CHROMOSOMAL ABERRATIONS OF CULTURED HUMAN BLOOD LYMPHOCYTES AFTER TREATMENT WITH SODIUM BISULFITE

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Presented by
Rania Ahmed Salah El-Din
M.B. B.CH. , M.SC. (Anatomy)

Supervised By

Professor Dr.Kariman ElGohary ElHodhod
Professor of Anatomy
Faculty of Medicine,
Ain Shams University

Professor Dr.Mostafa
Professor of Pediatrics
Faculty of Medicine,
Ain Shams University

Professor Dr.Shahera Youssef Sobki
Professor of Anatomy
Faculty of Medicine
Ain Shams University

Asst. Professor Dr. Ezzat El
Assistant professor of Genetics
Faculty of Medicine
Ain Shams University

Faculty of Medicine
Ain Shams University
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Introduction and Aim of the work

The antimicorbial properties of sulfite with its ability to inhibit discoloration have led to its wide spread use as an additive to food and beverages **(Chichester and Tanner,1972).**

Sodium bisulfite is a food and pharmaceutical additive. It is a pollutant in the form of sulfur dioxide.Epidemiological evidence links atmospheric sulfur dioxide with cardiac and respiratory illness and lung cancer **(Popescu and Dipaolo ,1988).**

Sulfite acting on the animal or human organisms originates from the ingestion of sulfite-treated food, beverages and drugs. Moreover,it might orginate from the inhalation of sulphur dioxide in the air or the endogenous degeneration of sulphur containing amino acids **(Renner and Wever,1983).**

Sodium metabisulfite is used as food preservative in food products like biscuits, chocolates, jam, sausages, salami and also in many alcoholic liquor like beer, wine and champagne **(Rencuzogullari , Basri, Kayraldiz,and Topakats , 2001).**

The aim of the present study is to investigate the effect of sodium bisulfite and sodium metabisulfite on human lymphocytes cultured in vitro.

Sodium bisulfite ($NaHSO_3$)

Nair and Elmore (2003) stated that Sodium bisulfite compound consisted of sodium bisulfite and sodium metabisulfite in varying proportions, but possessed the properties of the bisulfite. They described the compound as white or yellowish-white crystals or granular powder with an odor of sulfur dioxide. They stated that it was unstable in air, soluble in water and slightly soluble in alcohol.

Rowe, Sheskey and Weller (2003) specified some data about sodium bisulfite:

Molecular weight: 104.07

CAS number: [7631-90-5]

Synonyms: E222; sodium hydrogen sulfite.

Appearance: white crystalline powder.

Density: 1.48 g/cm3

Solubility: soluble 1 in 3.5 parts of water at 20°C, 1 in 2 parts of water at 100°C, and 1 in 70 parts of ethanol (95%).

They commented that most substances sold as sodium bisulfite contained significant but variable amounts of sodium

metabisulfite, since the latter was less hygroscopic and more stable during storage and shipment**.**

Sodium metabisulfite ($(Na_2S_2O_5)$)

Rowe et al, (2003) described synonyms for sodium metabisulfite: disodium disulfite; disodium pyrosulfite; disulfurous acid; disodium salt; E223; sodium acid sulfite; sodium pyrosulfite. They also specified some data about the compound:

Chemical name and CAS registry number:

Sodium pyrosulfite [7681-57-4]

Molecular weight: 190.1

Functional category: Antioxidant.

They described sodium metabisulfite as colorless, prismatic crystals or as a white to creamy-white crystalline powder, which had the odor of sulfur dioxide and an acidic, saline taste. Sodium metabisulfite crystallized from water as a hydrate containing $7H_2O$.

Stability and Storage Conditions:

Sodium metabisulfite might react with the rubber caps of multidose vials that should therefore be pretreated with sodium metabisulfite solution **(Schroeter, 1961).**

On exposure to air and moisture, sodium metabisulfite was slowly oxidized to sodium sulfate with disintegration of the crystals. Addition of strong acids to the solid liberated sulfur dioxide **(Schroeter, 1963).**

In water, sodium metabisulfite was immediately converted to sodium (Na^+) and bisulfite (HSO_3^-) ions. Aqueous sodium metabisulfite solutions also decomposed in air, especially on heating. Therefore, solutions which were sterilized by autoclaving should be filled into containers in which the air had been replaced with an inert gas, such as nitrogen. The bulk material should be stored in a well-closed container, protected from light, in a cool and dry place **(Schumacher and Hull, 1966).**

Methods of Manufacture:

Sodium metabisulfite was prepared by saturating a solution of sodium hydroxide with sulfur dioxide and allowing crystallization to occur; Hydrogen was passed through the solution to exclude air. Sodium metabisulfite might also be prepared by saturating a solution of sodium carbonate with sulfur dioxide and allowing crystallization to occur, or by thermally dehydrating sodium bisulfite **(Rowe et al., 2003).**

Applications in pharmaceutical formulation or technology and safety :

Popescu and Dipaolo (1988) noted that sodium bisulfite was used as a food and pharmaceutical additive. **Nair and Elmore (2003)** mentioned that sodium bisulfite was used in cosmetic preparations like hair dyes and colors, face and neck creams, lotions, powders and other skin preparations.

Sodium metabisulfite was used as an antioxidant at low pH, while sodium bisulfite at intermediate pH. Sodium metabisulfite was used as an antioxidant in oral, parenteral, and topical pharmaceutical formulations. It also had some antimicrobial activity, which was greatest at acidic pH, and might be used as a preservative in oral preparations such as syrups. In the food industry, and in wine production, sodium metabisulfite was similarly used as an antioxidant, in concentration 0.01-1.0 %, antimicrobial preservative, and antibrowning agent. However, at concentrations above 550 ppm it imparted a noticeable flavor to preparations. Sodium metabisulfite was accepted as a food additive in Europe. It was included in the FDA Inactive Ingredients Guide (epidural, IM and IV injections, ophthalmic solutions, and oral preparations). It was also included in nonparenteral and parenteral medicines licensed in the UK. Sodium metabisulfite contained small amounts of sodium sulfite and sodium sulfate **(Rowe et al., 2003)**.

Adverse Reactions:

Although it was extensively used in a variety of preparations, sodium metabisulfite, and other sulfites, had been associated with a number of severe, or fatal, adverse reactions **(Jamieson, Guill, Wray and May, 1985).**

Following oral ingestion, sodium metabisulfite was oxidized to sulfate and excreted in urine. Ingestion might result in gastric irritation due to liberation of sulfurous acid, while ingestion of large amounts of sodium metabisulfite caused colic, diarrhea, circulatory disturbances, CNS depression, and death. In Europe, the acceptable daily intake of sodium metabisulfite, and other sulfites, used in foodstuffs had been set at 3.5 mg/kg body-weight, calculated as sulfur dioxide (SO_2). The WHO had similarly also set an acceptable daily intake of sodium metabisulfite, and other sulfites, at 7.0 mg/kg body-weight, calculated as sulfur dioxide (SO_2) **(FAO.WHO, 1987).**

Hypersensitivity reactions might occur after exposure to sulfite. These included bronchospasm and anaphylaxis. Allergy to sulfite antioxidants was estimated to occur in 5-10% of asthmatics although adverse reactions might also occur in nonasthmatics with no history of allergy **(Deziel-Evans and Hussey, 1989).**

BIOLOGICAL DATA: -

Biochemical aspects: -

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Biotransformation: -

Sun, Cotgreave, Lindeke and Moldéus, (1989) studied the metabolic disposition of sulfite in isolated, perfused rat liver and in isolated rat hepatocytes. In particular, the kinetics of metabolism of sulfite ion to inorganic sulfate ion and the effect of sulfite ion on the concentrations of the endogenous, low-molecular-mass thiol-containing molecules as glutathione and cysteine. Sulfite was rapidly converted to sulfate by isolated hepatocytes at concentrations ranging from 200 µmol/L to 2 mmol/L. The rate of conversion was linear and quantitative over this range. These results confirmed the presence of substantial concentrations of sulfite oxidase in liver. Cytotoxicity was not seen, even at the highest concentration of sulfite.

Reported cases of sensitivity to sulfites in humans :-

Simon and Wasserman (1986) reported a case of an asthmatic patient that received a sulfite challenge of 5 mg by capsule, resulted in a drop in forced expiratory volume in one second (FEV_1). Skin-prick tests with sulfite produced inconsistent reactivity. They suggested that skin-sensitizing antibodies mediate sulfite-sensitive asthma through involvement of immunoglobulin (Ig) E.

Botey, Cozzo, Eseverri and Marin (1987) reported cases of six girls and two boys aged two to six were enrolled in a study for sensitivity to food additives and found to be sensitive to sulfite in an oral provocation test. The primary manifestation was urticaria with or without accompanying angio-oedema.

Frick and Lemanske (1991) reported an asthmatic two years old boy, who experienced attacks of wheezing in association with ingestion of foods containing sulfites. In order to confirm that sulfites were the precipitating agent in the attacks of wheezing, a double blind oral challenge test was conducted with gradual increasing doses of powdered potassium metabisulfite mixed with apple sauce. Measuring pulse, respiratory rate, and blood pressure assessed reaction to the challenge. A reaction to a dose of 25 mg was observed