

Garlic and Other Alliums: The Lore and the Science

Writing a book combining botany and chemistry

Eric Block

University at Albany, SUNY

248th ACS Meeting

San Francisco

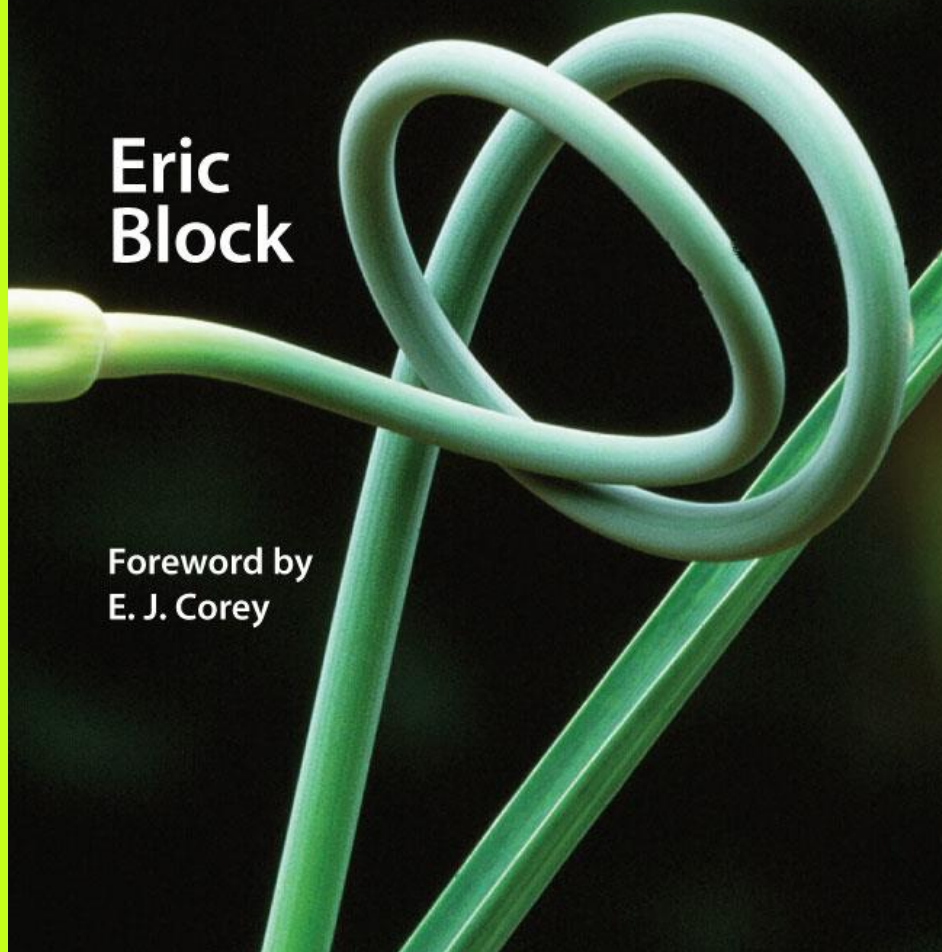
August 10, 2014

Garlic and Other Alliums

The Lore and the Science

Eric
Block

Foreword by
E. J. Corey



Publisher: Royal Society of
Chemistry, 2010 (hardback &
paperback); 454 pages

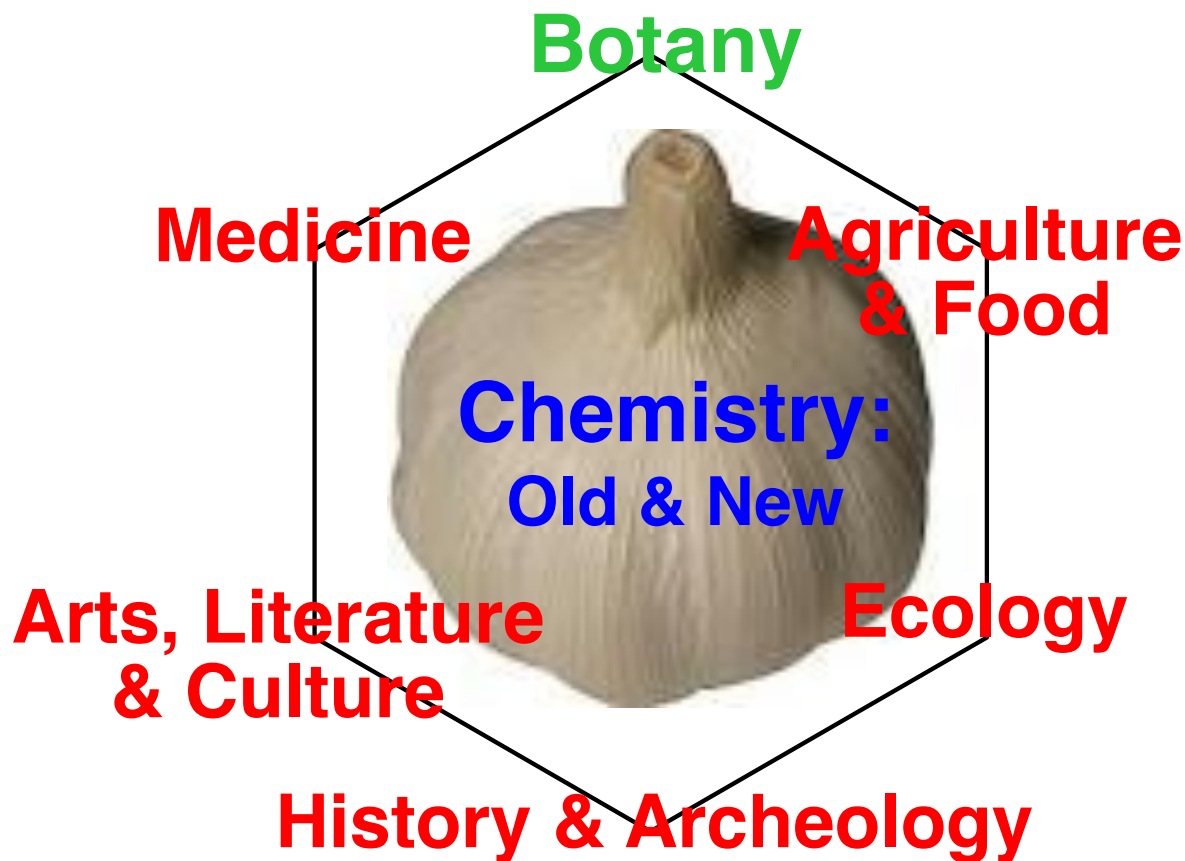
Includes 26 pages of full color
historical illustrations of 54
alliums from *Flora Germanica*
(L. Reichenbach, 1848)

Worldwide, in the holdings of
314 libraries; ~110 citations to
date

Reviewed by *NYTimes*, *Angew.
Chem.*, *J. Chem. Educ.*, etc.

Chinese edition in preparation!

While the core of the book is natural products chemistry, garlic and other alliums occupy a unique position in civilization, making for a fascinating story.



The Botany of the Genus *Allium*

A. Ascalonicum

Shallot

A. Cepa

Onion

A. Giganteum

**Giant Flowering
Onion**

A. Moly

Lily Leek

A. Porrum

Leek

A. Sativum

Garlic

A. Schoenoprasum

Chives

A. Tricoccum

Ramp

Total of 600-750 species in genus *Allium*

Ornamental Alliums



My source of botanical information

- Cambridge University Botanic Gardens (UK)
- Kew Gardens (UK)
- St. Petersburg Botanical Gardens (Komarov Botanical Institute of Russian Academy of Sciences; Russia)
- New York Botanical Gardens (Bronx, NY)
- Missouri Botanical Gardens (St. Louis, MO)
- Old herbals were found in the collections of major historical libraries.

St. Petersburg Botanic Garden (Komarov Botanical Institute, Russia)

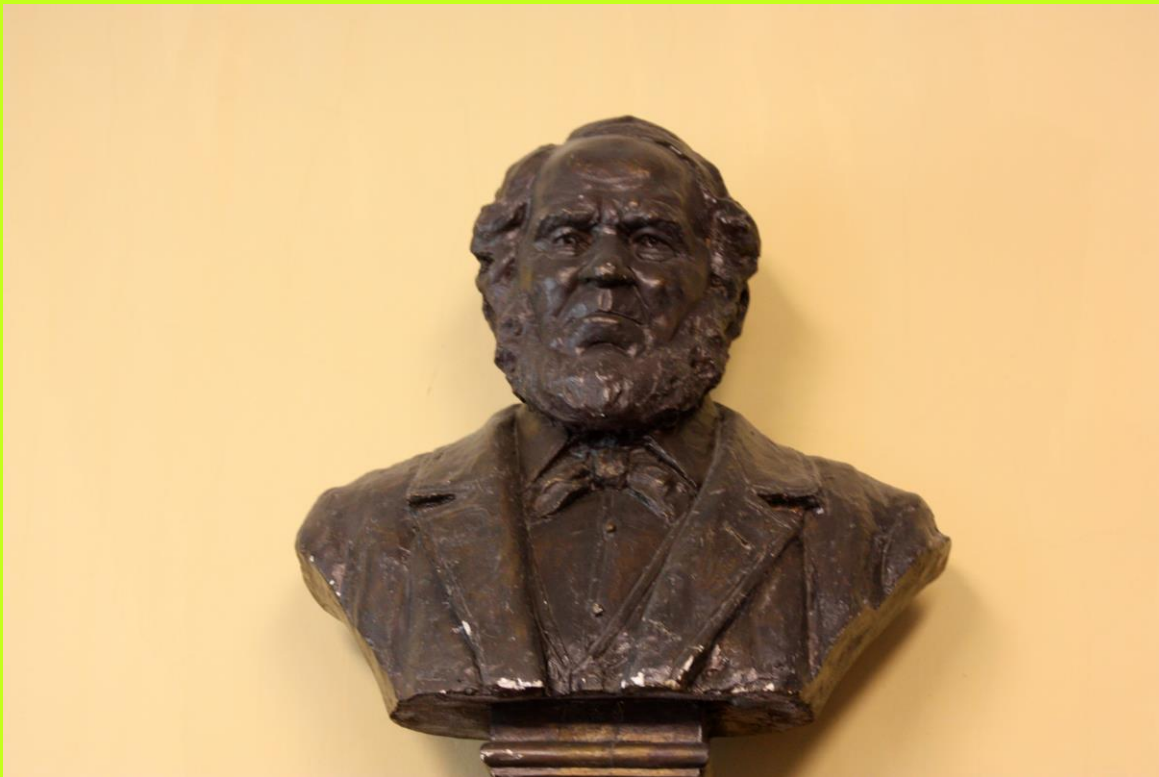


1714г. УКАЗ ПЕТРА I^{го}
АПТЕКАРСКИЙ ОГОРОД
1823. БОТАНИЧЕСКИЙ САД
1918. ГЛАВНЫЙ БОТАНИЧЕСКИЙ
САД РСФСР
1931. БОТАНИЧЕСКИЙ ИНСТИТУТ
АКАДЕМИИ НАУК СССР
1940. БОТАНИЧЕСКИЙ ИНСТИТУТ
ИМ. В.А. КОМАРОВА АН СССР



Kew Gardens (UK)

Eduard August von Regel (1815–1892): Director of Russian Imperial Botanical Garden of St. Petersburg. Directed biological collections around the world; described & named >3000 new plant species, including numerous alliums; published 3101 articles!



Allium alexeianum Regel, *Allium altissimum* Regel, *Allium andicolum* Regel, *Allium backhousianum* Regel, *Allium bakeri* Regel, *Allium bodeanum* Regel, *Allium boissieri* Regel, *Allium borszcaowii* Regel, *Allium bucharicum* Regel, *Allium caricoides* Regel, *Allium caricoides* Regel, *Allium cupuliferum* Regel, *Allium darwasicum* Regel, *Allium derderanum* Regel, *Allium derderianum* Regel, *Allium djimilense* Boiss. ex Regel, *Allium dolonkarense* Regel, *Allium drummondii* Regel, *Allium elatum* Regel, *Allium fetisowii* Regel, *Allium fibrosum* Regel 1887, *Allium filidens* Regel, *Allium filifolium* Regel, *Allium giganteum* Regel, *Allium gusaricum* Regel, *Allium herderianum* Regel, *Allium hoeltzeri* Regel, *Allium jacquemontii* Regel, *Allium karataviense* Regel, *Allium kaschianum* Regel, *Allium kaufmannii* Regel, *Allium kokanicum* Regel, *Allium longicuspis* Regel, *Allium longiradiatum* Regel, *Allium macrorhizon* Regel, *Allium maximowiczii* Regel, *Allium megalobulbon* Regel, *Allium oreophiloides* Regel, *Allium ostrowskianum* Regel, *Allium oviflorum* Regel, *Allium platystylum* Regel, *Allium renardii* Regel, *Allium sewerzowii* Regel, *Allium stipitatum* Regel, *Allium stoliczkii* Regel, *Allium suworowii* Regel, *Allium szovitsii* Regel, *Allium talassicum* Regel

Eduard August von Regel and family (~1890); botanist son **Johann Albert von Regel** is to right of father





The Komarov Institute Botanic Garden (St. Petersburg Botanical Gardens) was founded in 1714 as the pharmacy garden of Peter the Great. In 1905, more than 27,793 taxa were represented in the garden.

Center of Origin of Garlic is “Russian Asia,” explored by Regel’s son & his team





Expedition members having tea.



Readying plant specimens for transport from Russian Asia.



Transporting plant specimens from Russian Asia.



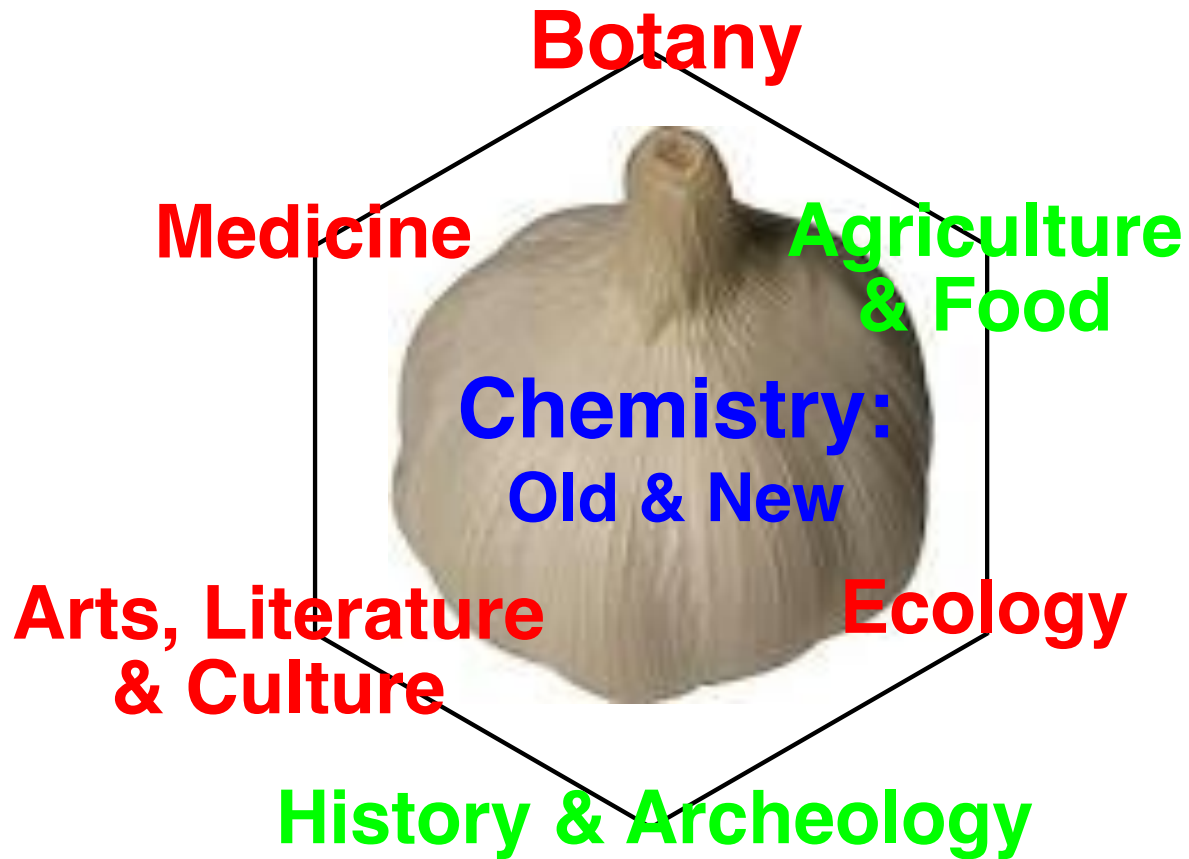
After the Seige of Leningrad during WWII only 300 of the 5000 indoor species survived.
As the result of restoration after the War, the garden now features >8000 species. 15



Restored greenhouses at the St. Petersburg Botanical Garden

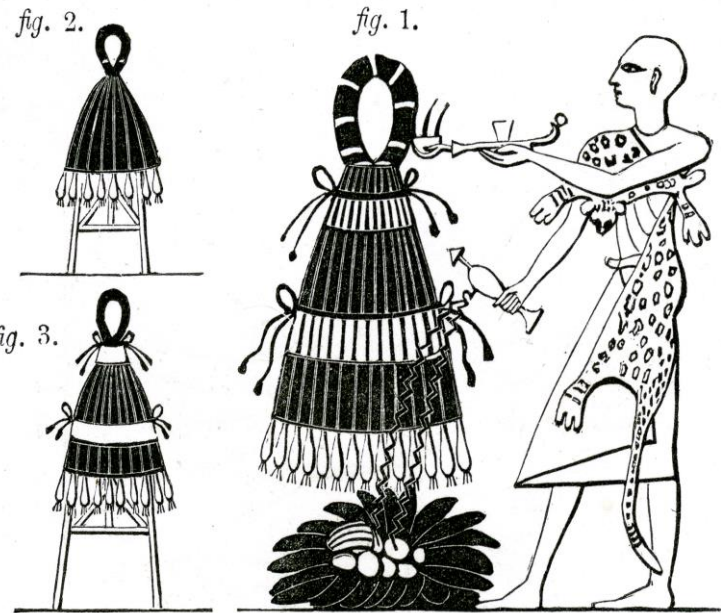


Restored greenhouses at the St. Petersburg Botanical Garden



Alliums in Ancient Egypt

Sprig of garlic buried with Nakhtefmut, 900 BC, Thebes, Egypt



No. 9.

Mode of tying up the onions for some offerings.

800,000 Acres of Garlic



Shandong, China



Ecospray: UK company sells garlic oil-based, environmentally benign pesticides: <http://www.ecospray.com/>



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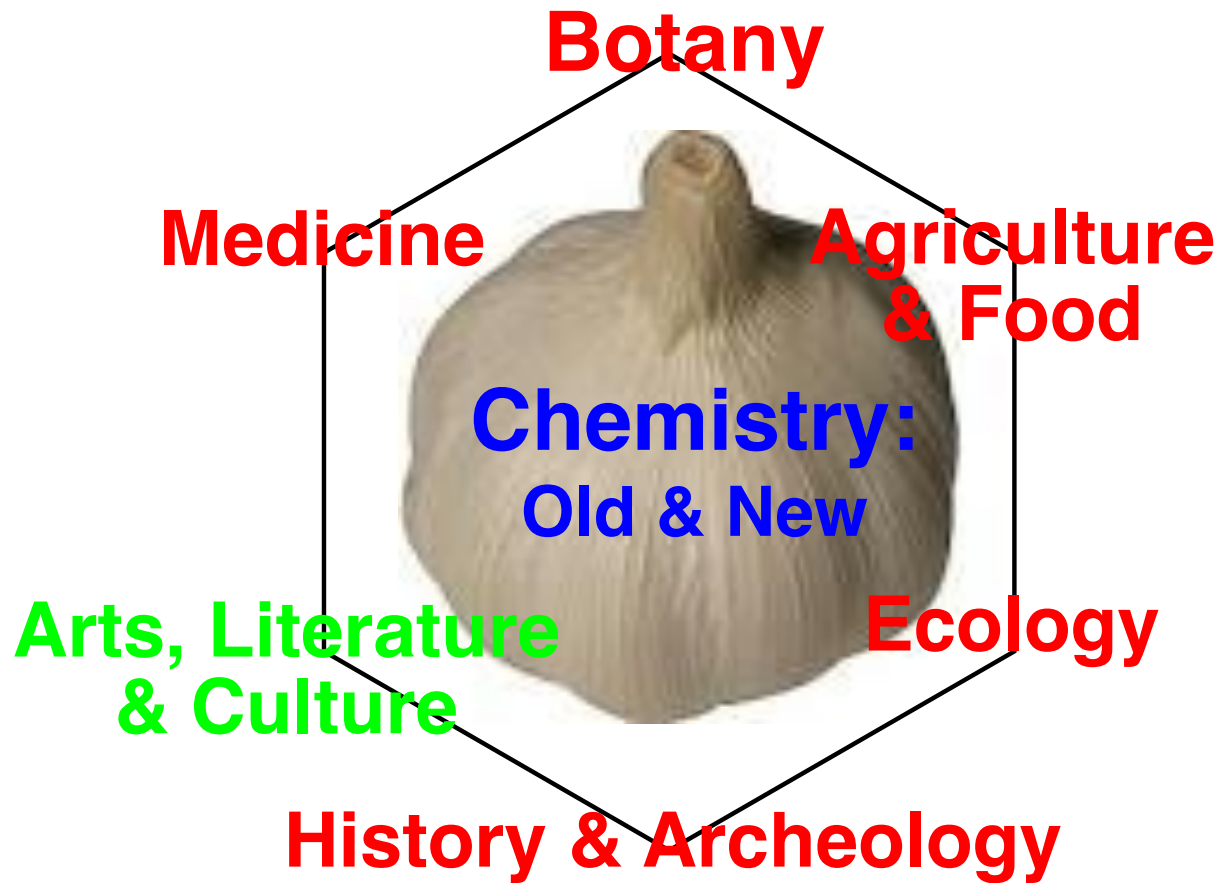
[Products](#)

[Research](#)

[Global distribution](#)

[What we do](#)

Annex 1 listing, EU directive 91/414; UK PSD approved



Historia Naturalis

Pliny the Elder (77 CE)

Garlic has powerful properties, and is of great benefit against changes of water and of residence. It keeps off serpents and scorpions by its smell ... It cures bites when drunk or eaten, or applied as ointment ... it is an antidote against the poisonous bite of the shrew-mouse ... powdered garlic has been given in milk to asthmatics ... The ancients used also to give it raw to madmen.

1480 edition: Collection of the Oxford University Bodleian Library



Shakespeare on Alliums



Antony and Cleopatra, Act 1, Scene 2

Indeed the tears live in an **onion** that should water this sorrow.

A Midsummer Night's Dream, Act 4, Scene 2

And, most dear actors, eat no **onions** nor **garlic** for we are to utter sweet breath; and I do not doubt but to hear them say, it is a sweet comedy

Henry V Act 4, Scene 7

Your majesty says very true: if your majesties is remembered of it, the Welshmen did good service in a garden where **leeks** did grow, wearing **leeks** in their Monmouth caps; which, your majesty know, to this hour is an honourable badge of the service; and I do believe your majesty takes no scorn to wear the **leek** upon Saint Davy's day.

Onions in Painting: Vincent van Gogh



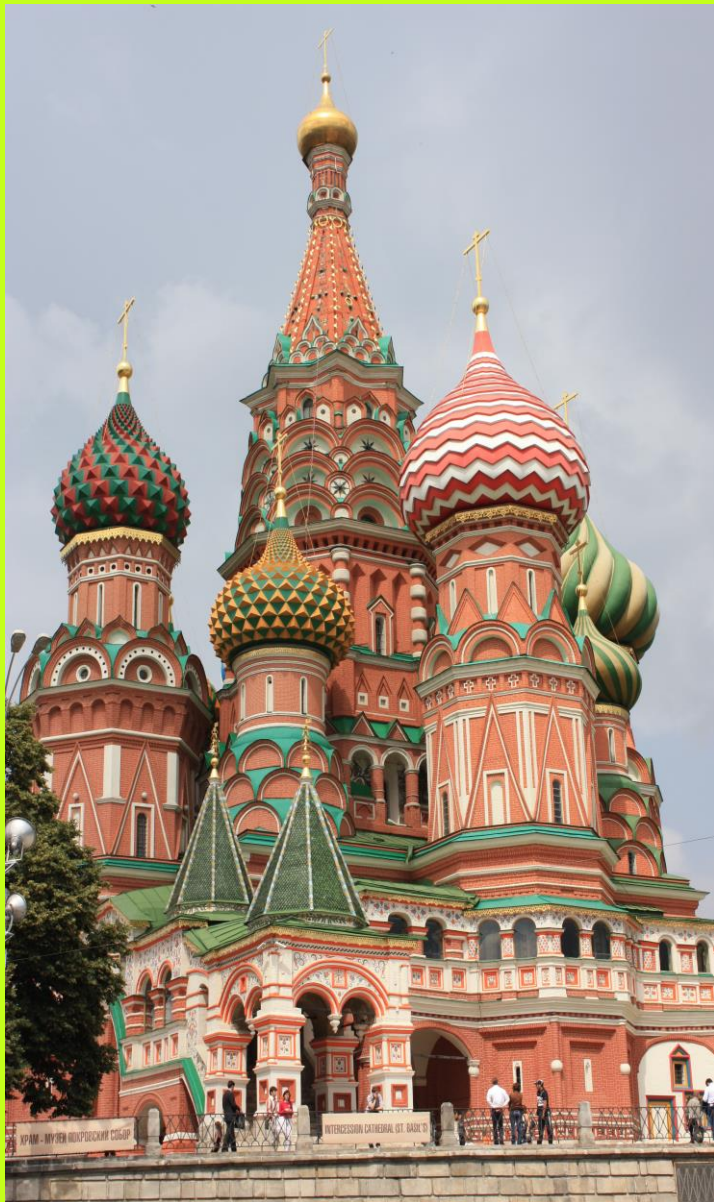
Alliums in Stamps and in the Bible

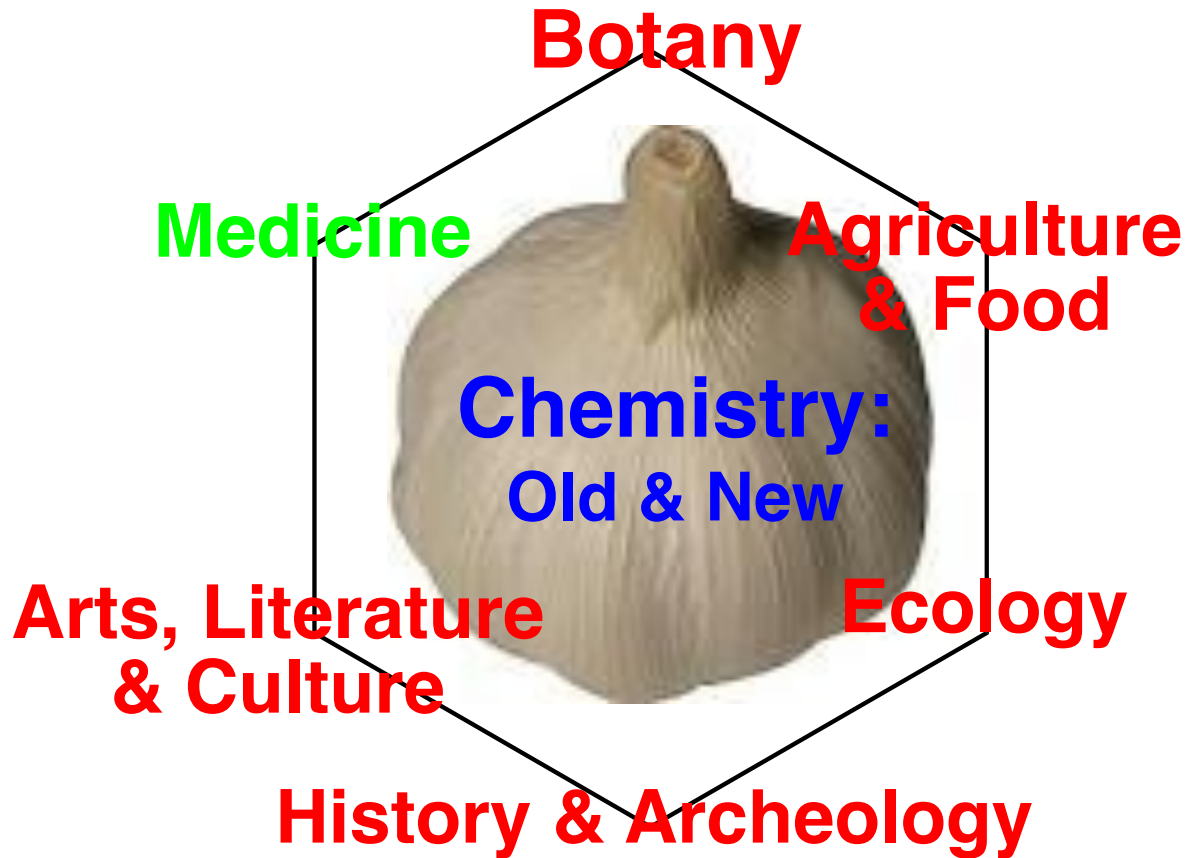


“We remember the fish which we did eat in Egypt, the cucumbers, the melons, leeks, onions and garlic”

Numbers 11:4-6

Onion Domes in Architecture: Saint Basil's Cathedral, Moscow





Garlic Health Supplements

US sales (2000)
\$61,200,000



Systemic Approaches Identify a Garlic-Derived Chemical, Z-ajoene, as a Glioblastoma Multiforme Cancer Stem Cell-Specific Targeting Agent

Yuchae Jung^{1,2}, Heejoo Park^{1,2}, Hui-Yuan Zhao¹, Raok Jeon¹, Jae-Ha Ryu¹, and Woo-Young Kim^{1,*}

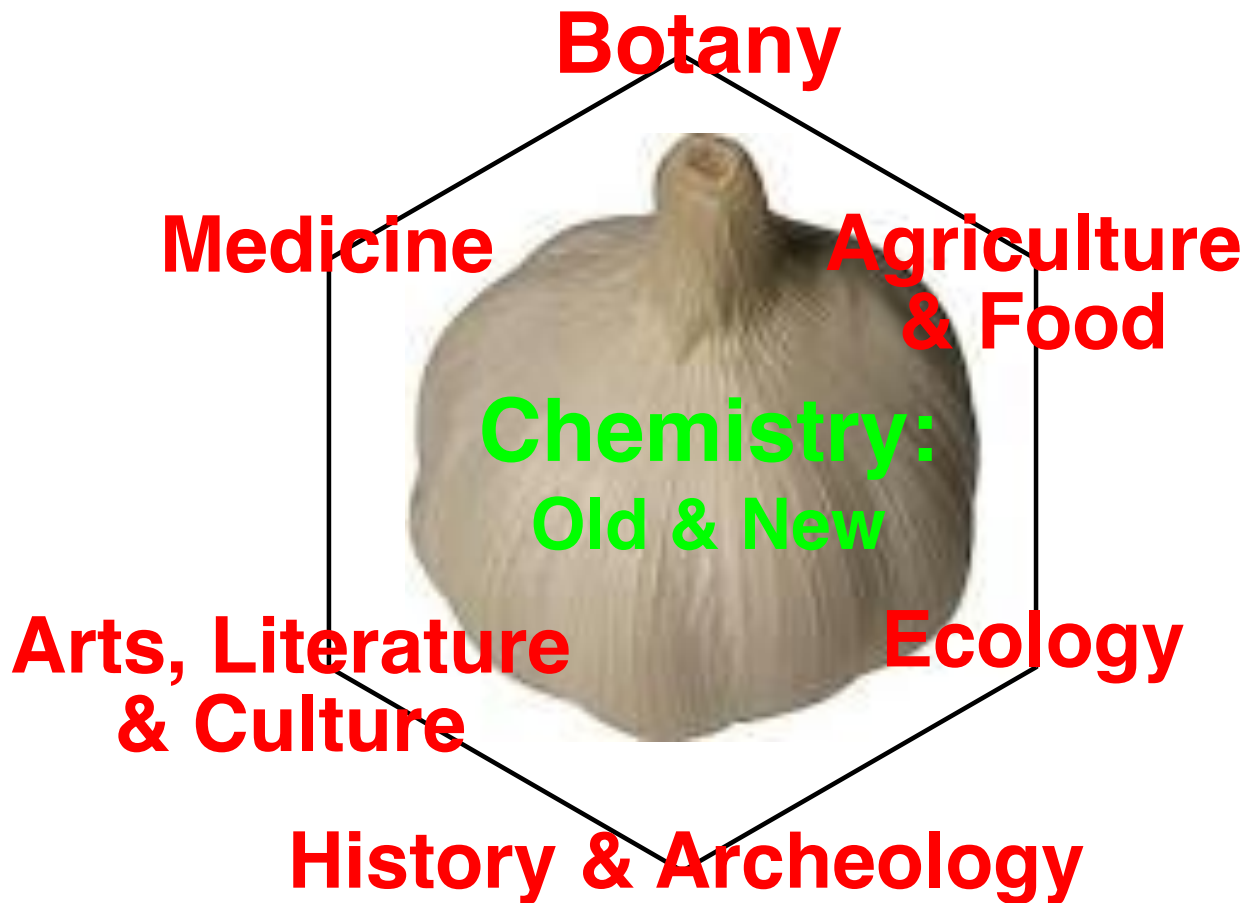
Glioblastoma multiforme (GBM) is one of the most common brain malignancies and has a very poor prognosis. Recent evidence suggests that the presence of cancer stem cells (CSC) in GBM and the rare CSC subpopulation that is resistant to chemotherapy may be responsible for the treatment failure and unfavorable prognosis of GBM. A garlic-derived compound, Z-ajoene, has shown a range of biological activities, including anti-proliferative effects on several cancers. Here, we demonstrated for the first time that Z-ajoene specifically inhibits the growth of the GBM CSC population. CSC sphere-forming inhibition was achieved at a concentration that did not exhibit a cytotoxic effect in regular cell culture conditions. The specificity of this inhibitory effect on the CSC population was confirmed by detecting CSC cell surface marker CD133 expression and biochemical marker ALDH activity. In addition, stem cell-related mRNA profiling and real-time PCR revealed the differential expression of CSC-specific genes, including Notch, Wnt, and Hedgehog, upon treatment with Z-ajoene. A proteomic approach, i.e., reverse-phase protein array (RPPA) and Western blot analysis, showed decreased SMAD4, p-AKT, 14.3.3 and FOXO3A expression. The protein interaction map (<http://string-db.org/>) of the identified molecules suggested that the AKT, ERK/p38 and TGF β signaling pathways are key mediators of Z-ajoene's action, which affects the transcriptional network that includes FOXO3A. These biological and bioinformatic analyses collectively demonstrate that Z-ajoene is a potential candidate for the treatment of GBM by specifically targeting

INTRODUCTION

Glioblastoma multiforme (GBM) is one of the most common and highly lethal brain malignancies (Bielen et al., 2011). GBM patients have a poor prognosis and a median survival of approximately one year after diagnosis (Bielen et al., 2011). The poor clinical outcome of the disease is unlikely to be overcome by conventional treatment, emphasizing the need to develop novel therapeutic strategies (Eyler et al., 2011).

Increasing evidence suggests that GBM contains a highly tumorigenic subpopulation of cells that is responsible for tumor initiation and progression (Hyun et al., 2011). Because these cells show stem cell-like properties, such as self-renewal and differentiation into other cell types, these cells are referred to as cancer stem cells (CSC) or tumor initiating cells (Soeda et al., 2009). Largely due to the dormant nature of stem cells, CSCs are resistant to chemo- and radiotherapy (Dean et al., 2005; Gangemi et al., 2009). Although conventional chemoregimens combined with aggressive radiation may kill the majority of cancer cells in a tumor mass, the treatment-resistant CSC population continues to survive and self-renew, ultimately leading to treatment failure and recurrence of the cancer (Hyun et al., 2011). Therefore, surgical resection with combined therapy for CSCs may be a potential solution to eradicate this malignant cancer (Lu et al., 2011).

Z-ajoene was first isolated from processed garlic in an E/Z-mixture (Block et al., 1984; Kaschula et al., 2012). It has been reported that Z-ajoene functions as an antioxidant agent and may be a potent antithrombotic agent (Kaschula et al., 2012). It



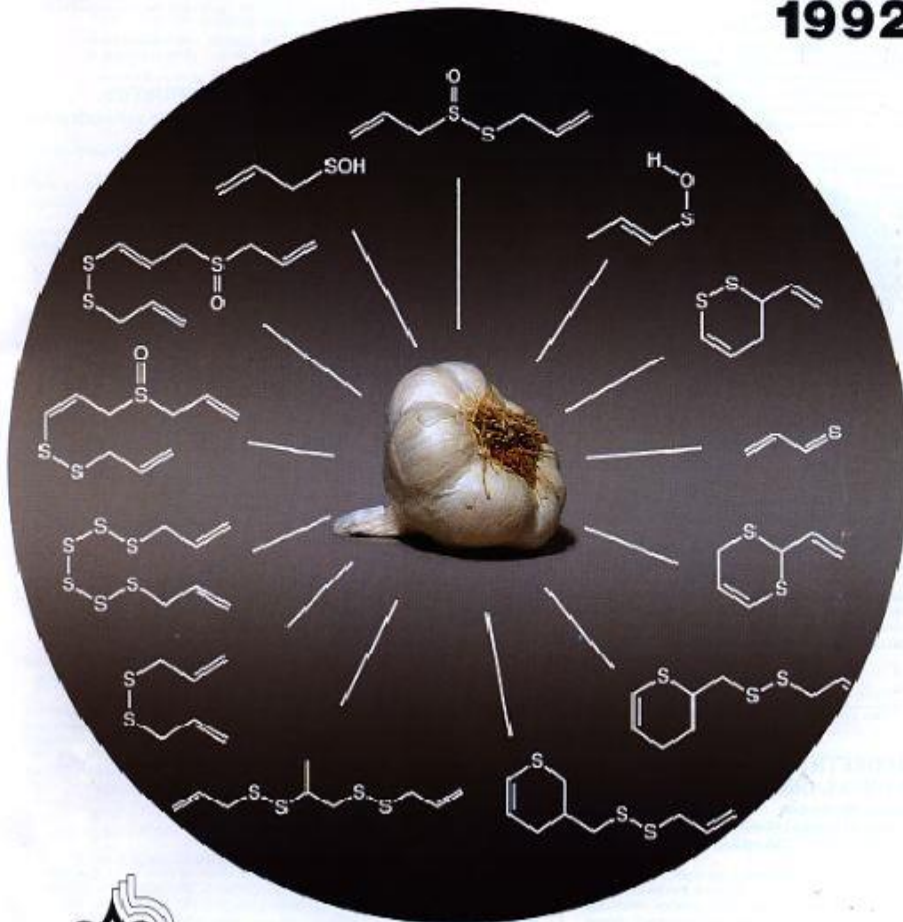
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ANGEWANDTE CHEMIE

A Journal of the Gesellschaft Deutscher Chemiker

International Edition in English

31/9
1992

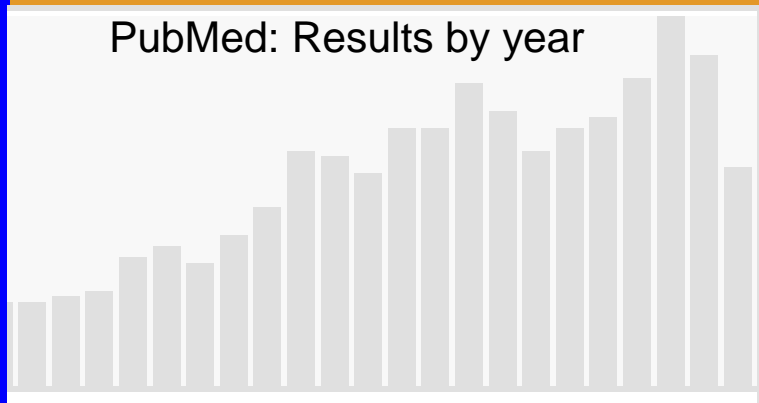


Reviews: Polyynes and Fullerenes · Chemistry of Garlic and Onion · Conformational Design
Highlights: [BPh₃]⁺ as Ligand · Asymmetric Syntheses · Inorganic Host-Guest Compounds

Supposed Health Benefits of Garlic:
Antibiotic, anticancer, antithrombotic, antioxidant, cholesterol-triglyceride lowering, blood pressure lowering

4445 (>1963) publications on garlic

PubMed: Results by year

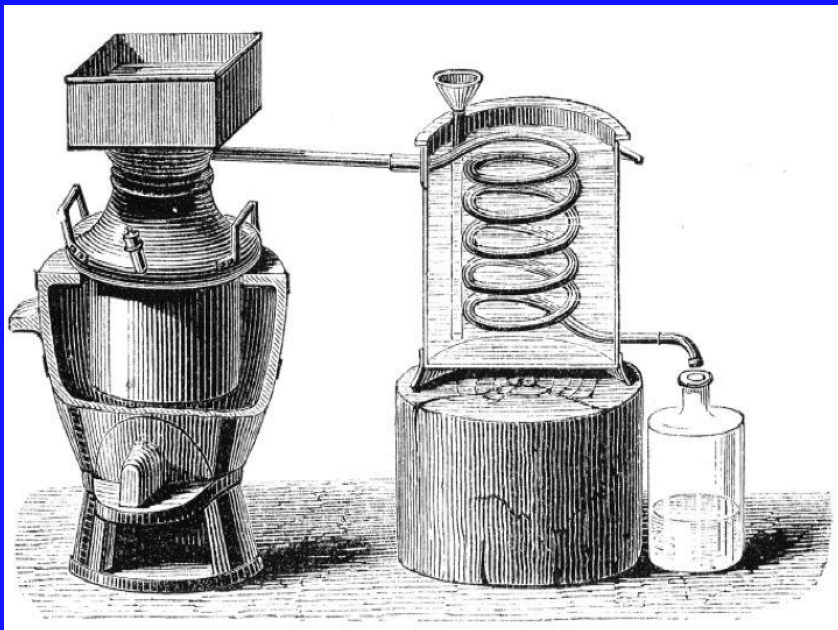


1993: 60

2012: 290

2014: 173

Early *Allium* Chemistry



An alembic of the type used to distil garlic oil

1844: Wertheim distills garlic and isolates garlic oil, “allyl sulfur”, the origin of the name “allyl” (from *Allium*)

1856: Hofmann synthesizes diallyl sulfide, having a “strong smell of garlic”, and allyl alcohol

1891: Semmler finds that garlic oil is in fact a mixture of diallyl disulfide and trisulfide



August Wilhelm von Hofmann, Director of the Royal College of Chemistry of London, and founder of the German Chemical Society

Allium Chemistry

Alliinase
Enzymes

Precursors

Intermediates

Distillates
(Headspace
volatiles)

Primary
Flavorants

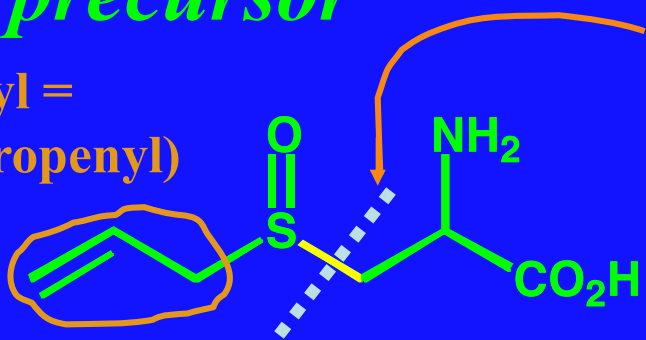
Secondary
Products



Garlic Chemistry

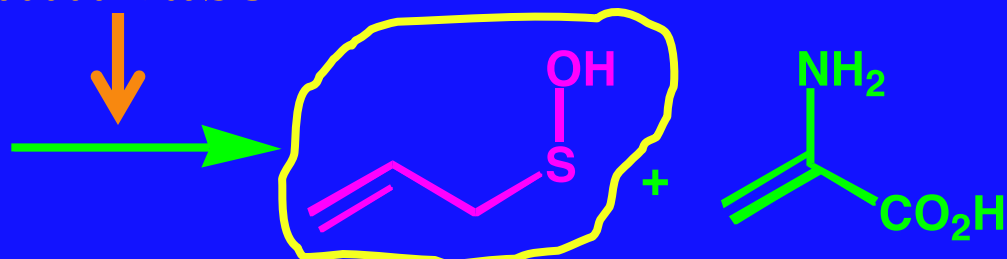
cysteine sulfoxide precursor

(allyl = 2-propenyl)



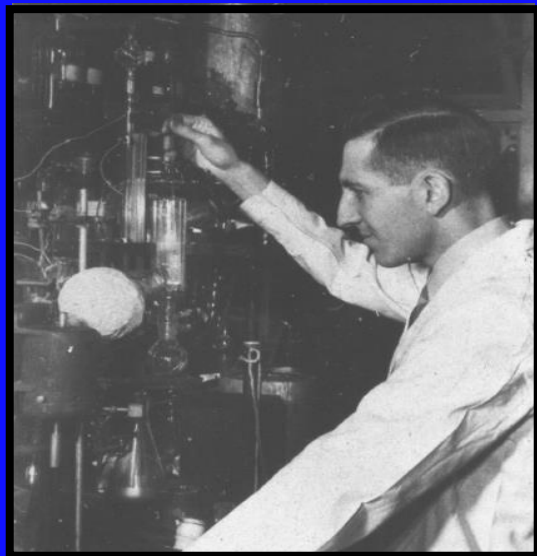
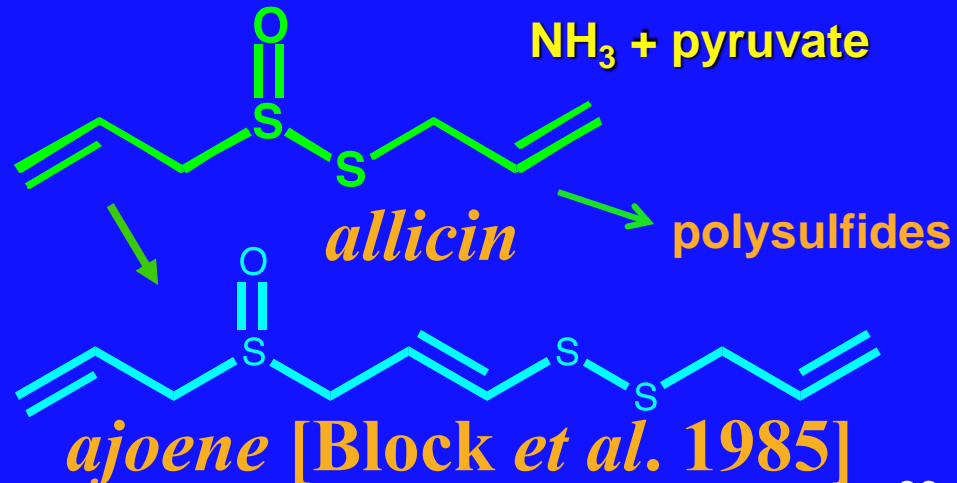
alliinase

sulfenic acid intermediate



X2 (-H₂O)

NH₃ + pyruvate



Chester J. Cavallito [1915-2010]
Sterling Winthrop Co., 1945

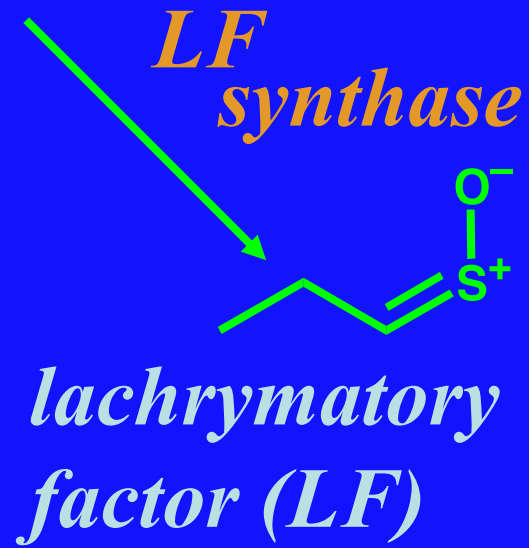
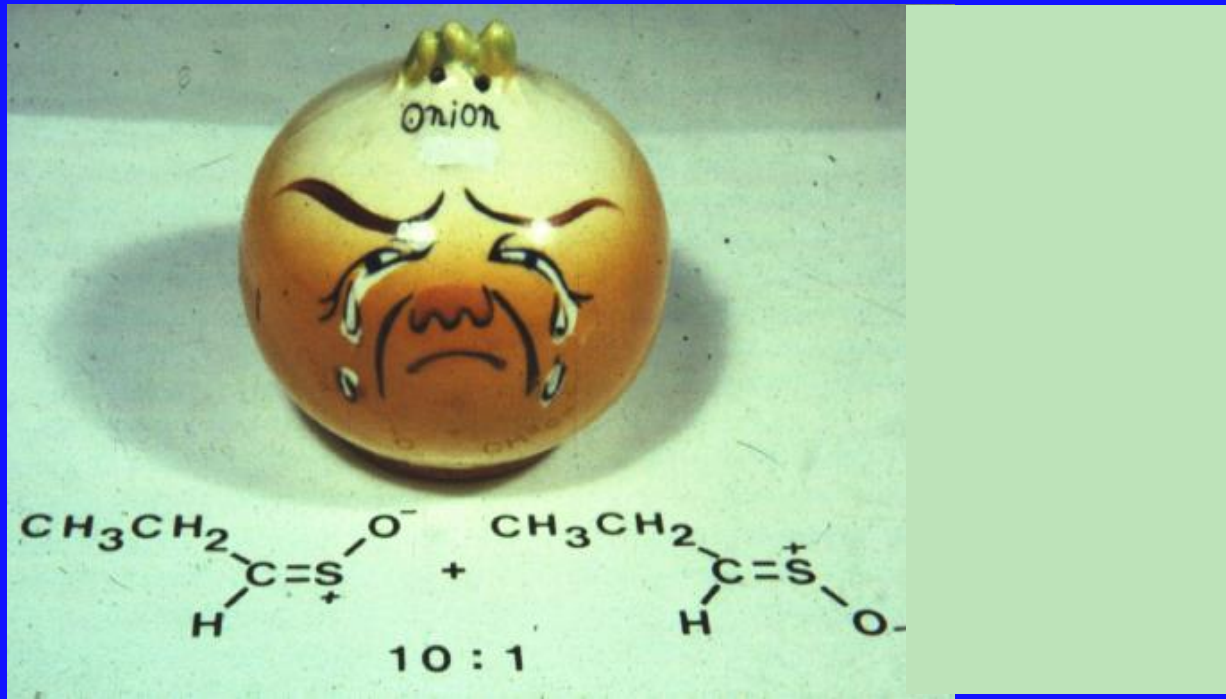
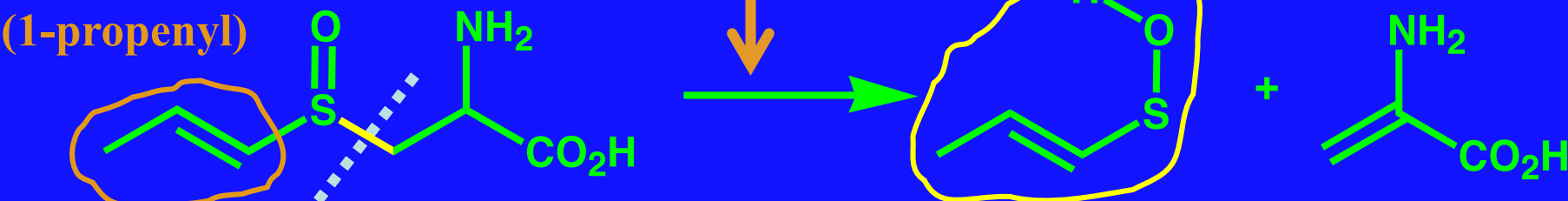
ajoene [Block et al. 1985]

Onion Chemistry

cysteine sulfoxide precursor

sulfenic acid intermediate

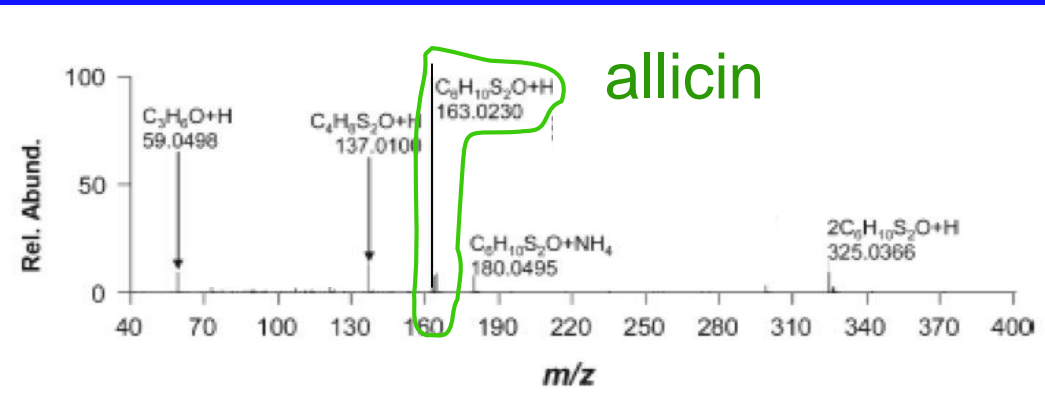
alliinase



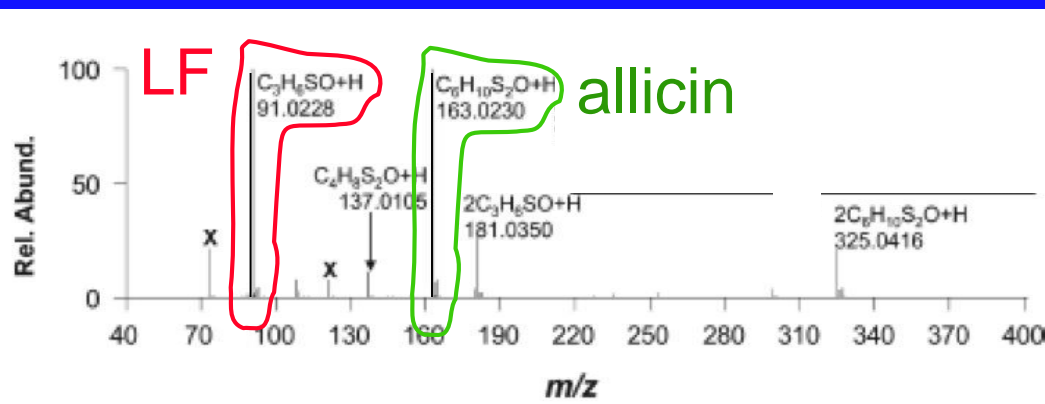
DART (Direct Analysis in Real Time) mass spectrometry allows high resolution measurement of mass spectra of plant samples at ambient atmospheric conditions with no sample preparation.



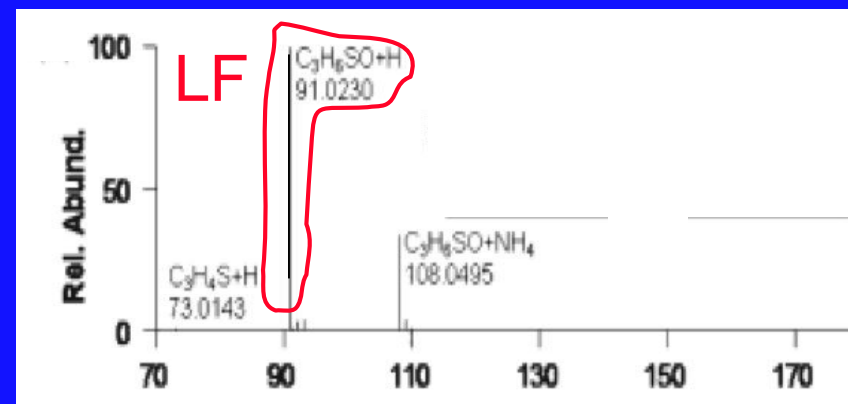
Elephant Garlic (*A. ampeloprasum*) but not Garlic Produces LF as well as Allicin



PI-DART mass spectrum of garlic
(allicin + H^+ = 163.0263)



PI-DART mass spectrum of elephant garlic
(LF + H^+ = 91.0235; LF + NH_4^+ = 108.0506;
allicin + H^+ = 163.0319)

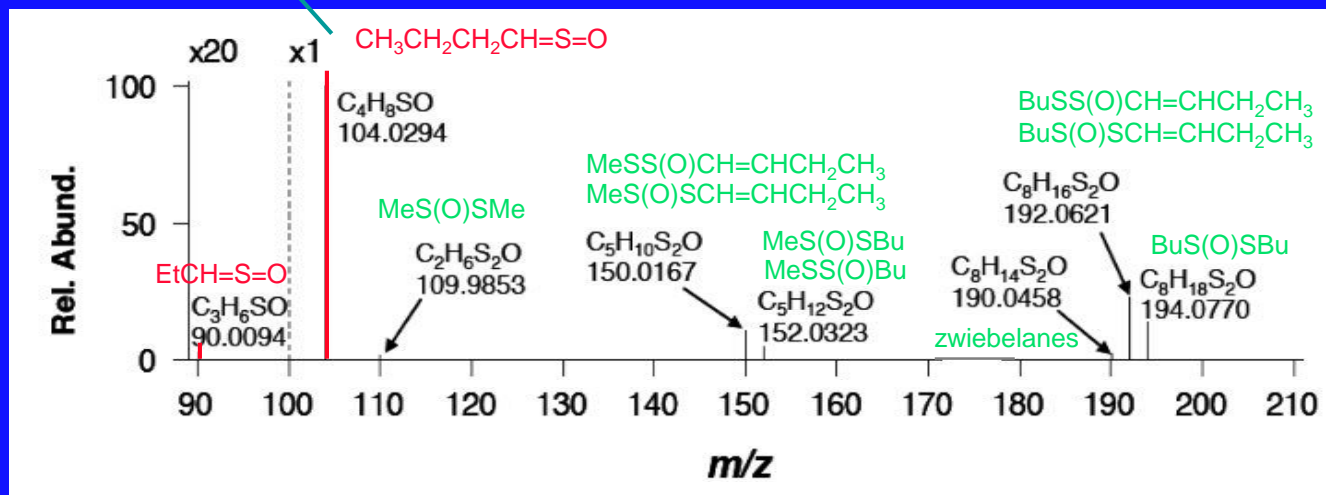
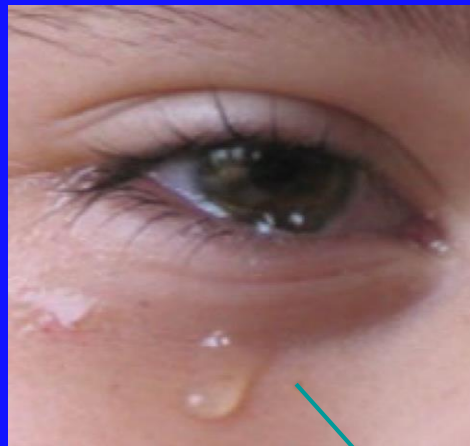


PI-DART mass spectrum of onion
(LF + H^+ = 91.0230; LF + NH_4^+ = 108.0506)

***Allium sicutum* (*Nectaroscordum sicutum*)
(used as a seasoning in Bulgaria)**

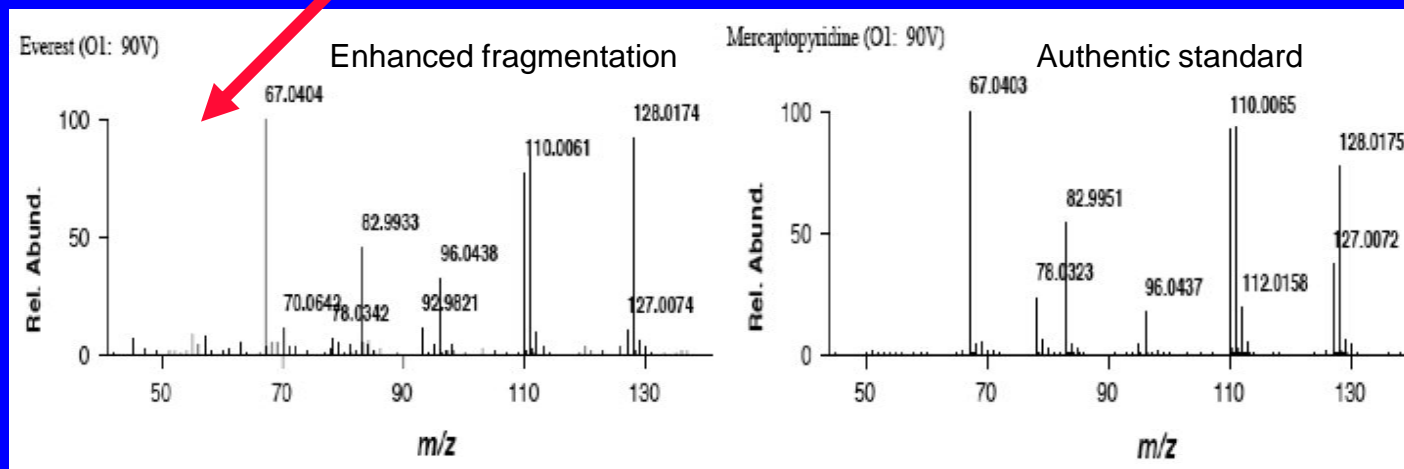
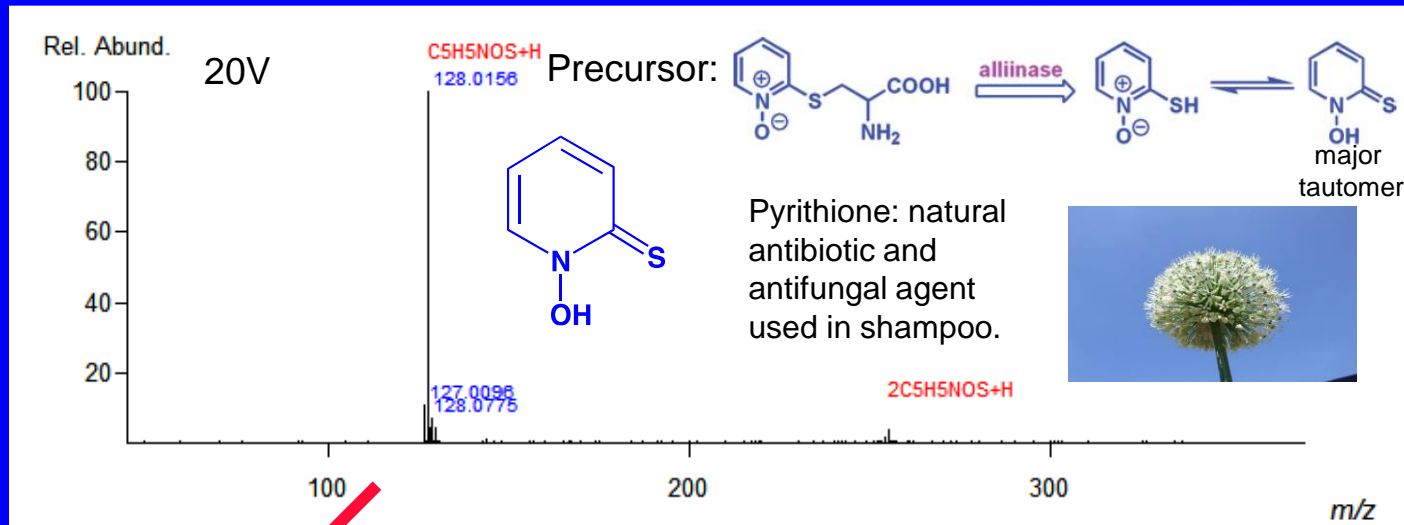


DART Results: A New Natural Lachrymator: (Z)-Butanethial S-Oxide



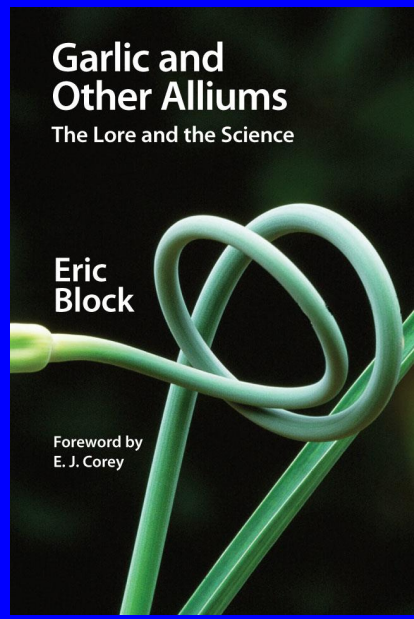
J. Agric. Food Chem. **2010**, *58*, 1121

Allium stipitatum: DART-MS Analysis Reveals that Major Volatile is a known Antibacterial and Antifungal Agent!



Phosphorus, Sulfur, Silicon Rel. Elements, 2011, 186, 1085

Thanks to: Dr. Dmitry Geltman, Komarov Botanical Institute (St. Petersburg, Russia)



RSC Publishing; JEOL USA

《神奇的葱蒜—传说与科学》
“Magical Scallions and
Garlic – The Lore and the Science”