Hydrazine Sulfate (PDQ®): Integrative, alternative, and complementary therapies - Health Professional Information [NCI]

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Overview

NOTE: The information in this summary is no longer being updated and is provided for reference purposes only.

This cancer information summary provides an overview of the use of hydrazine sulfate as a treatment for people with cancer. The summary includes a brief history of hydrazine sulfate research, results of clinical trials, and possible side effects of hydrazine sulfate use.

This summary contains the following key information:

- Hydrazine sulfate is a chemical that has been studied as a treatment for cancer and as a treatment for the body wasting (i.e., cachexia) associated with this disease.
- It has been claimed that hydrazine sulfate limits the ability of tumors to obtain glucose, which is a type of sugar used by cells to create energy.
- Hydrazine sulfate has been shown to increase the incidence of lung, liver, and breast tumors in laboratory animals, suggesting it causes cancer.
- There is only limited evidence from animal studies that hydrazine sulfate has anticancer activity.
- Hydrazine sulfate has shown no anticancer activity in randomized clinical trials, and data concerning its effectiveness in treating cancer-related cachexia are inconclusive.
- Hydrazine sulfate has been marketed in the United States as a dietary supplement or a nutraceutical by some companies; however, its use as an anticancer drug outside of clinical trials has not been approved by the U.S. Food and Drug Administration.

Many of the medical and scientific terms used in the summary are hypertext linked (at first use in each section) to the NCI Dictionary of Cancer Terms, which is oriented toward nonexperts. When a linked term is clicked, a definition will appear in a separate window.

Reference citations in some PDQ cancer information summaries may include links to external websites that are operated by individuals or organizations for the purpose of marketing or advocating the use of specific treatments or products. These reference
Hydrazine sulfate has been investigated as an anticancer treatment for more than 30 years. It has been studied in combination with established treatments as a chemotherapy agent. It has also been studied as a treatment for cancer-related anorexia (loss of appetite) and cachexia (loss of muscle mass and body weight). Similar to other hydrazine compounds, it has a core chemical structure that consists of two nitrogen atoms and four hydrogen atoms.

Hydrazine sulfate is marketed in the United States as a dietary supplement /nutraceutical by some companies. In the United States, dietary supplements are regulated as foods, not drugs. Therefore, premarket evaluation and approval by the U.S. Food and Drug Administration (FDA) are not required unless specific disease prevention or treatment claims are made. The FDA can, however, remove from the market dietary supplements that it deems unsafe. The use of hydrazine sulfate as an anticancer treatment outside of clinical trials has not been approved by the FDA. The FDA has not approved the use of hydrazine sulfate for any medical condition.

To conduct clinical drug research in the United States, researchers must file an Investigational New Drug (IND) application with the FDA. To date, the FDA has granted IND status to at least three groups of researchers to study hydrazine sulfate as a treatment for cancer.[1,2,3]

In animal studies, hydrazine sulfate has been added to the drinking water or the food supply, or it has been given by injection. In clinical trials involving cancer patients, hydrazine sulfate has been administered in pills or capsules.[4] In the clinical studies conducted thus far, the dose and the duration of hydrazine sulfate administration have varied.

References:


History

During the past 90 years, hydrazine compounds have been studied in animal cells grown in the laboratory, in live animals, and in humans.[1] More than 400 hydrazine analogs (related compounds) have been screened for their ability to kill tumors. In 1996, a retrospective review of scientific studies in which the anticancer activity of hydrazine analogs was investigated found that 65 of 82 evaluated compounds showed some anticancer activity in xenograft models (tumor cells of one species transplanted to another species).[1] Of the 82 tested compounds, seven showed activity against human tumor cells and were, therefore, selected for further testing in pilot studies and phase I clinical trials. Among these seven compounds, only procarbazine (a methylhydrazine derivative, also called ibenzmethyzin or natulan) completed preliminary testing in humans.

Procarbazine exhibited anticancer activity in patients with Hodgkin disease, melanoma, and lung carcinoma, and it was ultimately used in several first-line treatment regimens in the 1960s.[1,2,3] In view of the initial success with procarbazine, hydrazine sulfate, which is similar in chemical composition, was investigated for anticancer activity beginning in the 1970s. During this period, investigation of hydrazine sulfate as a treatment for cancer-related cachexia was also initiated. Research on hydrazine sulfate both as a single agent and in combination with standard chemotherapy regimens continued through the mid-1990s.[4,5,6,7,8,9]

Although it was proposed in the early 1900s that hydrazine compounds are toxic to animals and to humans, they have been administered as antidepressant (e.g., iproniazid), chemotherapy (e.g., procarbazine), and antituberculosis (e.g., isoniazid) drugs. In addition to medicinal uses, hydrazine compounds have been used in industry and agriculture as components of rocket fuel, as herbicides, and as antioxidants in boiler and cooling-tower water.[10,11,12] Many scientists consider hydrazine sulfate and other hydrazine analogs to be cancer-causing agents, and they have expressed concern about the safety of these compounds.[1,10,12,13,14,15,16,17,18,19,20,21] In the 10th Report on Carcinogens, hydrazine and hydrazine sulfate are listed by the U.S. Department of Health and Human Services' National Toxicology Program as "reasonably anticipated to be human carcinogens."[22] When the antituberculosis drug isoniazid and hydrazine antidepressants are combined with purified DNA in the laboratory, they produce hydrogen peroxide and free radicals that can damage the DNA.[14,17,23] Hydrazine compounds
have been reported to cause mutations and chromosome damage in bacteria and in plant and animal cells.[10]

Two mechanisms of action have been proposed for hydrazine sulfate to explain its potential antitumor and anticachexia properties. Both mechanisms involve the utilization of glucose (sugar), which tumors require as a main source of energy for growth. In one proposed mechanism, hydrazine sulfate blocks gluconeogenesis through inhibition of the enzyme phosphoenolpyruvate carboxykinase.[24,25,26,27,28,29] Gluconeogenesis is a process by which extra glucose (in addition to that obtained from the diet) can be formed in the liver and the kidneys from the breakdown products of sugars, lipids (fats), and proteins. It has been suggested that cachexia occurs because the body must use increasing amounts of energy and other resources, including its own protein, to meet the demand for glucose by tumors.[24,25,26,27,28,29,30] Blocking gluconeogenesis and interfering with the supply of nutrients to tumors has been proposed as one way to inhibit tumor growth and to prevent cachexia.

In the second proposed mechanism, hydrazine sulfate inhibits tumor necrosis factor (TNF)-alpha activity.[31,32,33,34] TNF-alpha, which is also known as cachectin, is one of a number of substances normally produced by white blood cells in the body in response to infection by microorganisms and in response to other stimuli such as tissue damage.[31,32,34,35,36] Higher-than-normal TNF-alpha production has been observed in white blood cells obtained from cancer patients. It has been suggested that higher-than-normal levels of TNF-alpha can cause the anorexia, increased energy expenditure, and increased muscle protein breakdown seen in cancer patients.[31,35,36,37] Some of the muscle protein breakdown products would become available for gluconeogenesis. Inhibition of TNF-alpha activity might, therefore, inhibit tumor growth and prevent cachexia.

References:

Laboratory / Animal / Preclinical Studies

Hydrazine compounds have been studied both as potential anticancer drugs and as cancer-causing agents. Early studies of hydrazines, including hydrazine sulfate, were conducted to determine whether these compounds could cause cancer in healthy laboratory animals.[1,2,3,4,5,6,7,8,9,10,11] Substantial increases in tumor incidence were observed in most studies that used rats, mice, or hamsters.[1,2,3,4,5,7,8,9] Hydrazine administration was associated with increases in lung, liver, and breast tumors in rats,[2,5] increases in lung and liver tumors in mice,[1,2,3,4,8] and increases in liver tumors in hamsters.[7,9] In one study, hydrazine sulfate increased the incidence of lung tumors in both males and females of the mouse strain C3H, but reduced the incidence of breast adenocarcinomas in C3H females.[3]

Animal studies of hydrazine sulfate as a treatment for cancer have investigated this compound as a single agent and in combination with established chemotherapy drugs.[12,13,14,15,16,17,18] In studies conducted in one laboratory, hydrazine sulfate alone was found to cause dose-dependent inhibition of tumor growth in rats bearing
Walker 256 carcinosarcoma or Murphy-Sturm lymphosarcoma tumors and in mice bearing B-16 melanoma tumors.[12,13,14] Hydrazine sulfate alone had no effect on solid tumors formed from L-1210 leukemia cells in mice.[13] In work performed in another laboratory, hydrazine sulfate alone inhibited the growth of FBCa bladder cancer tumors in one of two experiments in rats, but it had no effect on the growth of 13762NF mammary adenocarcinomas in rats.[17] Findings from a third laboratory demonstrated that hydrazine sulfate alone had no effect on the growth of Dunning prostate cancer tumors in rats.[18]

It is important to note that the best tumor responses to hydrazine sulfate as a single agent (i.e., tumor reductions of approximately 50% or more) were accompanied by substantial losses in animal body weight.[12,13,14] This finding appears to be inconsistent with the proposed use of hydrazine sulfate as an anticachexia agent.

In other experiments, hydrazine sulfate was combined with individual chemotherapy drugs (cyclophosphamide, mitomycin C, methotrexate, bleomycin, fluorouracil [5-FU], carmustine [BCNU], or neocarzinostatin) to treat Walker 256 carcinosarcoma tumors in rats and solid L-1210 leukemia tumors in mice.[13,14,15] For both tumor types, enhanced anticancer effects were observed. In the experiments with L-1210 tumors, cyclophosphamide and mitomycin C were more effective when combined with hydrazine sulfate than they were when used alone.[13] As indicated previously, hydrazine sulfate alone had no effect against solid L-1210 tumors.[13]

Addition of the drug clofibrate to the hydrazine sulfate plus chemotherapy drug combinations was reported to produce even greater antitumor effects.[15] Clofibrate lowers blood lipid levels and has the potential to inhibit gluconeogenesis by limiting the availability of lipid breakdown products for the synthesis of glucose. This three drug treatment regimen, however, was tested against only one type of tumor (Walker 256 carcinosarcomas in rats).[15]

Hydrazine sulfate has also been tested in combination with drugs that affect the uptake of glucose by cells. The combination of hydrazine sulfate and phloretin, a drug that blocks glucose uptake, showed greater activity against FBCa bladder cancer tumors in rats than was found with hydrazine sulfate alone; however, this combination did not exhibit enhanced antitumor activity against 13762NF mammary adenocarcinomas in rats.[17] When hydrazine sulfate was combined with the drug phloridzin, which is similar to phloretin, using the same two tumor models, no increase in anticancer activity was observed.[17] When hydrazine sulfate was combined with the drug phenformin, which increases glucose uptake by cells (and lowers blood glucose levels), enhanced antitumor activity against Walker 256 carcinosarcomas in rats was observed.[16]
In the 1980s, the National Cancer Institute (NCI) conducted preclinical studies of hydrazine sulfate as a single agent, using many of the animal tumor models described above. With the exception of borderline activity against Walker 256 carcinosarcomas in rats, no evidence of antitumor activity was found.[19] In view of these results, NCI recommended against further evaluation of hydrazine sulfate as an anticancer agent.[19] However, clinical investigation of this compound continued, largely because of its potential as a treatment for cancer-related anorexia and cachexia.

References:

Human / Clinical Studies

Most of the information presented here is summarized in a table located at the end of this section.

Hydrazine sulfate has been studied extensively in patients with advanced cancer. These studies have evaluated the following: a) tumor response and/or survival among patients with various types of cancer,[1,2,3,4,5,6,7,8,9,10,11,12,13] b) changes in body weight,[1,2,3,4,5,6,8,10,11,12,14] c) carefully measured quality of life,[4,5,6,15] and d) changes in nutritional or metabolic status.[1,4,12,13,16,17] Clinical studies of hydrazine sulfate have been funded by a pharmaceutical company,[3] the Russian government,[7,9,10,18] and by grants from the National Cancer Institute (NCI).[1,2,4,5,6,8,11,12,15,16] They have also been sponsored by the North Central Cancer Treatment Group (NCCTG) [5,6] and the Cancer and Leukemia Group B (CALGB).[4,15]

The first clinical tests of hydrazine sulfate as a treatment for cancer were conducted in the mid-1970s by a pharmaceutical company.[3] In an uncontrolled study of 158 patients with advanced disease, it was found that 45 of 84 evaluable patients had subjective improvements (i.e., the patients reported an increase in appetite, a decrease in weight loss, an increase in strength, or a decrease in pain) and that 14 had objective improvements (i.e., there was measurable tumor regression, stable disease, or improvement in a cancer-related disorder) in response to treatment with hydrazine sulfate. Among the patients with objective responses, two had long-term (17 and 18 months) stabilization of their disease and seven had measurable tumor regression, although the extent and duration of these regressions were not specified. Major weaknesses of this study included the absence of a control (i.e., comparison) group and the fact that 74 of the 158 initially recruited patients could not be evaluated because of poor prognosis, missing documentation, insufficient duration of treatment, and/or concurrent therapy (i.e., therapy given at the same time) with other anticancer drugs.[3]
In 1976, Russian investigators reported findings from 95 patients with advanced cancer who had been treated with hydrazine sulfate after all previous therapy (surgery, chemotherapy, and/or radiation therapy) had failed. Three partial responses (i.e., reductions in tumor size of greater than 50% observed for a period of 4 weeks or more) and no complete responses were noted after 1 to 5 months of treatment. Tumor regressions of 50% or less and stable disease (i.e., cessation of tumor growth for a period of 1.5 to 2.0 months or more) were reported for 16 and 20 patients, respectively.

In 1981, the same investigators published findings from 225 patients with advanced disease who had been treated with hydrazine sulfate after all previous therapy had failed. It appears that the 225 patients described in this second report included the 95 patients described in the first report. Partial responses and stable disease were reported for 4 and 95 patients, respectively, after 1 to 6 months of treatment. No patient experienced a complete response. Subjective improvements in appetite, weight stabilization or gain, pain, fever, breathing, and/or mental outlook were reported by 147 patients.

In 1995, the same Russian investigators published findings from 740 patients with advanced cancer. Once again, it appears that 225 of these 740 patients were described in the earlier reports. Partial responses and stable disease were reported for 25 and 263 patients, respectively. Complete responses were noted for six patients. Subjective improvements in cancer-related symptoms were reported by 344 patients.

In 1994, the same investigators reported findings from a clinical series involving 46 patients with malignant brain tumors (38 with glioblastomas, four with astrocytomas, and four with meningiomas) and six patients with benign brain tumors. These patients were not described in the other reports. All patients in this series appear to have been treated with surgery in addition to hydrazine sulfate therapy, and at least some of the patients were also treated with radiation therapy. Complete or partial regression of neurologic symptoms (e.g., seizures, headaches, sensory and motor disorders, and hallucinations) was reported for 73% of the patients. In addition, longer-than-average survival was reported for most patients. Among the patients with glioblastomas, the increase in average survival time was from 6 months to more than 13 months.

Evaluation of the findings from these Russian clinical series is made difficult by the limited information provided about the patients and their treatment histories. In addition, insufficient information was given about study design and methodology. The absence of control groups; the receipt of prior or concurrent surgery, chemotherapy, and/or radiation therapy by all patients; and the reliance on subjective measures of quality of life are major study weaknesses. Therefore, it is difficult to ascribe any of the positive findings to treatment with hydrazine sulfate. In contrast with the previously described clinical series, three NCI-funded clinical series found no complete responses or partial
responses among a total of 79 patients treated with hydrazine sulfate.\[2,8,11] In addition, only temporary, minor improvements in appetite, pain, and weight stabilization or gain were reported by the patients in these series. A weakness in these three clinical series was the absence of control groups.

Findings from four placebo-controlled, randomized clinical trials, however, also fail to support the effectiveness of hydrazine sulfate as a cancer treatment in humans.\[1,4,5,6,15] In these trials, survival,\[1,4,5,6,15] objective tumor response,\[1,4,15] and carefully measured quality of life \[4,5,6,15] were major endpoints.

One of the trials involved 65 patients with advanced nonsmall cell lung cancer and examined the effects of hydrazine sulfate on survival and nutritional status.\[1] In this trial, patients received either hydrazine sulfate or placebo in addition to a multiple-drug chemotherapy regimen. When all patients were evaluated, no improvement in survival was found with hydrazine sulfate therapy. In addition, no differences were noted in objective tumor response between the hydrazine sulfate group and the placebo group. However, on the basis of caloric intake and the maintenance of serum albumin levels, the nutritional status of the patients in the hydrazine sulfate group was judged better than that of the patients in the placebo group. However, the moderate increases in body weight associated with hydrazine sulfate use did not achieve statistical significance.

A CALGB-sponsored trial also evaluated the use of hydrazine sulfate as a treatment for patients with advanced nonsmall cell lung cancer.\[4,15] In this trial, 266 patients received either hydrazine sulfate or placebo in addition to a multiple-drug chemotherapy regimen. No differences in survival, objective tumor response, anorexia, weight gain or loss, or nutritional status were observed between the hydrazine sulfate group and the placebo group. However, the quality of life of the patients who received hydrazine sulfate was found to be statistically significantly worse than that of the patients who received placebo.

The use of hydrazine sulfate as a treatment for patients with nonsmall cell lung cancer was also evaluated in an NCCTG-sponsored trial.\[6] In this trial, 243 patients were randomly assigned to receive either hydrazine sulfate or placebo in addition to a multiple-drug chemotherapy regimen. No statistically significant differences were found between the hydrazine sulfate group and the placebo group with respect to either survival or quality of life.

Another NCCTG-sponsored trial tested hydrazine sulfate alone versus placebo in the treatment of 127 patients with metastatic colorectal cancer.\[5] In this trial, the patients who received hydrazine sulfate had, on average, shorter survival than the patients who received placebo, a finding that was statistically significant. There were no statistically significant differences between the hydrazine sulfate group and the placebo group with respect to weight gain or loss, anorexia, or quality of life.
Four other clinical trials did find some objective evidence of benefit with hydrazine sulfate therapy.[12,13,16,17] These trials had either nutritional status or metabolic status as the primary endpoint. In a placebo-controlled, randomized trial involving 38 patients with advanced disease, hydrazine sulfate was found to improve the abnormal glucose metabolism seen in cancer patients.[13] In another placebo-controlled, randomized trial that involved 101 patients with advanced cancer and weight loss, the use of hydrazine sulfate was associated with statistically significant improvements in appetite and either weight increase or weight maintenance.[12] However, the higher average caloric intake observed in this study for patients treated with hydrazine sulfate compared with patients treated with placebo was not statistically significant.[12] Two other clinical studies involving a total of 34 patients with either lung cancer or colon cancer found that hydrazine sulfate was able to reduce the body protein breakdown associated with cancer cachexia.[16,17] In view of the totality of evidence, the overall importance of the findings from these four clinical trials is not clear.

A search of the PDQ clinical trials database indicates that no clinical trials of hydrazine sulfate as a therapy for cancer are being conducted at this time.
### Studies of Hydrazine Sulfate in Which Therapeutic Benefit Was Assessed

<table>
<thead>
<tr>
<th>Reference Citation(s)</th>
<th>Type of Study</th>
<th>Type of Cancer</th>
<th>No. of Patients: Enrolled; Treated; Control</th>
<th>Strongest Benefit Reported</th>
<th>Concurrent Therapy</th>
<th>Level of Evidence Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>[1]</td>
<td>Randomized clinical trial</td>
<td>Advanced nonsmall cell lung</td>
<td>65; 32; 33, placebo</td>
<td>None</td>
<td>Yes</td>
<td>1iA</td>
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<tr>
<td>[4,15]</td>
<td>Randomized clinical trial</td>
<td>Advanced nonsmall cell lung</td>
<td>291; 135; 131, placebo</td>
<td>None</td>
<td>Yes</td>
<td>1iA</td>
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<tr>
<td>[5]</td>
<td>Randomized clinical trial</td>
<td>Advanced colorectal</td>
<td>128; 63; 64, placebo</td>
<td>None</td>
<td>No</td>
<td>1iA</td>
</tr>
<tr>
<td>[6]</td>
<td>Randomized clinical trial</td>
<td>Advanced nonsmall cell lung</td>
<td>243; 119; 118, placebo</td>
<td>None</td>
<td>Yes</td>
<td>1iA</td>
</tr>
<tr>
<td>[2]</td>
<td>Nonconsecutive case series</td>
<td>Various advanced</td>
<td>25; 25; None</td>
<td>Slight regression of some metastatic</td>
<td>No</td>
<td>3iiiDiii</td>
</tr>
</tbody>
</table>

No. = number.

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### Notes:

- **a** See text for more details.
- **b** Number of patients treated plus number of control patients may not equal number of patients enrolled; number of patients enrolled = number of patients initially recruited/considered by the researchers who conducted a study; number of patients treated = number of enrolled patients who were given the treatment being studied AND for whom results were reported; historical control subjects are not included in number of patients enrolled.
- **c** The strongest evidence reported that the treatment under study has anticancer activity or otherwise improves the well-being of cancer patients. See text and glossary for definition of terms.
- **d** Surgery, chemotherapy, or radiation therapy given/allowed at the same time as hydrazine sulfate treatment.
- **e** For information about levels of evidence analysis and an explanation of the level of evidence scores, see Levels of Evidence for Human Studies of Integrative, Alternative, and Complementary Therapies.
- **f** This study included six additional patients with benign brain tumors.
- **g** Insufficient information given to permit a level of evidence analysis.
<table>
<thead>
<tr>
<th>Reference Citation(s)</th>
<th>Type of Study</th>
<th>Type of Cancer</th>
<th>No. of Patients: Enrolled; Treated; Control</th>
<th>Strongest Benefit Reported&lt;sup&gt;c&lt;/sup&gt;</th>
<th>Concurrent Therapy&lt;sup&gt;d&lt;/sup&gt;</th>
<th>Level of Evidence Score&lt;sup&gt;e&lt;/sup&gt;</th>
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<td>[3]</td>
<td>Nonconsecutive case series</td>
<td>Various advanced</td>
<td>158; 84; None</td>
<td>Measurable tumor regression, 7 patients</td>
<td>Yes</td>
<td>3iiiDiii</td>
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<td>[7,9,10]</td>
<td>Nonconsecutive case series</td>
<td>Various advanced</td>
<td>763; 740; None</td>
<td>Complete tumor regression, 6 patients</td>
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<td>3iiiDiii</td>
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<td>[8]</td>
<td>Nonconsecutive case series</td>
<td>Various advanced</td>
<td>25; 25; None</td>
<td>None</td>
<td>No</td>
<td>3iiiDiii</td>
</tr>
<tr>
<td>[11]</td>
<td>Nonconsecutive case series</td>
<td>Various advanced</td>
<td>32; 29; None</td>
<td>None</td>
<td>Unknown</td>
<td>3iiiDiii</td>
</tr>
</tbody>
</table>

No. = number.

<sup>a</sup> See text for more details.

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<table>
<thead>
<tr>
<th>Reference Citation(s)</th>
<th>Type of Study</th>
<th>Type of Cancer</th>
<th>No. of Patients: Enrolled; Treated; Control&lt;sup&gt;b&lt;/sup&gt;</th>
<th>Strongest Benefit Reported&lt;sup&gt;c&lt;/sup&gt;</th>
<th>Concurrent Therapy&lt;sup&gt;d&lt;/sup&gt;</th>
<th>Level of Evidence Score&lt;sup&gt;e&lt;/sup&gt;</th>
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<td>[12]</td>
<td>Nonconsecutive case series</td>
<td>Various advanced</td>
<td>101; 71; 30, placebo</td>
<td>Improved weight maintenance or gain, 41 hydrazine sulfate treated vs. 17 placebo-treated patients</td>
<td>Yes</td>
<td>3iiiDiii</td>
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<tr>
<td>[18]</td>
<td>Nonconsecutive case series</td>
<td>Glioblastoma, astrocytoma, or meningioma&lt;sup&gt;f&lt;/sup&gt;</td>
<td>465; 46; None</td>
<td>Improved survival, patients with glioblastoma</td>
<td>Yes</td>
<td>None&lt;sup&gt;g&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

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<sup>f</sup> This study included six additional patients with benign brain tumors.

<sup>g</sup> Insufficient information given to permit a level of evidence analysis.

References:


Adverse Effects

The side effects associated with hydrazine sulfate use have been mainly gastrointestinal and neurologic.\[1,2,3,4,5,6,7,8,9,10,11,12\] Nausea and/or vomiting, dizziness, and sensory and motor neuropathies have been reported.\[1,2,3,4,5,6,7,8,9,10,11,12\] The sensory and motor neuropathies have included paresthesias (abnormal touch sensations, such as burning or prickling, in the absence of external stimuli) of the upper and lower extremities (i.e., the arms and the legs, including the hands and the feet), polyneuritis (simultaneous inflammation of several peripheral nerves), and impaired fine motor function (e.g., an impaired ability to write).\[2,5,7,8,9\] Other side effects have included dry skin and/or itching, insomnia, and hypoglycemia.\[1,2,7,9\] One case of fatal liver and kidney failure and one case of severe encephalopathy (an injury to the brain) have been associated with the use of hydrazine sulfate.\[13,14\] The former case involved a man aged 55 years with squamous cell carcinoma of the maxillary sinus who purchased hydrazine sulfate from a source found on the Internet and proceeded to take it without medical advice or supervision. After 4 months he presented with evidence of renal and liver toxicity, which eventually resulted in death. This case highlights the danger of accessing materials and medical information on the Internet and proceeding with self-medication without seeking proper medical advice and supervision.\[15\]

The side effects of hydrazine sulfate have been described as mild to moderate in severity, and their incidence appears to have been low. Most side effects are reported to resolve when treatment is stopped. However, limited evidence from animal studies suggests that hydrazine sulfate is highly toxic when combined with either alcohol or barbiturates.\[16,17,18,19\]

References:

Summary of the Evidence for Hydrazine Sulfate

Several clinical case series conducted by Russian investigators have indicated that hydrazine sulfate has marginal anticancer activity, but these results are considered inconclusive due to the lack of control groups and insufficient information provided about study methodology. Well-controlled clinical studies conducted in the United States have shown no evidence of anticancer activity. In addition, evidence concerning the effectiveness of hydrazine sulfate as a treatment for cancer-related cachexia and anorexia is inconclusive. Furthermore, hydrazine sulfate has been shown to increase the incidence of several types of tumors in animals, and it has been classified as a potential...
carcinogen by the National Toxicology Program of the U.S. Department of Health and Human Services. The use of hydrazine sulfate as an anticancer drug outside the context of clinical trials has not been approved by the U.S. Food and Drug Administration and, thus, cannot be recommended.

Separate levels of evidence scores are assigned to qualifying human studies on the basis of statistical strength of the study design and scientific strength of the treatment outcomes (i.e., endpoints) measured. The resulting two scores are then combined to produce an overall score. For additional information about levels of evidence analysis, refer to Levels of Evidence for Human Studies of Integrative, Alternative, and Complementary Therapies.

**Changes to This Summary (04 / 12 / 2016)**

The PDQ cancer information summaries are reviewed regularly and updated as new information becomes available. This section describes the latest changes made to this summary as of the date above.

Editorial changes were made to this summary.

This summary is written and maintained by the PDQ Integrative, Alternative, and Complementary Therapies Editorial Board, which is editorially independent of NCI. The summary reflects an independent review of the literature and does not represent a policy statement of NCI or NIH. More information about summary policies and the role of the PDQ Editorial Boards in maintaining the PDQ summaries can be found on the About This PDQ Summary and PDQ® - NCI's Comprehensive Cancer Database pages.

**About This PDQ Summary**

**Purpose of This Summary**

This PDQ cancer information summary for health professionals provides comprehensive, peer-reviewed, evidence-based information about the use of hydrazine sulfate in the treatment of people with cancer. It is intended as a resource to inform and assist clinicians who care for cancer patients. It does not provide formal guidelines or recommendations for making health care decisions.

**Reviewers and Updates**

This summary is reviewed regularly and updated as necessary by the PDQ Integrative, Alternative, and Complementary Therapies Editorial Board, which is editorially independent of the National Cancer Institute (NCI). The summary reflects an independent
review of the literature and does not represent a policy statement of NCI or the National Institutes of Health (NIH).

Board members review recently published articles each month to determine whether an article should:

• be discussed at a meeting,
• be cited with text, or
• replace or update an existing article that is already cited.

Changes to the summaries are made through a consensus process in which Board members evaluate the strength of the evidence in the published articles and determine how the article should be included in the summary.

Any comments or questions about the summary content should be submitted to Cancer.gov through the NCI website's Email Us. Do not contact the individual Board Members with questions or comments about the summaries. Board members will not respond to individual inquiries.

**Levels of Evidence**

Some of the reference citations in this summary are accompanied by a level-of-evidence designation. These designations are intended to help readers assess the strength of the evidence supporting the use of specific interventions or approaches. The PDQ Integrative, Alternative, and Complementary Therapies Editorial Board uses a formal evidence ranking system in developing its level-of-evidence designations.

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