The in vivo genotoxic effects of sodium metabisulphite in bone marrow cells of rats.

Kayraldiz A, Topaktaş M.


Biology Department, Faculty of Arts and Sciences, University of Kahramanmaraş Sütçü Imam, Turkey. akayraldiz@ksu.edu.tr

This study is designed to investigate the genotoxic effect of sodium metabisulphite (SMB), which is used as an antimicrobial substance in foods on bone marrow cells of rats. Four different concentrations of SMB (250, 500, 750 and 1000 mg/kg body weight) were given rats (Rattus norvegicus var. albinos) for 6, 12 and 24 hours treatment period by intraperitoneal (IP) and gavage (GV) administrations. In this study, we found that intraperitoneal implement of SMB generally more effective increasing the percentage of abnormal cells and CA/cell in all concentrations and treatment period. In addition, mitotic index (MI) data of intraperitoneal injection are lower than gavage. It can be concluded that potential genotoxic effects of SMB by IP injection is higher than GV injection.

PMID: 17958310 [PubMed - indexed for

The genotoxic effect of potassium metabisulfite using chromosome aberration, sister chromatid exchange, micronucleus tests in human lymphocytes and chromosome aberration test in bone marrow cells of rats.

Yavuz-Kocaman A, Rencuzoquillari E, Ilia HB, Topaktas M.

Department of Biology, Natural and Applied Science Institute, Cukurova University, Adana, Turkey.

Potassium metabisulfite (PMB) is used as an antimicrobial substance in many kinds of foods. In the present study, the effects of PMB on chromosome aberrations (CAs), sister chromatid exchanges (SCEs), and micronucleus (MN) formation in human lymphocytes and as well as its effect on CAs in bone marrow cells of rats were investigated. The human lymphocytes were treated with 25, 50, 100, and 200
microg/ml of PMB for 24 and 48 hr. PMB was also intraperitoneally (ip) injected to the rats as a single dose of 150, 300, and 600 mg/kg body weight (b.w.) for 12 and 24 hr before sacrifice. PMB induced abnormalities such as structural and numerical (total) CAs, SCEs, and MN formations in a dose dependent manner in the lymphocytes of the 24- and 48-hr treatment periods. In addition, PMB showed a cytotoxic effect by decreasing the replication index (RI), mitotic index (MI) and nuclear division index (NDI) in a dose dependent manner in human lymphocytes. The compound induced CA as well and decreased the MI in bone marrow cells of rats. It might be concluded that PMB had a high genotoxic and cytotoxic risk.


Food additive-induced chronic pruritus: further evidence.

Asero R.


[Food additives as a cause of medical symptoms: relationship shown between sulfites and asthma and anaphylaxis; results of a literature review]

Reus KE, Houben GF, Stam M, Dubois AE.

Academisch Ziekenhuis, afd. Allergologie, Groningen.

OBJECTIVE: To determine if a causal connection exists between food additives and various medical complaints. DESIGN: Literature study. METHOD: Medline over the period January 1966-January 1999 was searched for articles on the following substances not containing protein and lactose: monosodium glutamate (MSG), sulfites, azo-dyes (tartrazine, sunset yellow, azorubin, amaranth, cochineal red), benzoates, sorbates, butylated hydroxyanisole/butylated hydroxytoluene (BHA/BHT), parabens, cinnamon and vanilla, in combination with key words regarding food and side effects. Of those studies purporting to demonstrate an effect, only double-blind randomized placebo-controlled studies with oral challenge were assessed further, unless the complaint was anaphylaxis. Of studies not demonstrating an effect the design was assessed. RESULTS: Only for sulfites as causative agents of asthma and anaphylaxis, methodologically adequate studies demonstrating a causal connection could be found. For azo-dyes, benzoates, MSG, sorbates and BHA/BHT, no link with medical symptoms was demonstrable. For parabens, cinnamon and vanilla there were insufficient or inadequate data to justify a conclusion.
Adverse reactions to food additives.

Simon RA.

There are thousands of agents that are intentionally added to the food that we consume. These include preservatives, stabilizers, conditioners, thickeners, colorings, flavorings, sweeteners, antioxidants, etc. etc. Yet only a surprisingly small number have been associated with hypersensitivity reactions. Amongst all the additives, FD&C dyes have been most frequently associated with adverse reactions. Tartrazine is the most notorious of them all; however, critical review of the medical literature and current Scripps Clinic studies would indicate that tartrazine has been confirmed to be at best only occasionally associated with flares of urticaria or asthma. There is no convincing evidence in the literature of reactivity to the other azo or nonazo dyes. This can also be said of BHA/BHT, nitrites/nitrates and sorbates. Parabens have been shown to elicit IgE mediated hypersensitivity reactions when used as pharmaceutical preservatives; however, as with the other additives noted above, ingested parabens have only occasionally been associated with adverse reactions. MSG, the cause of the 'Chinese restaurant syndrome' has only been linked to asthma in one report. Sulfiting agents used primarily as food fresheners and to control microbial growth in fermented beverages have been established as the cause of any where from mild to severe and even fatal reactions in at least 5% of the asthmatic population. Other reactions reported to follow sulfite ingestion include anaphylaxis, gastro intestinal complaints and dermatological eruptions. The prevalence of these non asthmatic reactions is unknown. The mechanism of sulfite sensitive asthma is also unknown but most likely involves hyperreactivity to inhale SO2 in the great majority of cases; however, there are reports of IgE mediated reactions and other sulfite sensitive asthmatics have been found with low levels of sulfite oxidase; necessary to oxidize endogenous sulfite to sulfate.

PMID: 3302664 [PubMed - indexed for

The prooxidant effect of sodium metabisulfite in rat liver and kidney.

Elmas O, Aslan M, Çağlar S, Derin N, Agar A, Alicigüzel Y, Yargıçoğlu P.
Sodium metabisulfite (Na2S2O5) is used as an antioxidant and antimicrobial agent in a variety of drugs and functions as a preservative in many food preparations. In addition to their antioxidant activity, sulfites oxidize to sulfite radicals (SO3-) initiating lipid peroxidation. This study was performed to elucidate the effect of subchronic Na2S2O5 (520 mg/kg/day) ingestion on hepatic and renal antioxidant enzyme activities and lipid peroxidation in albino rats. The antioxidant effect of L-carnitine was also tested in rats treated with Na2S2O5. Plasma uric acid levels were monitored in all rats included in the study. Malondialdehyde (MDA) levels significantly increased in Na2S2O5 treated rats vs. controls, with kidney values of 2.21+/-0.21 vs. 1.22+/-0.35 and liver values of 79.85+/-19.5 vs. 31.36+/-5.0 nmol/mg protein, respectively. Selenium-glutathione peroxidase (GPx) activity was significantly increased in Na2S2O5 treated rats vs. controls, with kidney values of 38.22+/-2.21 vs. 8.09+/-0.76 and liver values of 31.11+/-6.37 vs. 11.70+/-1.02 U/g protein, respectively. Sodium metabisulfite treatment increased plasma uric acid levels in rats that were included in the study. No protective effect of L-carnitine was observed against lipid peroxidation in both liver and kidneys of rats treated with Na2S2O5. The presented data confirm the prooxidant activity of sulfites and suggest that increased GPx activity and plasma uric acid levels may partially reduce the observed renal and hepatocellular oxidative damage caused via the ingestion of sulfites.


**Antiperoxide activity of sodium metabisulfite. A double-edged sword.**

*Lavoie JC, Lachance C, Chessex P.*

Department of Pediatrics, Hôpital Ste-Justine, University of Montreal, Quebec, Canada.

Sulfites are chemical substances that are used widely in the pharmaceutical industry to reduce or prevent oxidation. Sodium metabisulfite (Na2S2O5) is still present in several parenteral amino acid solutions. Since intravenous lipid emulsions are contaminated by hydroperoxides, we evaluated whether metabisulfite had an antioxidant activity against hydroperoxides. In vitro, Na2S2O5 inhibited the oxidant activity of H2O2, tert-butyl-, and cumene hydroperoxides. The antioxidant capacity of metabisulfite was supported in vivo by the lower (P < 0.01) excretion of malondialdehyde, a stable end product of lipid peroxidation, in babies receiving metabisulfite in their parenteral nutrition. However, for concentrations outside the range found in solutions for parenteral nutrition, the reduction of hydroperoxides by Na2S2O5 could transform this compound into an oxidant, like a sulfite radical. It is suggested that metabisulfite has antiperoxide properties that, under specific conditions, contribute to the generation of toxic oxidants.

PMID: 8135862 [PubMed - indexed for...
Effect of sodium metabisulphite on germination, growth and yield of Vigna sinensis, Savi.

Teresa MV, Rekha K, Bindu A.

Department of Botany, St. Teresa's College, T.D. Road, Ernakulam, Cochin-682 035, Kerala, India.

In the present study, the impact of sodium metabisulphite (Na2S2O5), a food preservative, on seed germination, growth and yield of Vigna sinensis, Savi has been evaluated. Observations clearly reveal the deleterious effect of Na2S2O5 on germination, stomatal development, stomatal index, chlorophyll content and yield. The shoot length exhibited a steady rise in length, while the biomass showed a gradual decrease with the increasing doses of Na2S2O5.

PMID: 15248661 [PubMed - indexed for MEDLINE]

Contact dermatitis from sodium metabisulfite in a baker.

Lee A, Nixon R.

Department of Dermatology, Monash Medical Centre, Darling, Victoria, Australia.

PMID: 11205400 [PubMed - indexed for MEDLINE]

Allergic contact dermatitis from sodium metabisulfite in an antihemorrhoidal cream.

Sánchez-Pérez J, Abajo P, Córdoba S, García-Díez A.

Department of Dermatology, Hospital Universitario de la Princesa, Universidad Autónoma, Madrid, Spain.

PMID: 10727178 [PubMed - indexed for MEDLINE]

Eyelid dermatitis due to sodium metabisulfite.

Seitz CS, Bröcker EB, Trautmann A.
Active sensitization to sodium metabisulfite in hydrocortisone cream.

Heshmati S, Maibach HI.

Department of Dermatology, School of Medicine, University of California, San Francisco, 94143, USA.

PMID: 10475522 [PubMed - indexed for MEDLINE]

Sodium metabisulfite allergy is common but is it relevant?

Madan V, Walker SL, Beck MH.

Contact Dermatitis Investigation Unit, University of Manchester, School of Medicine, Hope Hospital, Manchester, UK. vishalmadan@doctors.net.uk

Positive patch tests to sodium metabisulfite (SMB) are frequent. Standard series patch testing to SMB in 1751 patients showed 71 reactions interpreted as positive and allergic. 33 (46.5%) reactions were originally reported as relevant and 38 (53.5%) were of unexplained relevance depending on the presence or absence of identifiable sources responsible for the presenting dermatitis. A breakdown of these findings is presented. An additional detailed study of the sources of SMB in the environment and a retrospective analysis of these results have been undertaken to identify further, possibly overlooked sources of SMB exposure based on the occupational and recreational history. Most of the positive reactions in the relevant group were attributed to the use of Trimovate cream (63%). 5 patients (13%) with positive reactions in the unexplained relevance group were potentially exposed to SMB in local anaesthetic solutions while at work. 3 patients in the unexplained relevance group (7.8%) and 4 (12.1%) in the relevant group had potential for occupational exposure to SMB as bakers or caterers. Overall, occupational exposure was considered as a possible source of sensitization in 10 (26.3%) patients in the unexplained relevance group. We propose that sensitization to SMB from parenteral solutions and occupational exposure from food handling may account for some of the otherwise unexplained positive patch test reactions. A detailed occupational history should be therefore be sought in otherwise unexplained positive reactions to SMB. We also propose that it is worthwhile including SMB in our standard series in the UK.

PMID: 17680867 [PubMed - indexed for MEDLINE]
Intolerance to sodium metabisulfite in beer.

Gall H, Boehncke WH, Gietzen K.

Department of Dermatology, University of Ulm, Germany.

PMID: 8863931

Metabisulfite sensitivity and local dental anesthesia.

Schwartz HJ, Gilbert IA, Lenner KA, Sher TH, McFadden ER Jr.

Department of Medicine, University Hospitals of Cleveland, Ohio.

A case of sulfite sensitivity first manifesting as urticaria and acute airway obstruction following local anesthesia is described. A positive parenteral provocation test to metabisulfite was observed weeks after recovery of the patient from the clinical event.

PMID: 2919806 [PubMed - indexed for MEDLINE]

Metabisulfite sensitivity: case report and literature review.

Jamieson DM, Guill MF, Wray BB, May JR.

Sulfiting agents have recently been identified as food and drug additives responsible for adverse reactions. These reactions are not rare and may result in life-threatening asthma and anaphylaxis. We report a 34-year-old female with intractable asthma and urticaria. Sensitivity to sulfites was suspected based on exacerbation after restaurant meals and metaproterenol 5% inhalant solution. Bronchial provocation challenge resulted in a 28% decrease in FEV1 and a 34% decrease in FEF25-75 at the 0.01 mg/ml dose. Thirty-two cases of sulfite sensitivity reported in the literature are reviewed. Foods and drugs containing sulfites are listed. The pathogenic mechanism is unknown. The FDA allows the addition of sulfites to foods and drugs without disclosure. Only recently has this potential hazard been recognized. The FDA is considering a labeling requirement on drugs that do contain sulfites.

PMID: 2578754 [PubMed - indexed for MEDLINE]
Pickled onion-induced asthma: a model of sulfite-sensitive asthma?

Gastaminza G, Quirce S, Torres M, Tabar A, Echechipía S, Muñoz D, Fernández de Corres L.

Servicio Alergología, Hospital Santiago Apóstol, Victoria-Gasteiz, Spain.

BACKGROUND: Asthma elicited by sulfite ingestion has been mainly described in steroid-dependent and in non-atopic asthmatics. We have studied a group of 18 young extrinsic asthmatics who presented with asthma attacks immediately after eating pickled onions. OBJECTIVE: The aim of this study is to ascertain if these asthma attacks are elicited by sulfites contained in pickled onions and the influence of the dose and pH of onions. METHODS: The bronchial hyperreactivity of the patients was assessed by a methacholine challenge test. Oral challenge tests were performed with sodium metabisulfite (MSB) diluted in lemon juice at pH 4.2 and at pH 3.3 (only in patients who did not react with pH 4.2). Two types of pickled onions, Spanish and Dutch pickled onions, were used for oral challenge in seven of the patients. The Monier-Williams method was used to measure the SO2 concentration in pickled onions. RESULTS: The oral provocation test with MBS, pH 4.2, elicited a positive response in six patients (33.3%) and the test at pH 3.3 was positive in three out of 12. No significant difference in PD20 values was found between these groups. Three of the seven patients challenged with Spanish pickled onions had a positive reaction but had no reaction with Dutch pickled onions. The SO2 concentration in Spanish pickled onions varied between 765 and 1182 ppm while in Dutch pickled onions were 200 ppm; this exceeded the permitted level (100 ppm). SO2 release in Spanish pickled onion samples was nearly 2.5 times higher when the pH of the sample decreased from 4.2 to 3.3. CONCLUSION: High levels of SO2 in Spanish pickled onions, and their low pH (3.3) would be the responsible factors of the asthmatic outbreaks after ingestion of Spanish pickled onions by these patients.

PMID: 7584680 [PubMed - indexed for MEDLINE]
blind challenge protocol was performed in 22 patients (sodium metabisulfite solutions at pH 2.2 to 2.6) and the positive responses were confirmed by double-blind challenge. The other 22 were tested directly in a double-blind manner (pH4). Initially, 6/44 presented a positive reaction. However, a careful analysis and the confirmation by double-blind challenge of the positive responses obtained with the single-blind test, allowed us to identify 4 false positive responses. Thus, the true prevalence of sulfite sensitivity in our population is 4.5%. A patient with intolerance to sulfite agents also suffered aspirin-induced asthma. The labile tendency of the pulmonary function of the asthmatic patients may have contributed to some false positive reactions and probably explain the very high prevalence found in some studies. It does not appear that the variations of pH decisively influence the result of the challenge test.

PMID: 3266541 [PubMed - indexed for MEDLINE]

Sulfite sensitivity: significance in human health.

Lester MR.

Department of Pediatrics, Children's Hospital, Boston, Massachusetts, USA.

Endogenous sulfite is generated as a consequence of the body's normal processing of sulfur-containing amino acids. Sulfites occur as a consequence of fermentation and also occur naturally in a number of foods and beverages. As food additives, sulfiting agents were first used in 1664 and approved in the United States as long ago as the 1800s. With such long experience with their use, it is easy to understand why these substances have been regarded as safe. They are currently used for a variety of preservative properties, including controlling microbial growth, preventing browning and spoilage, and bleaching some foods. It is estimated that up to 500,000 (< .05% of the population) sulfite-sensitive individuals live in the United States. Sulfite sensitivity occurs most often in asthmatic adults--predominantly women; it is uncommonly reported in preschool children. Adverse reactions to sulfites in nonasthmatics are extremely rare. Asthmatics who are steroid-dependent or who have a higher degree of airway hyperreactivity may be at greater risk of experiencing a reaction to sulfite-containing foods. Even within this limited population, sulfite sensitivity reactions vary widely, ranging from no reaction to severe. The majority of reactions are mild. These manifestations may include dermatologic, respiratory, or gastrointestinal signs and symptoms. Severe nonspecific signs and symptoms occur less commonly. Broncho-constriction is the most common sensitivity response in asthmatics. The precise mechanisms of the sensitivity responses have not been completely elucidated. Inhalation of sulfur dioxide (SO2) generated in the stomach following ingestion of sulfite-containing foods or beverages, a deficiency in a mitochondrial enzyme, and an IgE-mediated immune response have all been implicated.(ABSTRACT TRUNCATED AT 250 WORDS)

PMID: 8586770 [PubMed - indexed for
Sulfite hypersensitivity. A critical review.

Gunnison AF, Jacobsen DW.

Sulfiting agents (sulfur dioxide and the sodium and potassium salts of bisulfite, sulfite, and metabisulfite) are widely used as preservatives in foods, beverages, and pharmaceuticals. Within the past 5 years, there have been numerous reports of adverse reactions to sulfiting agents. This review presents a comprehensive compilation and discussion of reports describing reactions to ingested, inhaled, and parenterally administered sulfite. Sulfite hypersensitivity is usually, but not exclusively, found within the chronic asthmatic population. Although there is some disagreement on its prevalence, a number of studies have indicated that 5 to 10% of all chronic asthmatics are sulfite hypersensitive. This review also describes respiratory sulfur dioxide sensitivity which essentially all asthmatics experience. Possible mechanisms of sulfite hypersensitivity and sulfur dioxide sensitivity are discussed in detail. Sulfite metabolism and the role of sulfite oxidase in the detoxification of exogenous sulfite are reviewed in relationship to the etiology of sulfite hypersensitivity.

PMID: 3556020 [PubMed - indexed for MEDLINE]