for lowering of the BP and reducing hypertension. The lowering effect that garlic has on BP is said to be due to the fact that the nitric oxide (NO) system is more active than the renin-angiotensin system. NO and Hydrogen sulphide (H₂S) play major roles in the progression of diseases, both NO and H₂S are considered to be important vasodilators. In a recent study both serum NO and H₂S were measured in diabetic rats and it was shown that chronic administration of garlic normalised both gaseous molecules and reduce BP [26].

It was found that both aged garlic and raw RG produce the same amount of NO implying that nitric oxide synthase (NOS) is the key to lowering BP. Both forms of garlic resulted in an increase in the activation of NOS. An increase in NO will lead to an increase in the relaxation of the blood vessels, and will therefore lead to a decrease in the BP. However, studies have shown that both AGE and RG require at least 3-4 weeks of daily administration before their action is expressed and this suggests that there could be a different mechanism for the lowering of BP [27].

The administration of AGE improved the condition of arteries as well as prevented the stiffening of the blood vessels which is a key marker in aging. By doing this it also improves erythrocytes which are the main component of blood. And therefore improves peripheral circulation and leads to a decrease in erythrocyte deformation. The improvement of blood circulation caused by AGE could be one of the causes of lowering BP, but RG showed to cause an increase in erythrocyte deformation and could lead to anaemia [25]. Garlic's medicinal properties in relation to its ability to lower BP have been studied extensively. It has been shown to significantly reduce BP in hypertensive patients when compared to those receiving a placebo [28]. Chronic feeding of AGE and RG decreased BP. Unfortunately the exact mechanism is not entirely elucidated as of yet. However, RG showed more harmful than beneficial effects. These results suggest that with regard to decrease in hypertension aged garlic would be the better and safer option [24]. It is also a safer treatment to use in conjunction with conventional anti-hypertensive therapy [25].

3.3. Effects on diabetes

Diabetes mellitus, or simply diabetes, is an endocrine disorder that forms part of a group of metabolic diseases characterised by elevated blood sugar levels or an insulin deficiency. Between one and two percent of the global population is affected by diabetes and there are roughly 100 million patients worldwide [29]. The most common form of diabetes is type two diabetes mellitus and comprises 80 percent of all diabetic populations [30]. A predicted increase from 51 to 72 million individuals affected by diabetes is expected in developed countries in the next decade; this translates to an increase of more than 42 percent. Developing countries will however face the brunt of the pandemic as it is expected to show an increase of 170 percent [31].

Diabetes is divided into two categories based on its mechanisms. Type 1 diabetes results from an individual's body failing to produce insulin, and currently requires the person to inject insulin or wear an insulin pump. It is also referred to as insulin-dependent diabetes mellitus (IDDM) or juvenile onset diabetes due to the fact that it is prominent in children [32]. This is a rare case of diabetes in comparison to its counterpart. Type 2 diabetes results from insulin resistance, a condition in which cells fail to use insulin properly, in some cases it is combined with an absolute insulin deficiency. It is also referred to as non-insulin-dependent diabetes mellitus (NIDDM) or adult-onset diabetes [32].

An individual's dietary factors play a key role in both the onset as well as the prevention of diabetes and other metabolic disorders [33]. Garlic is recognised for its therapeutic potential for controlling diabetes and its subsequent metabolic complications. The hypoglycaemic effect that garlic is said to have is attributed to the presence of allicin and sulphur compounds. Studies have shown that the oral administration of RG significantly reduced blood glucose levels and improved insulin sensitivity in garlic treated rats. Administration of aqueous garlic in patients with Type 1 diabetes has been reported to increase insulin sensitivity. Furthermore, metabolic complications such as increased serum-triglyceride, insulin and uric acid levels usually observed in diabetic rats were normalised after garlic administration [30].

Interestingly it has been observed that chronic administration of RG significantly reduced body weight, however the mechanism as to how garlic contributes to a reduction in body weight is still unclear. A study by Elkayam [26] has shown that allicin administered for 2-3 weeks reduced weight gain in fructose fed rats. Together with reducing glucose levels allicin also has the added advantage of decreased weight gain.

Glycation is the spontaneous phenomenon that occurs whenever proteins are exposed to reducing sugars and is depended on the degree and duration of hyperglycaemia in the body. It has been suggested that a direct reaction referred to as the Maillard reaction takes place during hyperglycaemia. This is a reaction that occurs between the sugars and proteins in the body. Advanced glycation end products (AGEPs) are formed when glycated proteins react with dicarbonyl intermediates to form complex heterogeneous, cross-linked and fluorescent molecules. Little is known about the chemistry of AGEPs but AGEPs are said to generate free radicals and lead to oxidative damage and this inevitably leads to diabetic complications [29]. The exact mechanism as to how garlic decreases glycation is uncertain but it is said to be due to decreasing the free radicals in the body, and it also increases anti-oxidant enzymes. Garlic also plays a role in the regulation of the Maillard reaction by inhibiting AGEP production/formation, but more research is required on the exact mechanism [29].

3.4. Effects on dementia and the brain

Increased homocystein levels damages the endothelial cells that line blood vessels and prompts apoptosis by producing strand breaks in the DNA. This causes thrombotic activity that could result in heart attacks and strokes. Individuals living with dementia have a much higher level of homocystein than healthy people and there is a significant link between high levels of homocystein and loss of cognition. It has also been indicated that the intake of AGE decreases homocystein levels [20, 34].

Studies have also shown that there could be a link between heart diseases and dementia risks [34]. Risk factors such as hypertension, high cholesterol, increasing levels of homocystein, inflammation and oxidative stress are all related to both heart disease and dementia. These risks factors occur in the brain due to an increase in α - β peptide levels or a restriction in the blood supply to tissues. This could then result in cardiovascular or cerebrovascular diseases of which dementia and Alzheimer's disease (AD) is included [20, 34]. In addition to oxidative stress, free radicals such as ROS are closely associated with CVDs, cerebrovascular diseases such as dementia and cancer. It is believed that the damage done to DNA, proteins and lipids are considered of the foremost causes in the commencement and development of the diseases.

Free radicals increase in number when there is an infection, inflammation, hyperhomocysteinemia or exposure to smoking, drugs and radiation [35]. When the LDL cholesterol levels are changed due to oxidative stress and free radicals, the risk of atherosclerosis, cardio and cerebrovascular diseases increase. In addition neuronal apoptosis is triggered which leads to an increase in the risk of brain atrophy and dementia. AGE is known to lower homocystein levels, increase microcirculation and provide protection for endothelial cells from the effects of oxidation. Following a stroke the risk factors of neurodegenerative conditions and CVD include myocardial ischemic or reperfusion injury, AGE can protect the body against this by

increasing the production of constitutive NO [20, 34]. AGE has also been shown to possess anti-aging properties, in studies AGE prevented the deterioration of the brain's frontal lobe, and enhanced learning and memory retention.

3.5. Effects on cancer

Cancer or malignant neoplasm is a broad group of diseases involving unregulated cell growth. Cell division and uncontrollable growth of these cells form malignant tumours in individuals living with cancer. These tumours are very likely to invade nearby parts of the body. The lymphatic system or bloodstream may also spread the cancer to more distant parts of the body. However, not all tumours are cancerous. Benign tumours do not invade neighbouring tissues and do not spread throughout the body [36].

There are over 200 different known cancers that affect humans ranging from breast and prostate cancer to colorectal and lung cancer. In the year 2008 approximately 12 million people worldwide were said to be living with cancer and this figure is expected to rise to about 21 million by the year 2030. Lung cancer is responsible for the most deaths closely followed by breast and colorectal cancer [37].

Garlic is said to have chemo-preventive properties and its effects have been closely studied on various cancers. The antitumor effects that garlic potentially possesses are directly attributed to its anti-mutagenic properties [38]. The formations of tumours in vitro and in vivo were shown to be greatly decreased after the administration of fresh garlic, although the mechanism of action is still unknown. The timing and dose of the garlic could be the main factor in inhibition of the pro-carcinogens [38]. A possible mode of action as to how garlic can prevent cancer is by the effects of Diallyl trisulphide (DATS). DATS is a by-product of garlic that exhibits several pharmacological effects (e.g. anti-microbial and CVD), making this compound a promiscuous agent with possible beneficial chemo-prevention properties due to the complex pathways in cancers [39]. Oral ingestion of aged garlic (that is lacking enzymatically produced allicin due to the fact that it was not chopped) reduced 1, 2-dimethylhydrazine induced colon tumours significantly [40]. With specific reference to skin cancer, the treatment results are inconclusive and more research will have to be conducted [41]. Stomach tumours were greatly decreased by administration of AGE. The toxicity of garlic was not directly responsible for the death of cancer cells alone although it does play an important role. Another key role in the prevention of cancers is garlics effect on the immune system. Macrophage activity, NK and killer cells as well as the cytokine TNF were all shown to have increased activity after administration of garlic and this resulted in an increase in antitumor response [42]. Colorectal cancer is the third leading cause of cancer death in the world. In this respect normal garlic cannot be administrated and would need to be introduced as part of a strict diet. The Garlic and low meat diet did however show a decrease in colorectal tumour growth [43].

3.6. Effects on reproductive system

Infertility and especially idiopathic infertility has been on the increase during the last century. Infertility is the inability to conceive after having unprotected sexual intercourse for more than a year of trying [44]. In 19-57% of cases the male is at fault when a couple have infertility concerns [45]. This has led to a lot of research on male fertility and the male reproductive system. Garlic and its effects on the male reproductive system has caused a tremendous amount of interest in the Andrology and reproductive field as some researchers believe it to have a beneficial influence and others believe it to have a detrimental effect on the male reproductive system. The possible reason as to why these discrepancies exist could be due to the preparation and the dosage.

3.6.1. Spermatogenesis and sperm function

In a study performed by Qian and co-workers it was shown that the administration of garlic to rats showed a decrease in sperm quality and functionality. The amount and preparation of garlic will result in a decrease in specific seminal parameters. The crude extract of garlic results in an increase in the percentage of empty seminiferous tubules. It has been reported to reduce membrane disintegration and irreversible immobilization of sperm [46] while at the same time reducing sperm viability [47]. This is the reason as to why some researcher's believe that garlic acts as a natural contraceptive although more research would have to be performed [47]. The majority of data report garlic to have deleterious effects on specifically the male reproductive system. In another study testicular morphological alterations were noted after male adult rats were given 50 mg kg⁻¹ of garlic powder for 45-75 days [48]. Hammami and El May (2009) found that garlic improved male sexual dysfunction in direct contrast to the studies previously mentioned which claimed garlic to have a negative impact on male reproductive function. The main difference and possibly the reason between different results could be the lack of standardization between research models and the different amounts of garlic given to test subjects [3].

Spermatogenesis is the process whereby spermatozoa are produced. Needless to say it is a very important process in the male reproductive organs. The production of spermatozoa can be effected by various stimuli. ROS and heat are important in the formation of mature sperm but a large amount of ROS and higher than normal physiological temperatures levels may become hazardous to the spermatozoa.

The daily administration of garlic powder and aqueous garlic to adult rats caused spermicidal effects and spermatogenetic arrest. However, feeding a higher garlic supplementation over a longer period of time to the adult rats caused an increase in Epididymal spermatozoa [3]. Although an animal model was used, comparisons can be linked to a human model to the similarities in the reproductive systems of the respective models. The effect of garlic on spermatogenesis and on testis also yielded contrasting findings. Administration of garlic over a period of time showed to have histological alterations on the cells within the testes. Both the Leydig and Sertoli cells showed lipid droplets along with a decrease in volume. Spermatocytes showed interrupted nuclear development and an increase in apoptosis was also evident [49].

Apoptosis is a physiological term used to explain programmed cell death [50]. Caspase 3 formation is a vital step in the activation of the apoptotic pathway and an increase in crude garlic intake leads to an increase in caspase 3 formation. Apoptosis effects the formation of spermatocytes and spermatids and the testes have shown an increase in apoptotic germ cells after the rat is exposed to crude garlic feeding [51]. It was shown that supplementing the diet with crude garlic induced apoptosis in both spermatocytes and spermatids [51]. Dixit & Joshi [48] again noted that treating rats with garlic powder impaired spermatogenesis and led to an early arrest in the development of spermatozoa. This in turn reduced the amount of round spermatids converted into elongated spermatids furthermore impairing spermatogenesis. With regards to the testicular function, garlic and its metabolites have a protective function. The effects of garlic on the testes include prevention of hypogonadism caused by heat and protection against cadmium-induced testicular damage by reversing the alterations in the biochemical parameters [52]. Other beneficial properties are its ability to restore testicular histology and decrease free radicals in the testes which are detrimental when in large amounts.

3.6.2. Hormonal levels and libido

Garlic feeding has both positive and negative effects on testosterone production. It is important to note that between the different studies that were performed, different preparations, amounts and concentrations of garlic were administered. The preparation of the garlic could possibly be the key factor involved in the impact it will have. By administering crude garlic to Rat models it was recorded that there was a decrease in testosterone formation due to the decrease in responsiveness of the Leydig cells to the luteinizing hormone. This decrease in responsiveness is due to the histological alteration in the testes (Figure 1). In contrast Oi et al. [53] showed an increase in testosterone levels due to the increase in the luteinizing hormones after administration of 8g of garlic powder. Again, the different preparations of the garlic plant are vital.

Garlic's effects on the reproductive system have led to contradictory results. According to Hammami et al. [51] garlic has been used to improve male sexual dysfunction and this includes impotence. Heated garlic juice is effective in recovering testicular function after experimental hypogonadism, but powder or crude garlic (in large amounts) impairs male reproductive tract functions [51].

Benign prostatic hyperplasia (BPH) is an extremely common condition in older men and can affect the male reproductive system. Milk and other dairy products have been related to an increase in BPH but the results found are very inconsistent. The same trend applies for garlic as studies have shown that cooked garlic can decrease the onset of BPH but RG can increase the onset [54]. Aqueous garlic extract has however shown to improve disease parameters in patients with BPH [55]. Garlic extract also decreases the onset of prostatic cancers and other malignancies [56]. The results are however inconclusive and very contrasting amongst published articles and no real conclusion can be drawn until more research is done on the effects of vegetable- more specific garlic – has on the male reproductive system.

4. Mechanisms

The scientific and pharmacologic explanations for most of the medicinal effects attributed to garlic treatment are still eluding researchers. There is however a few mechanisms via which garlic more than likely exert its effects which are worth mentioning and highly plausible.

4.1. Antioxidant properties

An antioxidant is a molecule that inhibits the oxidation of other molecules in the human body [57]. A chemical reaction known as oxidation occurs when electrons or hydrogen atoms are transferred from a substance to an oxidizing agent. Once this oxidation reaction occurs, free radicals are produced and realised into the body. In turn, these radicals can start chain reactions. Antioxidants terminate these chain reactions by removing free radical intermediates, and inhibit other oxidation reactions [58]. Antioxidants are present in most of the foods we eat and drink like spinach, oranges, whole wheat bread and tea. Garlic is also very rich in antioxidants [59] (Table 1). The powerful odour that fresh garlic possesses is due to the amount of allicin that is present. This odour as well as the unique acquired flavour of garlic has resulted that not every one favours it [20]. This led to the emergence of the AGE. As mentioned previously AGE is obtained via a long and tedious process. The extract obtained through this process does not have the pungent flavour of garlic and is also odourless [60]. This is due to the fact that a large amount of allicin is lost and therefor it loses a lot of its beneficial properties. However, due to the amount of allicin lost, this means that the most prominent component in AGE is the organosulfurs like SAC and SAMC. These compounds are said to have potent antioxidant effects in the body. *S*-allylcysteine and *S*-allylmercaptocysteine increase with aging of the garlic. Therefore, the longer the garlic is aged the less allicin it will contain, but the more antioxidant effect it will have. This makes AGE the most potent form of garlic with regards to antioxidant ability.

Oxidative stress is the term used to describe the process that transpires when there are too many free radicals or not enough antioxidant agents in the body [20]. This oxidative damage is often associated with aging and age-degenerative conditions such as dementia and AD. AGE has shown to inhibit this oxidative damaged caused and helps with reducing the risk factor or onset of neurodegenerative disease as well as slowing down the aging process or to be more specific the onset of deteriorating skin. However, the administration of garlic did not decrease the levels of iron mediated oxidative stress [61]. The antioxidant actions of AGE are based on decreasing the amounts of ROS and reactive nitrogen species (RNS) as well as inhibiting LDL oxidation and lipid peroxide formation. An increase in ROS in the body can lead to a host of issues including endothelial dysfunction which is a key marker in the development of cardiac injury. Likewise LDL oxidation could lead to vascular dysfunction and promotes the onset of atherosclerosis and possibly myocardial infarction [20].

A study was done to compare the antioxidant potential of the different garlic preparations. AGE which is predominantly SAC and SAMC was compared to a water extract of fresh garlic containing mostly alliin and RG that contains allicin [62]. AGE had the highest antioxidant effect and surprisingly the other two preparations served more as an oxidant [62]. Although

the majority of the antioxidant effects are from the AGE there are incidents where other preparations were used as an antibiotic/antioxidant. A lot of the mechanisms by which garlic acquired its medicinal properties have been specifically ascribed to this potent antioxidant action. It has the ability to stimulate immunological responsiveness and its modulation of prostanooids synthesis. The antioxidant properties of garlic have been studied extensively and it does have a beneficial role in the body. AGE is however more effective in removing free radicals and LDL cholesterol than other preparations of the garlic root, but that does not mean the other preparations aren't important as well.

4.2. Antibiotic properties

Alllicin, found in the garlic bulb, serves as a powerful antibiotic which aids the body in inhibiting the growth and reproduction of bacteria [63]. One milligram of alllicin is equal to 15 standard units of penicillin [63]. Alllicin attacks over 23 types of bacteria, such as staph and salmonella, 60 types of fungi and yeast and is also effective against 17 of the most dangerous fungi [64]. Another example of where alllicin serves as a potent antibiotic is in the treatment of Streptolysin O (SLO). SLO is a powerful cytolytic toxin found in almost all group A streptococci. Treatment of SLO with Alllicin completely neutralized the haemolytic activity of the bacteria, while the aqueous garlic extract inhibited it altogether [65]. From these results it can be deduced that garlic and its metabolites have antibiotic properties. Extracts of fresh garlic contain antioxidant phytochemicals that prevent oxidative damage.

4.3. NO and H₂S

NO and H₂S play major roles in the progression of diseases, both NO and H₂S are considered to be important vasodilators. In a recent study both serum NO and H₂S were measured in diabetic rats and it was shown that chronic administration of garlic normalised both gaseous molecules [26] and this decreased hypertension by inhibiting certain enzymes such as N omega-nitro-L-arginine-methyl-ester (L-NAME) [66].

5. Conclusion and recommendations

From this review it is evident that garlic certainly has some medicinal properties. Various studies highlighted its cardio protective, antibiotic, anti-hypertensive and cholesterol lowering effects. Some evidence also points to its ability to lower the risk of developing cancer. Not all the research data are as clear and conclusive and certain remain ambiguous. Garlic appears to exert both positive and negative effects on the male reproductive system. Interestingly enough crude garlic (if taken in large amounts) shows the most detrimental and AGE garlic the most beneficial results. The most crucial factor in determining the effects observed is possibly the manner in which the garlic was prepared as well as the amount that is being administered. Interestingly, large amounts are deemed to be

more detrimental. Some of the results found showed that the administration of garlic affected testicular function, histological properties and sperm quality [46, 48 & 51]. Hormone levels were subsequently also altered and an increase in testicular tissue apoptosis was recorded [51]. Furthermore crude garlic extracts and garlic juice showed to cause sperm immobilization (administered as 15g/100g and 30g/100g respectively) [51, 67, 68]. More research definitely needs to be performed on the effect of garlic on acrosome and DNA integrity of spermatozoa.

In general it can be said that garlic's therapeutic properties warrants further investigation in order to develop its full treatment potential as a phytotherapeutical agent impacting on human health and used for the treatment of various disease conditions. The specific mechanism of action also need to be identified as it can possible shed more light on and help with the development of more effective pharmacological agents. Additional human studies on AGE and its constituents are needed to elucidate their role in protecting human health, and molecular studies should be intensified to reveal the underlying mechanisms.

Product	Source of commercial sample	Lot#	% Inhibition ² (SD)
AGE	Kyolic liquid (Mission Viejo)	5LO1	+121.8 (2.73)
A	Garlinase 4000 (Enzymatic Therapy, Green Bay, WI)	213Y46QD	-213.0 (4.67)
B	Garlic powder (McCormick, Baltimore, MD)	0208A	-217.2 (5.20)
C	Quintessence caplet (Pur- Gar, Takoma, WA)	36698	-239.5 (4.85)
D	Quintessence capsule (Pur- Gar, Takoma, WA)	63121	-242.1 (5.15)
E	Garlicin (Nature's Way Product, Springville, UT)	503369	-246.8 (9.24)
F	Kwai (Lichtwerpharma, Berlin, Germany)	94080700	-250.7 (3.01)
G	Garlique (Sunsorce HealthProducts, Kihei, HI)	5J0010	-251.0 (10.6)
H	Garlic Time (ArizonaNatural Products,Scottsdale, AZ)	896210	-254.4 (7.14)

¹Laboratory Report, Wakunaga Pharmaceutical, Hiroshima, Japan, October 1995. Courtesy of Wakunaga of America Company. Garlic products were purchased from stores, as in Freeman and Kodera 1995. Each analysis was performed three times.

²Antioxidant properties were measured by the ability of the various products to inhibit the emission of low level chemiluminescence, in a liver microsomal fraction, initiated by t-butyl hydroperoxide (Imai et al. 1994). Inhibition (+) denotes antioxidant activity, resulting from scavenging of reactive oxygen species (ROS) and reflected in the inhibition of light emission. Inhibition (-) denotes prooxidant activity of a product as reflected in an increased light emission, induced by increased ROS activity.

*Table reproduced from "Recent Advances on the Nutritional Benefits Accompanying the Use of Garlic as a Supplement" held November 15-17, 1998 in Newport Beach, CA. The conference was supported by educational grants from Pennsylvania State University, Wakunaga of America, Ltd. and the National Cancer Institute. The proceedings of this conference are published as a supplement to *The Journal of Nutrition* 131:1010S-1015S, 2001.

Table 1. Antioxidant effects of aged garlic extract (AGE) compared with other garlic supplements^{1*}

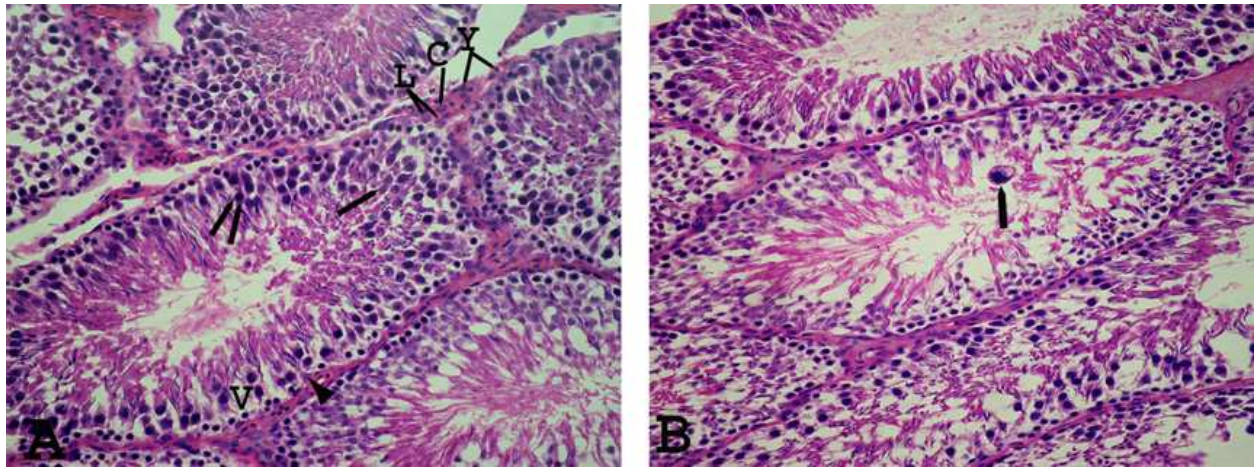


Figure 1. Photomicrographs of sections of testes of albino rats having received 20% of their daily food as crude garlic for two months (subgroup B1) showing: (A) intraepithelial vacuoles of variable sizes (V). Sertoli cell nuclei (S) on the basal portion of the tubules. Primary spermatocyte nuclei either dividing normally (\uparrow) or with condensed chromatin ($\uparrow\uparrow$). Some seminiferous tubules possess irregular basal lamina and are separated from each other. Interstitial tissue with Leydig cells (L), plasma cells (c) and lymphocytes (Y) ($\times 200$). (B) Giant cell (\uparrow) formation and exfoliation in the lumen of the seminiferous tubules ($\times 200$). (Reproduced from Abdelmalik, 2011)

Author details

Carlo Valente¹, Guillaume Aboua^{2*} and Stefan S. Du Plessis¹

*Address all correspondence to: abouay@cput.ac.za

1 Division of Medical Physiology, Faculty of Medicine and Health Sciences, Stellenbosch University, Tygerberg, South Africa

2 Department of Biomedical Sciences, Faculty of Health and Wellness, Cape Peninsula University of Technology, Bellville, South Africa

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