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Histological Profile of Liver of Albino Rats on Oral Administration of Sodium Benzoate for Sixty Days

Dr. Amit Agarwal1

Assistant Professor, Department of Anatomy, Rama medical College Hapur
Uttar Pradesh, India

Dr Deepanjali gupta2

CMO(NFSG), Hindu Rao Hospital, NDMC Medical college, Delhi, India
Email: amitk2012.2012@gmail.com]

Abstract

The present study evaluates the histological effects of oral sodium benzoate on liver of albino rats. The study comprises of 4 groups of albino rats. Each group consists of 10 albino rats. Of these, first group was given 400mg/kg body weight sodium benzoate orally in distilled water, second group was given 800mg/kg body weight sodium benzoate in distilled water, and the third group was given 1200mg/kg body weight sodium benzoate in distilled water and the fourth group served as a control which received distilled water only. All rats were sacrificed at the end of 60 days. The changes which occurred in rats as compared to control were swelling (vacuolization), disorganization of hepatocytes, dilated central vein, hemorrhage, venous bleeding, large area devoid of hepatocytes and syncytium formation.

Introduction

Humans are exposed to complex mixtures of chemical compounds in their food. One of these substances are antioxidants which are used as food preservatives. Preservatives are added into the products for preventing and delaying losses due to microbiologic, enzymatic or chemical changes and for prolonging shelf life (1). The food additives means any substance that is normally used as typical ingredient of the food (2). Sodium benzoate occurs naturally in some foods about 40% mg/kg e.g. Apple, milk products and cinnamon, but, is more to be chemically produced (3).

Such substances are introduced into food to improve food appearance, taste and aroma (e.g. colouring matters, flavouring agent and emulsifiers) and keeping good food qualities (antioxidant, preservation) such as: sodium benzoate which is a very widespread food preservative in many foods (4,5). It is used in soft drinks, fruit products, pickles and sauces[6]. lt is classified as 'class 2' preservatives and is also present naturally in many food stuffs and in

plants extract. In physical form it is solid and its chemical formula is NaC7H5O2Na. Sodium benzoate at a general optimum concentration of 0.1% could be used for preservation of such products as soft drinks, fruit drinks, margarine, and certain fish products (7,15) .
The present study has been conducted to elucidate some lights on histological changes in the liver of albino rats on oral administration of sodium benzoate.

Material and Methods

The present study was conducted in the department of Anatomy, LLRM Medical College after obtaining approval from the Institutional Ethical Committe. Total 40 albino rats weighing 150 to 200 grams were used for the study. They were maintained in the animal house under control conditions and were allowed to acclimatize for 3 weeks before the experiment.
Forty rats were classified as follows:

Treated group: first group was given 400mg/kg body weight sodium benzoate orally in distilled water, second group was given 800mg/kg body weight sodium benzoate in distilled water, and the third group was given 1200mg/kg body weight sodium benzoate in distilled water . All rats were sacrificed at the end of 60 days. All these treated groups consisted of ten rats each.

Control group: ten animals were administered 2ml distilled water orally. All animals were fed with a nozzle fitted into a measuring syringe.

The rats were sacrificed and liver dissected out and immediately preserved in 10% formalin solution. This solution was discarded after 24 hours and another fresh solution taken and tissue preserved for secondary fixation.

After suitable fixation the tissue underwent standard steps of dehydration, clearing and wax impregnation. After this sections 4-5 μm thick were cut and stained with haematoxylin and eosin stain.

Observations

In the present study remarkable increase in histopathological changes in liver of albino rats during treatment periods were observed as compared to control group. Fig 1 shows liver of control rats which were administered distilled water only for 60 days. Distortion of hepatic architecture was observed in all the dose groups. In the group of 400 mg dose of sodium

benzoate , liver of rats showed loss of most of the architecture of liver with dilated central vein and syncytium formation (Fig. 2) , vacuolization of hepatocytes (Fig. 3), interstitial hemorrhage with vacuolization of hepatocytes (Fig.4).

In the 800 mg dose group of sodium benzoate and rats sacrificed after a period of 60 days liver showed dilated central vein (Fig.5), loss of hepatic architecture, large area devoid of hepatocytes and formation of syncytium with interstitial hemorrhage (Fig.6).

In the 1200 mg dose group of sodium benzoate and rats sacrificed after a period of 60 days liver showed, in addition to above features, venous bleeding (Fig.7).

The above findings are summarized below.

Table: Observation

	Control (10 rats)	**400 mg (10 rats)**	**800 mg (10 rats)**	**1200 mg (10 rats)**
Distortion of hepatic architecture	_	9	9	9
Dilated central vein	_	7	7	8
Vacuolated cytoplasm of hepatocytes	_	7	8	8
Interstitial hemorrhage	-	6	6	8
Venous bleeding	_	_	6	6
Syncytium	_	6	6	7

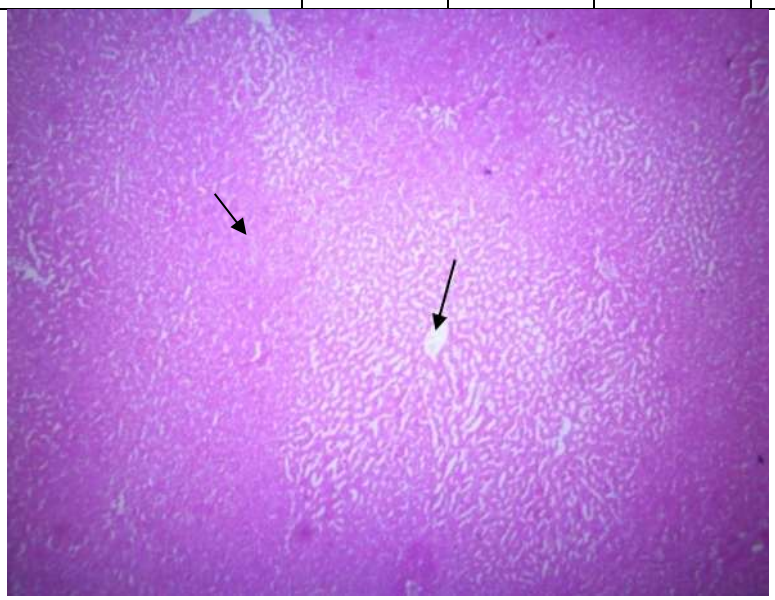

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Fig. 1 (10 × magnification): A photomicrograph of a liver section of control rats administered with distilled water for 60 days showing polyhedral hepatocytes and their radiation from central vein (arrow).

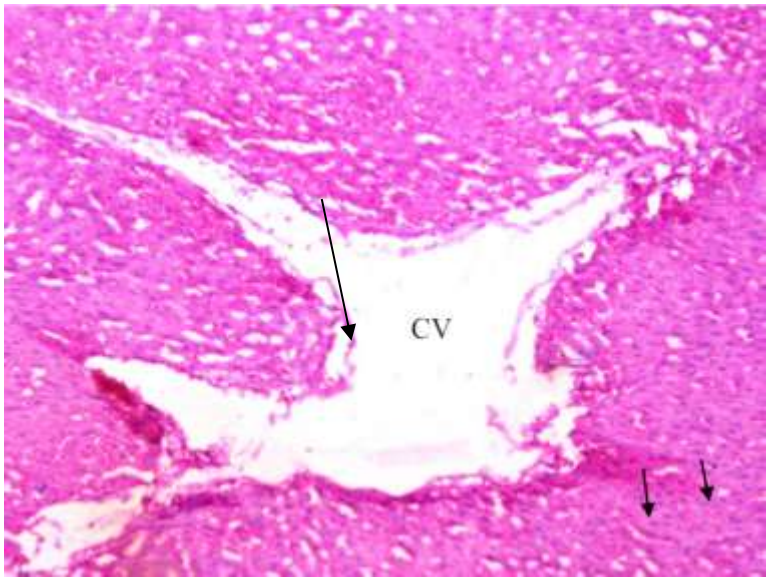

Fig.2 (10 × magnification): A photomicrograph of a liver section of rats administered with sodium benzoate 400 mg for 60 days showing dilated central vein (CV) and syncytium (arrows) and loss of architecture of Liver

CV

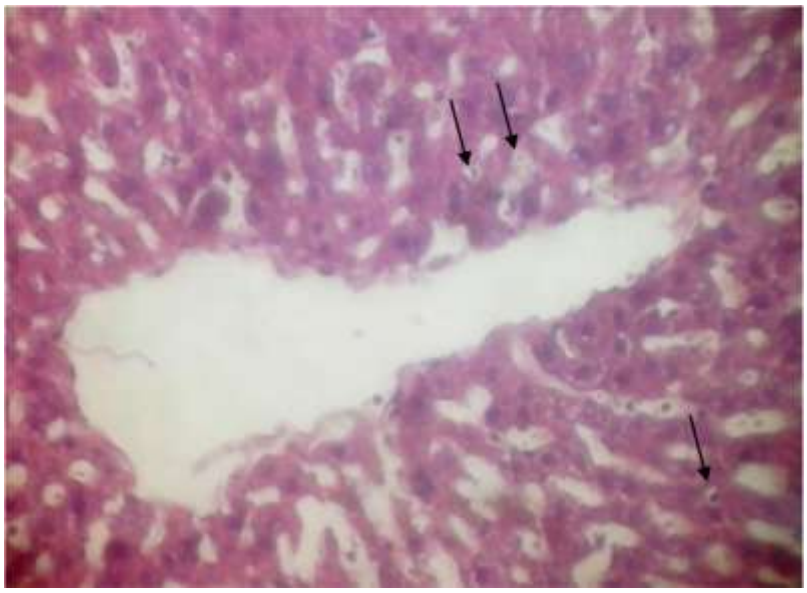

Fig.3 (40 x magnification): A photomicrograph of a liver section of a rat administered with sodium benzoate 400 mg for 60 days showing vacuolated hepatocytes (arrows).

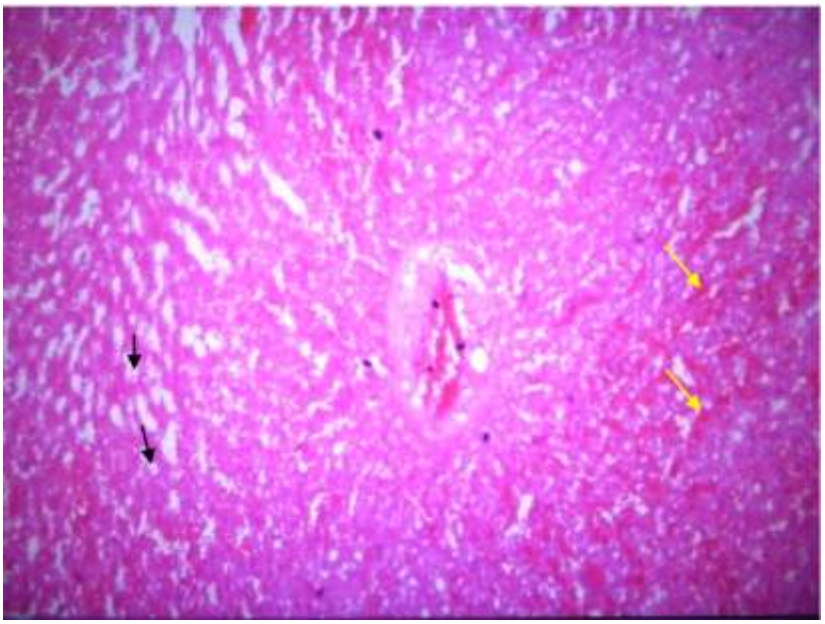

Fig.4 (40 x magnification): A photomicrograph of a liver section of a rat administered with sodium benzoate 400mg for 60 days showing cytoplasmic vacuolization of hepatocytes (arrows) and loss of hepatic architecture with interstitial hemorrhage (yellow arrows).

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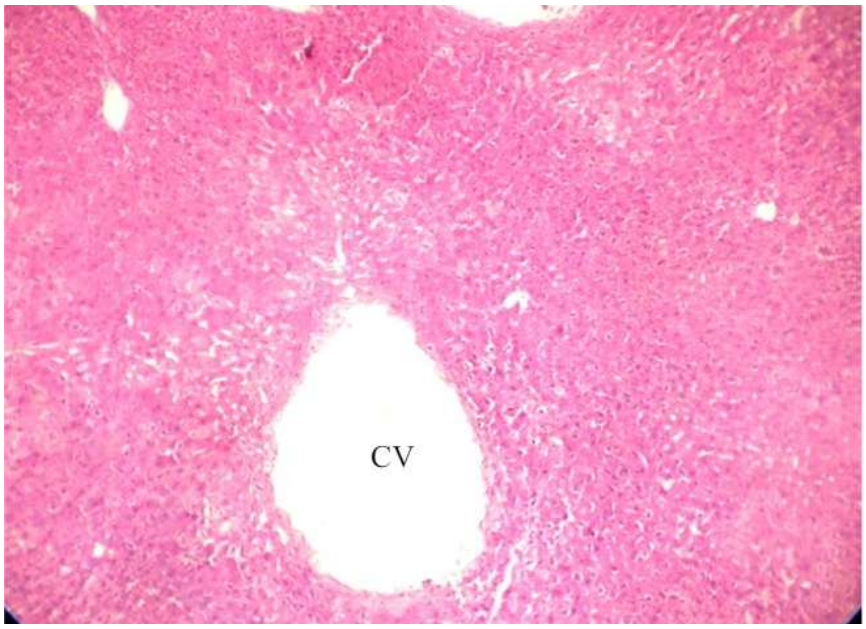

Fig.5 (10 x magnification): A photomicrograph of a liver section of a rat administered with sodium benzoate 800mg for 60 days showing dilated central vein (CV).

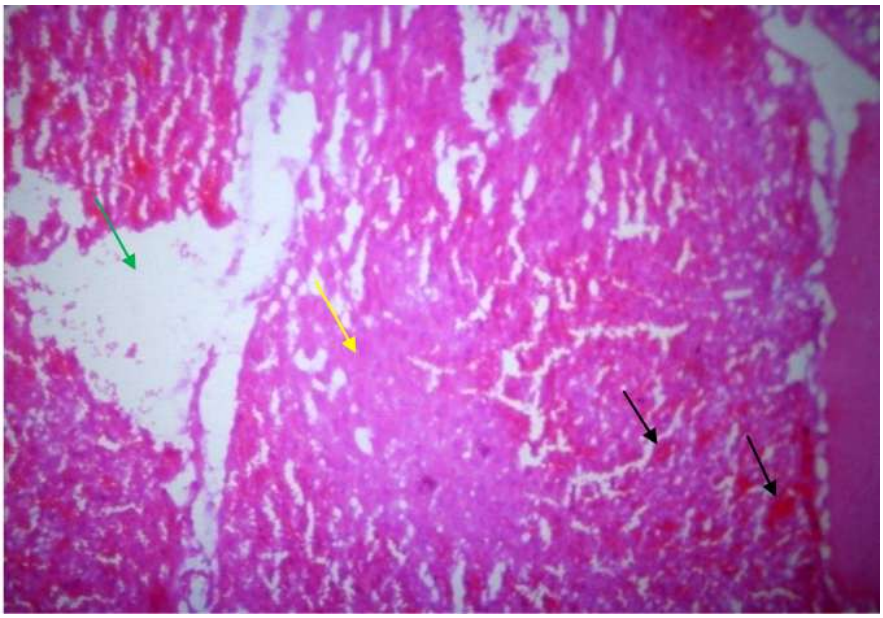

Fig.6 (10 x magnification): A photomicrograph of a liver section of a rat administered with sodium benzoate 800mg for 60 days showing loss of hepatic architecture, interstitial hemorrhage (arrows) and most of the hepatocytes have lost their cell boundaries forming a syncytium (yellow arrow) with large area devoid of hepatocytes (green arrow).

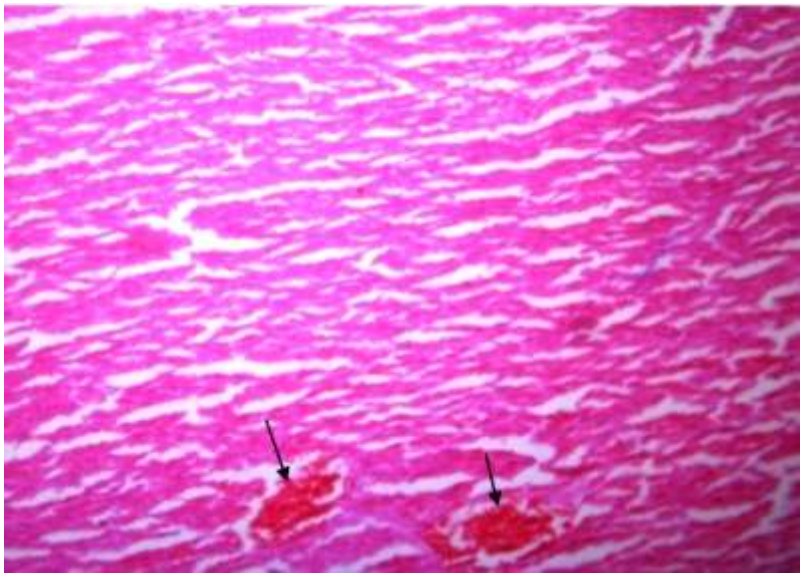

Fig.7 (40 x magnification): A photomicrograph of a liver section of a rat administered with sodium benzoate 1200mg for 60 days showing venous bleeding (arrows).

Discussion

Marked enlarged vacuolated cytoplasm (cellular swelling), loss of most of the architecture of liver, dilated central vein, Interstitial hemorrhage and formation of syncytium are a constant finding in all the sodium benzoate treated dose goups.

It is evident from the present study that the administration of sodium benzoate resulted in distinctive alteration of architecture of liver and on increasing the dose the histopathological changes in liver were increased on serial increment of dose of sodium benzoate from 400 mg to 1200 mg especially in terms of number of rats affected.

The drug administered resulted in swelling (vacuolization), disorganization of hepatocytes, dilated central vein, hemorrhage, and syncytium formation and venous bleeding.

Similar swelling of hepatocytes were also obtained by Fujitani (8) (1993), Tulin Aktac et al (9) (2003), Resham Sinha and Doris D'Soza (10) (2010) and also in 2012 in another study with sodium benzoate (14), Bothaina M. Khidir et al (11) (2012) and Elvan Bakar, Tulin Aktac (12) (2014), Khodaei et al(17) (2019). This swelling of hepatocytes was also found by Xiaognang et. al(13) 2013 with citric acid.

Khodaei et al (17) observed that 300 and 600mg/kg of SB caused histological alterations in the liver, such as focal acute inflammation and moderate portal inflammation in the hepatocytes, respectively. Also, SB at a dose of 600 mg/kg caused mild interstitial inflammation. Hypertrophy of the hepatocytes in the periportal area was a characteristic feature

in the liver of treated mice with SB at doses of 300 and 600mg/kg. The histology of the liver, in 150mg/kg of SB, was the same as the control groups; the central vein and normal hepatocyte were evident.

Shimma Mohammad et al (18) reported- A rat administrated with sodium benzoate showing; disorganized hepatic architecture. Some hepatocytes showed necrosis with pyknotic nuclei and others with karyolitic nuclei

S.A. Al-Ameen et.al (19) noticed some changes in the liver tissue that was congestion of portal vein, mild hydropic degeneration of hepatocytes and stenosis of sinusoids in group treated with 300mg/kg.bw of sodium benzoate, and shows congestion of portal vein, hydropic degeneration of hepatocytes, necrosis of others and stenosis of sinusoids in group treated with 400 mg/kg.bw of sodium benzoate, Also observed some changes in liver represented by portal vein congestion, mild hydropic degeneration of hepatocytes, stenosis of sinusoids, fatty change steatosis and hepatocytes necrosis with sodium benzoate treatment groups in compared to control group.

In the year 2023 an article was published by Yasmina M. Abd-Elkanam et al(20) in which they found that Sodium benzoate treated group showed periportal degeneration of hepatocytes with dilated Central vein, dilatation of Hepatic sinusoids.

Dina Akter et al in 2024(21) found in sodium benzoate treated group of mice showed central vein enlargement (CVE), congestion (C), sinusoids disintegration (SD), portal vein disintegration (PVD), hemorrhage (H), molecular degeneration (MD), leukocyte infiltration (LI), degeneration(D), portal vein disintegration and hemorrhage

Onengiyeofori et al (22) in 2025 administered a dose of 240mg/kg dose of Sodium benzoate in Albino rats and reported degenerating hepatocytes, Lymphoid cells in sinusoids, mild deposit in Central vein as well as perivascular distortion- H&E*400

Distortion of hepatic architecture was also obtained by all the above workers. Distortion of hepatic architecture was also reported by Tulin Aktac et al (9) (2003) with another preservative citric acid in addition to sodium benzoate. Similar findings were also seen in our study.

In the present study dilated central vein was seen which was also reported in a study by Bothaina M. Khidir et al (11) (2012) with sodium benzoate and Yasmina M. Abd-Elkanam et al(20).

The venous bleeding was seen with 800 mg and 1200 mg dose of sodium benzoate in present study and also with same dose groups in a study by Amit Agarwal, Archana sharma et al when

albino rats were sacrificed after 30 days of oral administration of sodium benzoate (16).. This has not been reported by above workers and only small venule bleeding is reported by Xiaoguang et. al.[13] (2013) with another preservative, citric acid.

Syncytium formation is seen in our study in all study groups.

It has been reported by Resham Sinha and Doris D'souza (14) (2012). Bothaina M. Khidir et al (11) (2012), and Elvan Bakar, Tulin Aktac (12) (2014) obtained same results with sodium benzoate.

Bothaina M. Khidir et al (11) (2012) found hemorrhage in areas of degenerated hepatocytes after 90 days of sodium benzoate administration at a dose of 1gm/kg body weight. He used rats in the range of 200 to 300 gms. That means a 200 gms. rat was fed 200 mg. of sodium benzoate for 90 days but in our study hemorrhage is widespread and is found even after 60 days of sodium benzoate administration probably due to higher doses used up to a maximum of 1200 mg.

Hence the present study showed that sodium benzoate caused considerable damage to liver of rats. Sodium benzoate induced swelling (vacuolization), disorganization of hepatocytes, dilated central vein, hemorrhage, and syncytium formation and venous bleeding.

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