Garlic has a long tradition as a food and as a medicinal plant. Therapeutic effects, routes of application and modes of preparation of garlic are very varied. In order to be able to assess which mode of preparation is suitable for which application, it is necessary to explain certain substance characteristics of garlic. The garlic bulb contains cysteine sulphoxides belonging to the secondary plant components. During the processing these compounds undergo a rapid enzymatic respectively non-enzymatic conversion. Depending on the mode of preparation, different substances with different effects can be found in the resulting products. Most of the data available on the chemopreventive and curative effects of garlic is based on the use of the freshly prepared garlic. Epidemiological studies prove that the risk for different malignant diseases, especially of the gastro-intestinal tract is significantly reduced by regular consumption of large amount of garlic. In numerous investigations it was possible to demonstrate different pharmacological properties, for some cysteine sulphoxides, like antimicrobial, anticancer, and antioxidant activity. The antioxidant potential of garlic is of great interest in connection with the antiatherosclerotic and cardioprotective effects observed epidemiologically and clinically.

Botany
Garlic belongs to the genus *Allium*, which comprises of approximately 600 known species distributed over the whole northern hemisphere. Characteristic for *Allium* species are herbaceous, perennial bulbous plants with a typical leek odour. The bulb of Garlic, *Allium sativum* L., is of a compound nature, consisting of numerous bulblets, so-called cloves, of different size, the whole surrounded by layers of white scale leaves. The ovoid cloves are 3-4 sided with an acute summit, narrowed into a thread like portion of fibre, and the base truncate. Each clove is separately enclosed in a white scale and covered with a pinkish-white skin. From the central clove, the plant shoots a quill-like, round, hollow, and unbranched stalk, which is encased at the bottom by long, narrow and flat, grass-like leaves. The whitish flowers are placed at the end of a stalk rising direct from the bulb, and grouped together in a globular head. The flowers develop numerous egg-shaped bulbils, which have an important function in the propagation of the plant (Fig. 1) [1, 2].

**Fig.1 :** Garlic, *Allium sativum* L. lowering plant, bulb, and bulb cross section. (From Weber H (1962) Botanik, eine Ein-führung für Pharma-zeuten und Mediziner. WVG, Stuttgart)

Historical aspects
*Allium sativum* is supposed to originate from Central Asia, from where its cultivation has spread to Southwest Asia and the Mediterranean region. The use of the garlic bulb as a food as well as a medicinal plant has a very long tradition. In all ancient civilisations of the Eastern Mediterranean garlic was known and highly respected, as with the Egyptians where the plant was attributed to
certain deities. The most important textbooks of Sanskrit medicine, known as Ayurveda, probably codified about 500 A.D., though the content of which is much older, mention garlic as a remedy to treat skin diseases, dyspepsia, anorexia or rheumatism. From India the cultivation of garlic seems to have been brought to China and following to Japan, where it was used to treat colds for example. In middle and northern Europe originally unknown, *Allium sativum* was introduced by the Romans. Though garlic was frequently used in therapy of European physicians of the 15th-17th century it was not equally accepted due to its strong smell [1, 3].

Today garlic is cultivated in regions with moderate or subtropical climate all over the world mainly for the use of its bulb as a spice or as a vegetable. *Allium sativum* prefers a well-fertilized open ground with sandy or loamy soil. As the plant is very sensitive to excessive moisture, the location should be warm and sunny [1].

**Different forms of preparations of the garlic bulb**

Equal to the use of garlic in culinary practice, only the bulb is of importance for medicinal purposes. Hence, the monograph for garlic in the British herbal pharmacopoeia specifies the fresh or dried compound bulbs of *Allium sativum* as the part of the plant used for medicinal preparations [4]. The greatest part of the agricultural production of garlic bulbs is processed to garlic powder. For this procedure the bulb is peeled, cut and freeze dried or dried at a temperature not exceeding 65°C. Garlic powder is monographed in the European Pharmacopoeia [5]. Besides the typical powder-drug there are other preparations of the garlic drug. By maceration, a cold extraction method, garlic oil is produced, the essential garlic oil is derived from fresh bulbs by steam-distillation and the fermentation of the bulbs leads to a product, called aged-garlic.

During the manufacturing techniques applied with this, compared to the fresh bulb, the concentration of certain substances is changed and even whole compound classes can be decomposed or lost by physikal or biochemical processes. Due to residual moisture, even in the garlic powder continuously proceeding enzymatic processes are still active and slowly leading to a volatilisation of the sulphur compounds [6].

Conditions like these make clear that the key to obtaining consistent benefits from garlic, in the sense of a rational phytotherapy, meaning that the therapy is based on herbal preparations, which have been tested in regard to their quality, effectiveness and safety, is to investigate the compounds substantially and to understand the underlying biochemical processes and their significance for the pharmacological potential of the medicinal plant [7].

**Compounds of the garlic bulb**

Besides compounds belonging to the substance metabolism and metabolism of activity the garlic bulb contains a dominant group of secondary plant components, which are noticeable through their sulphur content. These are primarily cysteine sulphoxides, e. g. alliin and derivatives of gamma-glutamyl cysteine. In the bulb they are present in considerable amount, about 4 %, based on the fresh weight, and with the usual modes of preparation they are responsible for the characteristic garlic odour.

Further compounds present in a small amount are flavonoids, steroids and triterpene saponins from the beta-sitosterol or F-gitogenin type [8].

A special characteristic of the group of the cysteine sulphoxides is that upon disrupting the cells of the garlic bulb by bruising, crushing, chewing, or mincing they undergo a rapid, spontaneous enzymatic conversion. The enzyme responsible for this, is the so-called allinase. As a result of this mechanical action the cell integrity is lost, so that the enzyme allinase comes into contact with the
amino acid alliin, causing its rapid transformation into allylsulfenic acid, and subsequent conversion to the so-called thiosulfinate allicin. This enzymatic metabolite, allicin, is a highly reactive substance which is transformed more rapidly or more slowly, depending on the surrounding medium, in further non enzymatic stages, into various different substances, such as vinyl dithiines, ajoen and / or alkyl sulphides (Fig. 2) [9].

**Pharmacology**

After a multitude of research publications and a long history of traditional use, there can be little doubt that garlic has a remarkable medicinal potential. The most important of which are antibiotic, cardiovascular and anticancer effects. These effects have been assessed in pharmacological and clinical studies.

**Antimicrobial activity**

From folk medicine and empirical treatment it has been learned that ample amounts of fresh garlic can have a beneficial effect on the human intestinal flora. This effect is attributed to the fact that the susceptibility of pathogenic gram-positive bacteria to the antibacterial components of garlic is higher than that of the physiologically desirable intestinal bacteria. According to the present state of knowledge, the key substances responsible for the antibacterial effectiveness of garlic are the thiosulphinates, particularly allicin [1, 8, 10]. Thiosulfinates are also in a dominant position with respect to the antimycotic activity of garlic. In *in vitro* studies allicin proved to be ten times more effective against candida cells, compared with ajoen, a catabolite of allicin [11]. The number of publications dealing with the antiviral or antiparasitic activity of garlic or its components is relatively small, however, some very encouraging results could be demonstrated. In these studies allicin again is dominant as the main active substance, yet some of its catabolites were assessed to be active too [1].

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**Fig. 2: Metabolic cascade of the cysteine sulphoxides;** During the crushing of the garlic bulb cysteine sulphoxides undergo a rapid, spontaneous enzymatic conversion. From two molecules of alliin, an antioxidant that acts as a reaction partner of hydroxyl radicals, the enzyme alliinase, via the intermediate allylsulphenic acid, forms one molecule of allicin. Metabolically allicin is converted into diallyl disulphide. Diallyl disulphide also acts as an antioxidant and as an enzym inhibitor. It is rapidly metabolised to allyl mercaptan, among other things, an excellent heavy metal chelator (Pb, Cd, Hg). Depending on the preparation, allicin can be transformed, non-enzymatically, to vinyl dithiines, ajoenes and di-, oligo- and polysulphides, which again display antioxidative and fibrinolytic effects and weak antibacterial effects. Finally, alliin, itself already effective following intact absorption by applying fresh garlic or corresponding preparations, can metabolise to diallyl disulphide. Diallyl disulphide is on its part metabolised to allyl mercaptan [1, 8].
**Anticancer effects**

Epidemiological studies, in which thousands of persons kept under observation over a long period of time, indicate that a regular consumption of large amounts of garlic is associated with a lower risk for cancer, especially cancer of the gastro-intestinal tract. In a Chinese study where large amounts of fresh garlic were consumed, the primarily allicin-induced antibacterial properties of garlic were suggested to be responsible for the protective effects of garlic against this particular form of cancer. The underlying mechanism is explained by the killing of nitrate-reducing bacteria that results in a decreased level of gastric nitrite, which is known to produce carcinogenic nitroso compounds [1, 12, 13]. Since there were also positive results from other epidemiological studies, where cooked garlic that no longer contains allicin was applied, allicin-derived catabolites or unidentified compounds not associated with antibacterial activity must be of importance too. In *in vitro* and animal studies anticancer activity could be demonstrated for different allicin-derived metabolites [1, 10].

Numerous publications have attempted to explain the mechanism of the anticancer activity of garlic. Some authors mention antioxidant effects, which lead to a reduction of the presence of free radicals and the induction of endogenous radical scavenging activities to be of certain importance in the field of cancer prevention with garlic [14]. It is commonly proceeded from the assumption that radicals, reactive oxygen species, are involved in the development of degenerative and malignant diseases. Antioxidants possess radical scavenging properties and thus may play a role in the prevention of these diseases as well as in providing a certain protection against environmental sources of free radicals (Fig. 3). Allicin, allyl sulphides and possibly other compounds are related with the radical scavenging activity of garlic. Also alliin and S-alkyl cysteine are active as antioxidants, although the experimental findings available up to now were obtained in dosage ranges that bear no relationship to the amounts of these substances that can be provided by garlic. In this respect, further and better-coordinated trial designs are necessary in order to determine the relevance or the irrelevance of these compounds in connection with radical scavenging [1, 8].

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**Fig. 3:** Simplified diagram on the development and effect of radicals and reactive oxygen species as well as enzymatic and non-enzymatic protective mechanisms against radicals and reactive oxygen species. Among others, also the antioxidant effects of certain substances of the secondary plant metabolism belong to the non-enzymatic protective mechanisms. Depending on the chemical characteristic of the antioxidants, they metabolise peroxide radical anions (O2⁻ . ) to hydrogen peroxide (H2O2) and further to water or inactivate hydroxy-radicals (HO . ) or peroxy-radicals (ROO . ). [from: Kreuter MH, Lardos A (1999) in: Phytopharmaka V, eds. Loew D, et al., Steinkopff, Darmstadt]
Cardiovascular-protective effects
Radicals can have a multitude of deleterious effects on the organism. Free radicals affect the cell at the level of DNA, protein synthesis and membrane function. In the arterial blood vessels they are supposed to play an important role in the development of atherosclerosis, since it is generally believed that through oxidation of the low-density lipoproteins (LDL) free radicals trigger the cascade of the formation of atherosclerotic plaque. For this reason the antioxidant potential of garlic is also of great interest in connection with antiatherosclerotic and cardioprotective effects. The active substances of garlic prevent the formation of free radicals, support the endogenous radical scavenging mechanism and protect LDL against oxidation. These effects substantially contribute to explain the cardioprotective effects of garlic [1, 8, 15].
The components responsible for these effects have still not been fully explored. An explanation, however, is difficult, mainly due to the fact that not only the parent components of the garlic bulb, such as cysteine sulfoxides, are pharmacologically active but also the products of degradation and metabolisation [1, 8].
However, in the cardiovascular-protective action of garlic also certain other mechanisms, not related to antioxidant effects, must be active. The results from various publications show that fresh garlic or certain garlic preparations and compounds inhibit platelet adhesion and aggregation in arterial blood vessels, a pathogenic process which is brought in connection with atherosclerosis. Human and in vivo studies indicate that allicin or allicin-derived compounds are responsible for the antiaggregatory activity [1,15].
In other studies the beneficial potential of garlic in regard to increased cholesterol and blood lipid levels, or possible effects on blood pressure, vascular resistance and heart function were investigated and supplied encouraging results [1, 15].

Therapeutical use of garlic
Pharmacological investigations have shown that garlic is very effective in regard to cardiovascular diseases. Applied in an appropriate form garlic may protect blood vessels from the destructing effects of free radicals, prevent blood platelets from aggregation or adhesion on the wall of the vessel, balance increased cholesterol or lipid levels in blood, increase capillary flow and lower elevated blood pressure.
According to this, today garlic is used mainly as an antithrombotic and antiatherosclerotic agent. The German commission E recommends garlic as a support of dietary measures at an elevated level of blood lipids and in the prevention of age-dependent vascular changes [17]. The WHO monographs mention the treatment of elevated levels of blood lipids and the prevention of atherosclerotic vascular changes as the field of indications supported by clinical data. Besides, also the uses described in pharmacopoeias and traditional folk medicine are given, such as the treatment of respiratory and urinary tract infections, ringworm and rheumatic conditions [18]. The ESCOP monograph on garlic indicates as therapeutical use the prophylaxis of atherosclerosis, the treatment of elevated blood lipid levels, the improvement of the circulation in peripheral arterial vascular disease, upper respiratory tract infections and catarrhal conditions [Table1] [19].
Table 1: Clinical Use of Garlic

<table>
<thead>
<tr>
<th>Monographs</th>
<th>ESCOP Monographs Published July 1997</th>
<th>Commission E Monographs Published July 6, 1988</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Definition</strong></td>
<td>Garlic powder is produced from the bulbs, or from the separated cloves, of <em>Allium sativum</em> L., cut and dried at a temperature not exceeding 65°C, or freeze-dried, then powdered. It contains not less than 0.45 percent of alliin (C6H10O5S2; Mr 162.3), calculated with reference to the dried drug. The material complies with the draft monographs of European Pharmacopoeia.</td>
<td>Garlic bulbs, consisting of fresh or carefully dried bulbs that consist of the main bulb with several secondary bulbs (cloves) of <em>Allium sativum</em> L. as well as its preparations in effective dosage. Garlic contains alliin and its degradation products and sulfur-containing essential oil.</td>
</tr>
<tr>
<td><strong>Therapeutic indications</strong></td>
<td>Prophylaxis of atherosclerosis Treatment of elevated blood lipid levels insufficiently influenced by diet. Improvement of the circulation in peripheral arterial vascular disease. Upper respiratory tract infections and catarrhal conditions.</td>
<td>Supportive to dietary measures at elevated levels of lipids in blood. Preventative measures for age-dependent vascular changes.</td>
</tr>
<tr>
<td><strong>Dosage</strong></td>
<td>Prophylaxis of atherosclerosis Adults: The equivalent of 6-10mg of alliin (approx. 3-5mg of allin) daily, typically contained in one clove of garlic or in 0.5-1.0g of dried garlic powder, or in other preparations. Upper respiratory tract infections. Adults: 2-4g of dried bulb or 2-4 ml of tincture (1:5, 45% ethanol), three times daily.</td>
<td>Unless otherwise prescribed: Average daily dosage: 4g fresh garlic equivalent preparations.</td>
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</table>

The greatest part of the data available on the chemopreventive and curative effects of garlic is based on freshly prepared garlic as used in the normal everyday diet. In the German Commission E monographs the fresh or dried garlic bulb containing alliin and its transformation products and sulfur containing essential oils is mentioned in the description of drug (17). Depending on the mode of processing of the garlic bulb, different substances can be found in the resulting product. As a consequence the substance composition of certain preparations does no longer correspond to the monographed drug. The studies conducted on garlic have clearly shown that the various garlic compounds can have different pharmacological properties. From that it can be followed that for different forms of preparations different therapeutic effects of different quality have to be expected, while certain effects may be absent at all [8].
**Toxicology, Contraindications and Side effects**

Apart from being effective, for the therapeutic use of every drug, synthetic or natural, the proof of its safety has to be given.

The German Commission E reported that no contraindications were known. WHO notes that garlic is contraindicated in those individuals who have a known allergy to garlic. Other sources give a warning that garlic may increase bleeding times, which may be of importance prior to surgery. Rare side effects may be gastrointestinal symptoms or changes to the flora of the intestines. During pregnancy and lactation the use of garlic is not recommended [9]. In this sense garlic – applied in appropriate form and dosage – can be considered a safe drug. [Table 2]

**Table 2 Cautions for use of Garlic preparation**

<table>
<thead>
<tr>
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<th>Monographs</th>
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<tbody>
<tr>
<td></td>
<td>ESCOP Monographs Published July 1997</td>
</tr>
<tr>
<td><strong>Contraindications</strong></td>
<td>None known</td>
</tr>
<tr>
<td><strong>Special warnings and special precautions for use</strong></td>
<td>Caution is advised after surgical operations.</td>
</tr>
<tr>
<td><strong>Interactions with Other Drugs</strong></td>
<td>None reported.</td>
</tr>
<tr>
<td><strong>Pregnancy and lactation</strong></td>
<td>There are no objections to use during pregnancy and lactation (because neither long term nutritional experience nor any other important circumstances give reason for suspicion). From a controlled trial it is known that major sulphur-containing volatiles from garlic are transmitted to human milk leading to improved drinking habits of the babies</td>
</tr>
<tr>
<td><strong>Effects on ability to drive and use machines</strong></td>
<td>Nothing reported.</td>
</tr>
<tr>
<td><strong>Undesirable effects</strong></td>
<td>In rare cases gastro-intestinal irritation or allergic reactions.</td>
</tr>
<tr>
<td><strong>Overdose</strong></td>
<td>None toxic effects reported.</td>
</tr>
</tbody>
</table>
References


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