

Diallyl disulfide, an organic sulphur compound found in garlic, has several biological applications.

S.Swapna Rani ¹,Mudigonda Naga Raju²,B.Shekar³,Manchala Ramesh ⁴,
Dept.: Humanities & Science
Nagole Institute of Technology and Science,
Kuntloor(V),Hayathnagar(M),Hyderabad,R.R.Dist.-501505

ABSTRACT

It's generally agreed that garlic is a healthful addition to the diet and a great way to get your fill of medicinal compounds. Anti-inflammatory, antioxidant, antibacterial, cardiovascular protective, neuroprotective, and anticancer actions are only some of the many positive biological effects of diallyl disulfide (DADS), a key bioactive component of garlic. Does this evaluation follow a systematic approach? the biological roles of DADS and elucidated the molecular processes by which it plays these roles. For these reasons, we're keeping our fingers crossed that this review facilitates future study and the creation of DADS for by shedding light on the present literature and pointing the way toward its future evolution. illness diagnosis and treatment in a nutshell.

Introduction

Medicinally useful substances may be found in plants in great abundance. The use of garlic as a functional food and traditional herb for the treatment and prevention of a variety of diseases has gained widespread acceptance. illness therapy, including cancer and infectious conditions [1-4] Organic sulphur is thought to most biological processes may be attributed to chemicals made with garlic [5]. Two disulfide bonds in an allyl group (composed of two allyl groups attached to sulphur atoms, see Figure 1) is a crucial sulfur-containing component found in garlic [6, 7]. There has been some research that DADS serves a variety of biological purposes, including anti inflammatory ones, cancer-preventative, detoxifying, and antioxidant effects, the nature of which may be deduced from its chemical make-up [4, 7-9]. Extensive prior analyses have focused on the encouraging The importance of DADS in the management of a variety of wide spectrum of illnesses [6]. Our job here is a methodical Biological Roles of DADS: A Review with an emphasis on the cellular and molecular processes, with the make available the most recent scientific data and expert analysis experiments.

Methodologies

We looked for DADS-related articles in PubMed, Web of Science, and GreenMed up to June 2021. The International Clinical Trials Database was also searched. Register System and Clinical Trials.gov as Possible Resources for medically relevant trials Bibliographic citations and references A supplementary product was the result of a manual search of reviews.

Biological Functions of DADS

Anti-inflammatory Effects, Section 3.1. Injury, toxicity, or microbial infection may trigger inflammation as an adaptive response by the host. The right kind of inflammatory tissue growth and protection by removing potentially damaging stimuli. recovery [10]. Nonetheless, unchecked inflammation causes repeated insult to the body's organs and tissues, which may lead to deterioration of these structures due to disease [11]. Academics have observed that DADS may reduce inflammation in a variety of illnesses include arthritis and pancreatitis [12, 14]. As shown by Fasolino et al. [15], mucosal edoema

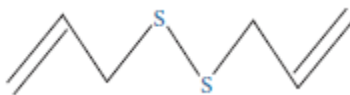


Figure 1: Chemical structure of DADS.

colonic mucosa and submucosa in DADS-treated rats was drastically reduced. In addition, decreases in body weight were seen when subjects took modest doses of DADS (between 0.3 and 10 mg/kg). based on the proportions of colonic weight to colonic length Inflammation of the intestines caused by dinitrobenzene sulfonate. damage. Studies on animals have shown that the anti-inflammatory and The DADS's anti-oxidant properties were also verified by Acute inflammatory reaction caused by carrageenan injection a model based on mouse paws [9]. Critical to the inflammatory response is the protein DADS. through the aid of immune cell regulation. As stated by Hashizume et al. [16], the quantity of circulating DADS might be adjusted absolute numbers of lymphocytes, leukocytes, and monocytes, as well as their dosage and methods that rely on the passage of time. In most cases, immune cells become active receptors inside the cell and send signals to the harmful stimuli. To begin, the cell signalling mechanism involving the nuclear factor kappa B (NF- κ B). The results of a study results demonstrated that DADS suppressed the progression of cerulein-induced inflammation of the pancreas and the resulting lung damage in mice by dampening NF- κ B p65 transcriptional activity and deterioration of IB [14], findings that were in line with in contrast to the results of earlier studies [17, 18].

As stated in Section 3.2, Antioxidant Capacity. Tissue damage caused by reactive oxygen species can be avoided, mitigated, or repaired with the help of antioxidants (ROS). There have been a number of Antioxidant effects of DADS have been studied extensively. characteristics [9, 28-30]. There is an immediate impact on reactive oxygen species (ROS) This was discovered in an in vitro experiment showing that DADS mitigated deoxycholic acid-induced reactive oxygen species (ROS) levels in Barrett's epithelial cells within the usable window of concentration [31]. Another Research demonstrated that DADS significantly decreased Percentages of reactive oxygen species (ROS) in IL-1-treated bone marrow mesenchymal embryonic cells [17] Nonetheless, research by Filomeni et al. [32] neuroblastoma cells were subjected to oxidative stress after being exposed to DADS. SHSY5Y cells, in line with the results of a research on cells from patients with lung cancer [33]. Together with the other sulfur-containing chemicals found in garlic, for instance diallyl trisulfide (DATS), which triggered the apoptosis resulting from an increase in reactive oxygen species (ROS) in human breast cancer cells and blocked its effects in high-glucose conditions cardiac muscle cells (cardiomyocytes) by decreasing reactive oxygen species (ROS) generation [34, 35]. There might be explanations for the inconsistencies in these research, including tumor-cell-specificity and treatment-modality variants In each trial, researchers used a different dose of DADS. Research into Treatment with 20 MDADS was shown to be neuroprotective in PC12 neuronal cells. had no observable impact on cellular function. That said, the membrane lipid peroxidation and amounts of free radicals rose noticeably after treatment with higher than 50 mM concentrations. Also, the number of the potential for cytotoxicity when 100 M DADS was treatment given to these cells [36]./e The findings of this corresponding to what was shown in the N18D3 neuron cell line [37].

Antimicrobial Activity

Antibacterial Activity, to put it in its drier form. Antibiotic resistance has emerged as a critical public health issue. Some people use garlic as a supplemental or alternative treatment for due to their potent antibacterial effects, medicines [44, 45]. Research suggests that garlic extracts may reduce the strength of *Pseudomonas aeruginosa* biofilms and make them receptive to phagocytosis and streptomycin by white blood cells that have several different types of nuclei (or "lobes") [46]. As it turns out DADS decreased virulence factor production, according to studies. features, such as elastase, pyocyanin, and swarming motility, the deactivation of a virulence factor in *Pseudomonas aeruginosa* DNA sequences involved in quorum sensing (QS) [47-49]. The expression of luxI and luxR genes was shown to be suppressed in *Hafnia alvei* H4 due to the anti-QS impact of DADS [50]. QS modulates these processes, although the mechanisms by which this occurs are not well understood. functions are still a mystery. Some studies have shown that DADS can protect Diabetic patients with MRSA (methicillin-resistant *Staphylococcus aureus*)

infections mice [51], prevent *Escherichia coli* from expanding and multiplying as an used in conjunction with gentamicin [52, 53], inhibits the both in vitro and in vivo against *Helicobacter pylori* [54, 55], and the pathogenicity of commonly isolated bacteria may be reduced. due to a problem with their ears [56]. What's more, a number of recent DADS has been shown to have regulatory effects on the small intestine flora. A byproduct of DADS processing is H₂S gas. inhibited or counteracted the effects of naproxen on structure of the microbiota in the gut [57]. If the research in which live animals were given a little amount of DADS to see what would happen. *Bacteroides* levels in mice who eat a typical diet firmicutes rose, but coliforms decreased, in the intestines [58].

Anti fungal Activity, Section 3.3.2.

In order to determine whether DADS has an antifungal effect, Alam et al. [59] gave it to mice with a *Candida albicans* infection. In their research, they discovered that the lysosomal The secretion was drastically reduced once DADS was created. yeast protease and phospholipase from *Candida albicans* and promoted longer life spans for infected animal hosts. Researchers found that DADS might slow the spread of *Aspergillus. toxigenic versicolor* and its byproducts [60].

DADS's antiviral action was originally described in 1993;

According to these findings, DADS slowed the growth of HIV-1 infected cells [61]. And moreover DADS was able to reduce inflammation and boost antioxidant levels. dengue virus research has shown that treating symptoms and the disease's degree of seriousness [62]. According to recent studies, garlic suggested as a possible treatment for COVID- On the basis of the results of multiple preclinical and clinical studies, research [63, 64]. Using a molecular docking analysis, garlic The essential oil has a significant inhibitory impact on SARSCoV-. 2 [65, 66]. Whether or not DADS has a role in garlic's ability to fight SARS-CoV-2, and The research gap calls for more investigation.

Detoxification

DADS has been proven in a number of studies [4] to protect organs against the toxicity of a variety of chemicals. One way in which DADS might help save money is through medicines such triglycerides [67], lessen the hearing loss that might result from it harmful effects of gentamicin and cisplatin [67-69], the liver damage caused by carbon tetra chloride bleed [18, 70], and stop the bleeding from a cystitis caused by treatment with cyclophosphamide in rats [71, 72], and a reduction in cyclophosphamide- chemically induced developmental toxicity [73], and significantly counteract the loss in renal function caused by methotrexate renal function decline, and the resulting damage [74].

Consuming garlic has been shown to significantly lower risk factors for cardiovascular disease [3, 84, 85].

The available data suggest that DADS plays a pivotal part in the heart-healthy benefits showing off the angiogenesis-blocking properties possessed by garlic. Anaphylaxis amines in the diet (DADS) substantially suppressed the angiogenic cell differentiation in endothelial tissues via dampening activation secretion of MMPs and other matrix metalloproteinases Endothelial morphogenesis and the role of tissue inhibitor of metalloproteinase-1 [86, 87]. Furthermore, DADS was shown to successfully suppress the production and transcription of factors in HL-60 cells over time and vascular endothelial growth factors dosage-dependent ways [88, 89]. mounting proof implications for the role of connections and gap junctions with regards to heart disease and stroke [90]. This DADS variant was found to increase gap-junctional intercellular communication in rat liver epithelial cells. cell-to-cell-communication-regulatory mechanisms of vascular smooth muscle multiplication and a marked uptick in the expression of connection 43, It is crucial to keeping everything running smoothly improvement in vascular function [91, 92]. In addition, DADS is a productive agent that may protect density lipoprotein from atherosclerotic damage.to protect low-density lipoprotein (LDL) against oxidation and glycation

[93, 94]. As an added bonus, DADS shielded endothelium cells against oxidised damage caused by oxidised LDL (ox-LDL).endothelial nitric oxide synthase (eNOS) activation by ox-LDL [95].

Anticancer Activity

The anti-invasive and anti-migratory effects of DADS in cancer cells have been connected to an increase in tight junctions, with a dampening of MMP activity [113, 114]. Steady rises in Resistance measured across the epithelium suggests DADS is present. improved cell-to-cell adhesion in human prostate cancer When tested, DADS was shown to prevent both migration and invasion (see [113]). via suppressing expression in human colon carcinoma 205 cells the MMPs (MMP-9, MMP-2, and MMP-7) [115]. Additional Assessment showed that DADS had a negative impact on MMPs controlled by the PI3K/Akt and NF- κ B pathways [116]. DADS has been proven to decrease tumour necrosis factor- α motif chemokine ligand 2 is released in response to, leading to Keeping cancer from spreading by preventing monocyte recruitment invasion of malignant cells [117, 118]. suppressing the metaplastic change from epithelial to mesenchymal Exploring the role of (EMT) in tumour metastasis is a current area of interest. C3 botulinum toxin substrate (Rac)-1 inhibition in tumour cells, whereas -catenin expression has been shown to suppress EMT [119]. Su et al. [120] found that DADS inhibited Rac1, -catenin, p21 activated kinase, and p53 function. 1, and Rho kinase-1, which ultimately prevents gastric development, invasion, and spread of cancer cells.

Controlling the Breakdown of the Cell Cycle.

DADS's capacity to decrease the cell ratio in the G1 phase and raise the cell ratio in the S phase was shown to be responsible for its anti-tumor effects. cells in the G2/M ratio [127]. After going through therapy with Increases in DADS led to a rise in the percentage of cells in the S phase and M phase, respectively. intensity, and length of exposure. Additional Molecular Statistical testing revealed that cyclin B1 (a cell cycle regulator) levels were significantly cells in the cell cycle (cdc) 25C, cdc2, and phosphorylated-cdc2 proteins could have been involved in preventing the G2/M phase transition. phase in esophageal squamous cell carcinoma patients treated with DADS cells [128]. Researchers have shown that DADS raised the level of p21 and p53 mRNA and protein in cancer cells and induced cell-cycle arrest and death by activating the p53/p21 signalling pathway [128, 129]. An earlier research shown that DADS has the potential to inhibit Histone acetylation was also linked to the cell cycle. [130]. Research elucidated that DADS triggered an acetylation of histones H3 and H4 in the CDKN1A gene increases promoter, which results in a rise in CDKN1A expression. protein levels of p21WAF1 and gene expression [131]. Moreover, DADS inhibited DNA damage response activation during the G2/M phase. Mec1 (ATR) and Tel1 (ATM) checkpoints. the efficiency of by preventing DNA from being repaired cancer treatments based on DNA damage [132].

Regulation of Metabolism

Controlling Blood Glucose Levels. Dose-dependent elevations in blood glucose concentration and free fatty acid levels have been seen in many in vivo investigations involving rats treated with DADS included. These results imply that DADS has an effect on glucose. biochemistry [161]. On the other hand, a different research found that Effects on glycemic control were similar between garlic oil and DADS, although garlic oil was more effective. suppression of diabetes-related complications in streptozotocin-treated rats [162]. In this way, DADS has very precise impacts on glucose metabolism, In order to maintain good health and prevent complications from diabetes,

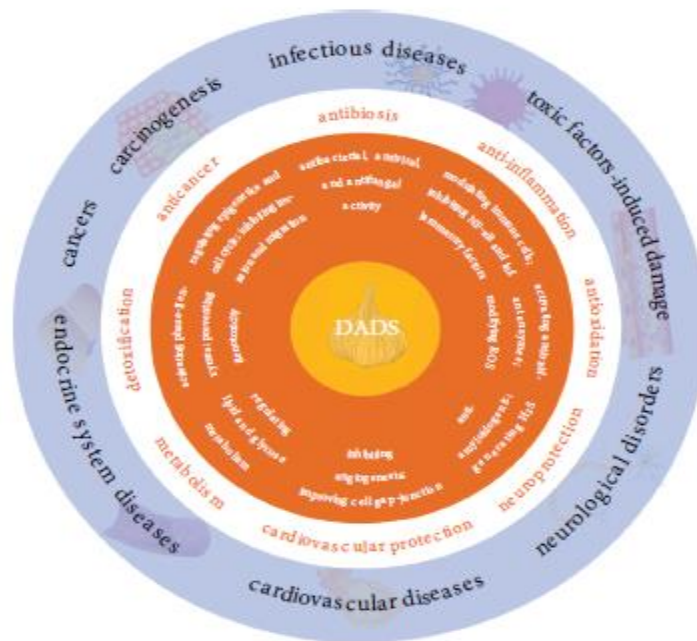


Figure 2: Overview of the biological functions of DADS.

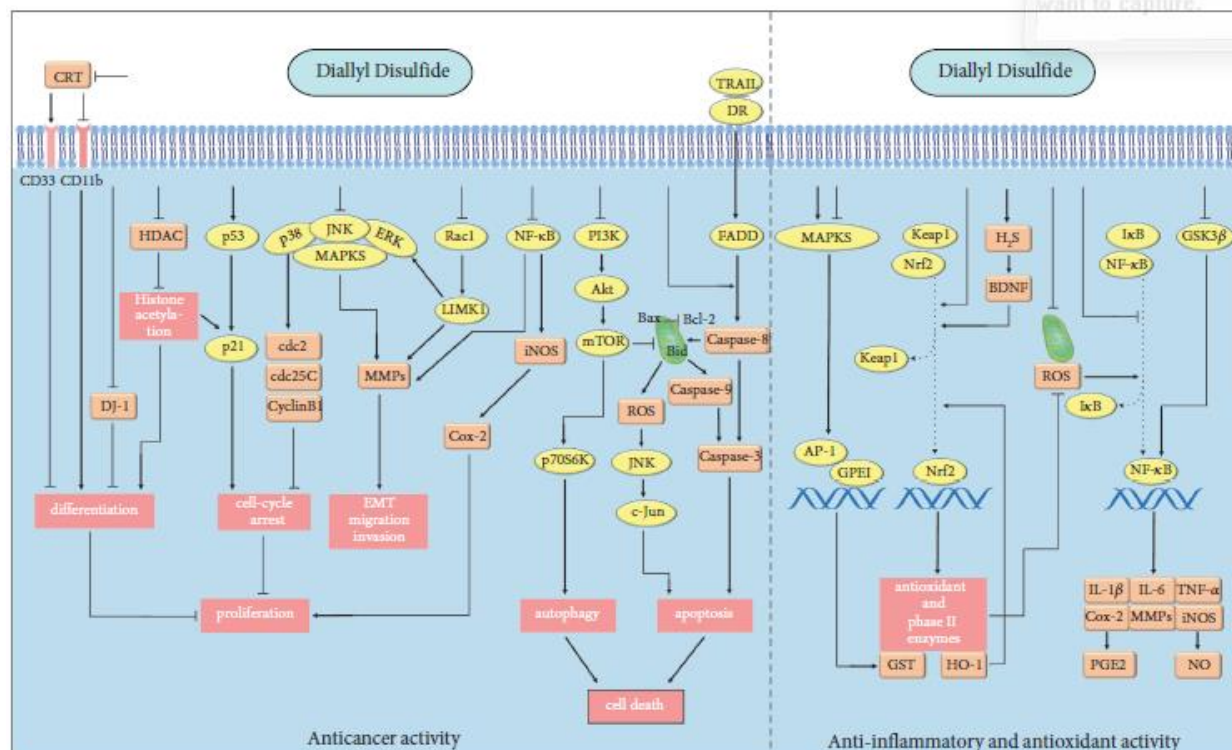


Figure 3: Signaling pathways affected by DADS.

be explained in further detail. Furthermore, DADS was shown to block the CD44/pyruvate kinase M2/AMPK pathway [163], which in turn suppressed glucose metabolism of breast cancer stem cells.

Controlling Fat Metabolism (3.8.2) Reports claim

Lipid metabolism may be controlled by DADS via (a) sterol Protein-1c, apolipoprotein A1, and Regulatory Element-Binding Protein. FGF21, and cyclin-dependent kinase inhibitors; (b) reducing lipotoxicity through CREB-H and FGF21 in part through elevating the expression of peroxisome proliferator-activated receptor- blocking stearyl coenzyme activity The Desaturase enzyme-1; (c) markedly suppressing lipid peroxidation through control of MDA and SOD [164–166]. The lipid has also been linked to potential impact on health, DADS's ability to regulate metabolism has shown benefits for the liver (hepatoprotective effects) [3]. Moreover, DADS has the potential to presupposition of the inflammatory response caused by monocyte chemo attractant protein-1 and the accumulation or activation of macrophages in enrichment adipose tissue. extra weight [167].

3.9, Various Other Effects. The dose of DADS that was taken orally increased up when compared natural antibody activity in chicken serum [168]. Chromosome aberration was also produced by DADS, and DNA replication in the ovary of the Chinese hamster involves the exchange of sister chromatic. In addition to controlling iron homeostasis, DADS [169] may Changes in Ferrite and Transferral Receptor Expression genes in cultured and animal hepatocytes [170] (see Figure 2).

Conclusion

The organic sulphur compound DADS has widespread culinary use. Recent studies have shown that DADS may be an effective medication for the treatment of drug therapy for several disorders, this study aimed to comprehensively learn how DADS helps the body and what it does biologically, briefly describe the chemical processes at play physiologic roles of DADS may be mediated The first group consists of the preventative measures taken for typical tissues and its disease-blocking inhibitory impact. /e anti inflammatory DADS' anti-oxidant properties also play a key role in order to keep tissues (including the nervous system and blood vessels) at a constant temperature and pressure, safeguarding, metabolic balancing, and combating pathogens There are connections between anti-inflammatory along with oxidative stress protection through NF-kappa B and reactive oxygen species essential parts in the plot or cast. The Biological Processes Are Affected By DADS internal and external characteristics of cancer cells mechanisms. Since this is the case, DADS has a major impact on effects that work against cancer, including induction of apoptosis and autotroph as well as dissimilarity. Moreover, DADS has room for growth. chemotherapy's effectiveness and mitigate its side effects drugs. Reducing inflammation and protecting cells using antioxidants, among others, such as AP-1, JNK, and STAT, play crucial parts in DADS's biological processes. Pathways related to apoptosis and autotroph include Contributions from PI3K, Akt, mTOR, MAPKs, Bcl-2, and Bax are also present. to DADS's role in fighting cancer. The signalling is especially Comparable DADS-affected pathways exist between normally developing cellular components of tissue and malignant tumours. It's important to note that various doses and Different administration strategies may have various outcomes, This needs more testing to confirm See also: Figure 3.

DADS plays a key role in garlic's efficacy when used by humans. It's important to keep in mind that certain major problems still require fixing before clinical studies of DADS. /e First, DADS is has a high rate of metabolism after ingested, and availability issues [6]; second, the technical challenges DADS processing tasks, including categorization, enhancement, plus the development of effective transport mechanisms [174, 175]. The pharmaceutical investigations of Improvements might be made to DADS and its byproducts. Currently, many nations are exploring new approaches to disease prevention and treatment. COVID-19, a virus that has had a devastating effect on the world economy, wellbeing of the people and the economy. Plant material that is easily accessible items could be an excellent place to begin the search for medicines with therapeutic potential. Science devoted to the study of life DADS's potential to perform its role might give us cause for optimism.

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